Atlas of Dermoscopy

Second Edition

Edited by
Ashfaq A. Marghoob
Josep Malvehy
Ralph P. Braun

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Dedication

To Alfred W. Kopf, mentor par excellence, who introduced me to dermoscopy and encouraged me not to settle for mediocrity.

To Allan Halpern, a chief unmatched, for providing the opportunity and means for me to pursue my passions and for allowing me to reach heights I could never have imagined.

To my fellows, residents, and students, for all your valuable insights, inquisitive nature, and hard work. You have all profoundly influenced my career and knowledge. I will remember each and every one of you forever!

To my children, Adam, Nadeem, Hannah, and Samir, remember to strive to do your best in all endeavors you undertake. Always be just, kind, and loving. Remember your Creator and thank Him every hour of every day for all that He has provided for you.

To Iman, my wife of more than 25 years, thank you for standing by my side. I could not have journeyed so far without your love, support, help, and patience.

To my parents, Mamnoon and Monika, for your love and for providing me with the foundation to successfully navigate through this life. To you both I owe everything!

To my sister, Azra, for always being there for me.

AAM

To my son Alexander
To my parents Ulrike und Paul, for always beeing there for us.

RPB

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Foreword

While the diffusion of dermoscopy into routine dermatology practice has been quicker in some circles than in others, there is little question it is now routinely used by most dermatologists. Increasingly, the dermoscopy audience has broadened beyond dermatologists and the focus is no longer exclusively on pigmented lesions. With the wider adoption of the technique has come affirmation of its utility, with multiple lines of evidence supporting an associated improvement in diagnostic accuracy, earlier detection of melanoma, and a reduction in unnecessary biopsies. One of the critical resources that helped educate the current generation of dermoscopists was the outstanding first edition of the *Atlas of Dermoscopy*. It is therefore a genuine privilege to write this brief forward to the new and improved 2nd edition of this important reference work.

The quality of the second edition of the *Atlas of Dermoscopy* comes as no surprise to anyone familiar with its distinguished contributors. The authors are all leaders in the field who have helped lay the academic foundations for the subjects they cover. The editors are renowned not only for their expertise but also as gifted educators. Through the outstanding courses and conferences they have organized they have educated many dermoscopists, myself included. The current iteration of this book will serve a growing readership and will help novice and experienced dermoscopists alike to improve their knowledge and skills.

The second edition has much important new material. Unlike most dermoscopy atlases, it highlights the differences observed with polarized and non-polarized dermoscopy. In keeping with the rapidly expanding dermoscopic literature, it details many newly recognized structures and patterns and addresses the many new areas benefiting from dermoscopy such as evaluation of the hair and nails. I especially enjoyed how the authors, throughout the atlas, have attempted to highlight principles on integrating dermoscopy into general clinical practice and I also like the inclusion of checklists of criteria used to diagnose skin lesions.

My congratulations to all those who contributed to this excellent volume and to you the reader, who I am confident will benefit from their labors.

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1 Introduction

Ashfaq A. Marghoob, Ralph P. Braun, and Josep Malvehy

The time for clinicians to use dermoscopy in evaluating and managing cutaneous malignancies is fast approaching. Currently, many dermatologists are using dermoscopy (Noor et al., 2009; Terushkin et al., 2010; Venugopal et al., 2011) and questions pertaining to dermoscopy have become part of the final qualifying examinations for many dermatologists. There is also a mounting interest being expressed by general practice (GP) physicians (i.e, family physicians), subspecialty physicians, nurse practitioners, and physician's assistants in learning dermoscopy. The added benefit of dermoscopy has been documented for dermatologists, GPs, and even medical students. In other words, the use of dermoscopy has begun to diffuse beyond the hands of dermatologists. Dermoscopy has even become part of the clinical practice guidelines in some countries. In the publication "Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand," the training and utilization of dermoscopy is recommended for clinicians routinely examining pigmented skin lesions. These guidelines are evidence-based best practice guidelines with grade A evidence, which means that the body of evidence can be trusted to guide practice.

The editors opine that it is only a matter of time for the truth to be known to all that the use of dermoscopy makes for a better clinician. With that said, let us explore some of the reasons for why clinicians should learn to use dermoscopy (Table 1.1).

1. *Dermoscopy significantly improves the in vivo diagnostic accuracy of melanoma.* Dermatologists only diagnose 65–80% of melanomas on routine naked-eye examination. For example, in the Oncology Section of the Skin and Cancer Unit of NYU Langone Medical Center the diagnostic accuracy was found to be only 64% using strict criteria (e.g., allowing a single diagnosis for all lesions) (Grin et al., 1990). Dermoscopy improves diagnostic accuracy by 10–27% (Kittler et al., 2002).
2. *Dermoscopy can differentiate most lesions of the skin from melanoma.* With naked-eye examination it is not unusual to come upon a pigmented lesion, which has some or all of the clinical attributes of melanoma, but on dermoscopy the lesion can be definitively diagnosed as some other type of cutaneous lesion.
3. *Dermoscopy reduces unneeded biopsies.* Studies have shown that the "benign/malignant ratio" of pigmented lesions of the skin is decreased when dermoscopy is used compared with visually unassisted diagnoses (Carli et al., 2004).
4. *Basic instrumentation for dermoscopy is affordable.* Compared with some other available instruments used by dermatologists (e.g., reflectance confocal microscopy), dermoscopes are relatively inexpensive, thus making such technology affordable for most practitioners.
5. *Dermoscopes are easy to use.* Placing liquid or gel onto the skin prior to placement of the glass plate of the dermoscope onto the lesion allows the clinician to view the lesion, through the magnifying ocular lens of the dermoscope, with exceptional clarity. The liquid interface, by matching the refractive index of the stratum corneum and glass plate, allows the clinician to visualize structures below the surface of the skin. The advent of polarized dermoscopes, however, has eliminated the necessity for a liquid interface or direct skin contact (see chapter 2 for details).
6. *Several helpful algorithms have been created to aid in classifying lesions of the skin.* These algorithms have been created primarily for those who are beginning to use dermoscopy. Details on a number of such algorithms are presented in chapters 4 and 6b–h.
7. *Dermoscopy has added a new powerful dimension to the clinical diagnosis of early melanoma.* The qualities of a "good test" are accuracy, no adverse effects, target disorder dangerous if left untreated, and effective treatment if diagnosed early (Jaeschke et al., 1994). Dermoscopy has all of these attributes since the target disorder, melanoma, if diagnosed and removed early in its evolution, is curable.
8. *Dermoscopy is a noninvasive technique that allows microscopic visualization of subsurface skin structures not visible to the naked eye.* Thus, the use of dermoscopy does not require additional expense to the patient for invasive procedures, such as the performance of biopsy, cost of processing the biopsy specimen, and interpreting the dermatopathologic diagnosis. Eliminating unneeded biopsies translates to overall reduced health care costs.
9. *Adding dermoscopy to complete skin examinations is not overly time consuming.* Zalaudek et al. (2008) have shown that, on average, complete skin examination takes 70 seconds without dermoscopy and 142 seconds with dermoscopy. The authors conclude that complete skin examination, with or without dermoscopy, usually takes less than 3 minutes. They profess this is a reasonable time to potentially prevent mortality from cancers of the skin.
10. *Meta-analysis of the literature has demonstrated the superiority and usefulness of dermoscopy.* Numerous studies (Vestergaard et al., 2008; Bafounta et al., 2001) have provided data to indicate that the diagnostic accuracy of dermoscopy is superior to that of naked-eye examination.
11. *Dermoscopy allows the observer to focus (concentrate) on the lesion.* The procedure forces a pause during the busy total cutaneous clinical examination allowing time to think and formulate a logical differential diagnosis. Dermoscopy provides another chance to rethink the naked-eye examination conclusion allowing for a second opportunity to make the correct diagnosis.
12. *Dermoscopy helps differentiate melanocytic from nonmelanocytic lesions.* This concept is explained in chapter 10 on the "two-step" initial dermoscopic procedure, which differentiates melanocytic from nonmelanocytic lesions.
13. *Dermoscopy increases the observers' confidence in their clinical diagnoses.* It has been shown that, compared with naked-eye examination of lesions of the skin, dermoscopy engenders greater degree of confidence in the correctness of the clinical diagnosis (Wang et al., 2008). The procedure also assures the patient that additional steps have been taken regarding the decision whether or not the lesion should be biopsied. When the confidence in a dermoscopic examination of a lesion reaches 100% that the lesion is benign, biopsy is almost always avoided.
14. *Dermoscopy helps isolate suspicious foci within larger lesions.* Identifying such foci can be useful for directing pathology sectioning of such suspicious sites within a lesion (Marghoob et al., 2009).
15. *Dermoscopy can aid in more precisely defining borders of some lesions for improved presurgical margin mapping.* An example of this is the ability to recognize subclinical extensions of facial lentigo maligna melanomas using dermoscopy (Robinson, 2004).
16. *Dermoscopy helps in the surveillance of patients with many melanocytic nevi.* In such patients certain lesions have attributes that do not meet the full criteria for melanoma but have

Table 1.1 How Can Dermoscopy Help?

Allows observer to concentrate on lesion and formulate a logical differential diagnosis
Helps differentiate melanocytic from nonmelanocytic lesions
Helps differentiate benign from malignant lesions
Improves diagnostic accuracy
Increases the observers' confidence in their clinical diagnoses
Confirms naked-eye diagnosis (clinical–dermoscopy correlation)
Improves malignant to benign biopsy ratio (avoids unnecessary biopsies)
Helps isolate suspicious foci within lesions—directing pathology step-sectioning—clinical–dermoscopy–pathology correlation
Helps more precisely define borders of some lesions for improved presurgical margin mapping
Helps in the surveillance of patients with many nevi
Helps reassure patients

Source: From Benvenuto and Marghoob (2006).

some "suspicious" features. By using a comparative approach and short-term (i.e., every three months) sequential dermoscopic digital imaging, the lesions that appear similar to each other or remain unchanged or changed in a benign way can be followed (Altamura et al., 2008; Argenziano, 2011).

Now, a word regarding the second edition of this atlas. This edition has been completely rewritten with the aim of providing the most up-to-date information possible regarding dermoscopy. The editors solicited experts in this field to contribute chapters pertaining to their respective area(s) of interest and expertise. However, many chapters were subsequently edited and/or substantially rewritten by Dr. Ashfaq A. Marghoob and Ralph Braun with the aim of providing a more interwoven view of the subject matter. For this we ask the authors of the edited chapters for forgiveness. Schematics, to help readers visualize certain dermoscopic structures, were added to many chapters by Josep Malvehy. Furthermore, many of the submitted dermoscopic images were replaced by better examples from the editors' personal image database. This was all done so as to provide a textbook on dermoscopy that will speak to the reader with one unified point of view. It is our sincere hope that this book will help novices and experts in the field of dermoscopy to improve upon their dermoscopic skills. Without doubt, we, the editors, poured our hearts and souls into this work and thereby further perfected our own dermoscopy knowledge and skills. For this we will forever be indebted to all those that contributed to this atlas.

Melanoma writes its message on the skin with its own ink, and it is there for all to see. Unfortunately, some see but do not comprehend.
Neville Davis (Davis, 1978).

REFERENCES

Altamura, D., Avramidis, M., & Menzies, S.W., 2008, Assessment of the optimal interval for and sensitivity of short-term sequential digital dermoscopy monitoring for the diagnosis of melanoma, *Arch Dermatol*, 144, 502–6.

Argenziano, G., 2011, Dermoscopy of patients with multiple nevi. Improved management recommendation using a comparative diagnostic approach, *Arch Dermatol*,147, 46–9.

Bafounta, M.L., Beauchet, A., Aegerter, P., & Saiag, P., 2001, Is dermoscopy useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests, *Arch Dermatol*, 137, 1361–3.

Benvenuto, C., Marghoob, A.A., 2006, Ten reasons why dermoscopy is beneficial for the evaluation of skin lesions. *Expert Rev Dermatol*, 1, 1–6.

Carli, P., De Giorgi, V., Crocetti, E., Mannone, F., Massi, D., Chiarugi, A. & Giannotti, B., 2004, Improvement of malignant/benign ratio in excised melanocytic lesions in the 'dermoscopy era': a retrospective study 1997–2001, *Br J Dermatol*, 150, 687–92.

Davis, N., 1978, Modern concepts of melanoma and its management, *Ann Plast Surg*, 1, 628–9.

Grin, C., Kopf, A., Welkovich, B., Bart, R. & Levenstein, M., 1990, Accuracy in the clinical diagnosis of malignant melanoma, *Arch Dermatol*, 126, 763–6.

Jaeschke, R., Guyatt, G. & Sackett, D.L., 1994, Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group, *JAMA*, 271, 389–91.

Kittler, H., Pehamberger, H., Wolff, K. & Binder, M., 2002, Diagnostic accuracy of dermoscopy, *Lancet Oncol*, 3, 159–65.

Marghoob, A.A., Changehien, L., DeFazio, J., Dessio, W.C., Malvehy, J., Zalaudek, I., Halpern, A.C., & Scope, A., 2009, The most common challenges in melanoma diagnosis and how to avoid them, *Australasian J Dermatol*, 50, 1–15.

Noor, O., Nanda, A. & Rao, B.K., 2009, A dermoscopy survey to assess who is using it and why it is or is not being used, *Int J Dermatol*, 48, 951–2.

Robinson J.K., 2004, Use of digital epiluminescence microscopy to help define the edge of lentigo maligna, *Arch Dermatol*, 140, 1095–100.

Terushkin, V., Oliveria, S.A., Marghoob, A.A. & Halpern, A.C., 2010, Use of and beliefs about total body photography and dermatoscopy among US dermatology training programs: an update, *J Am Acad Dermatol*, 62, 794–803.

Venugopal, S.S., Soyer, H.P. & Menzies, S.W., 2011, Results of a nationwide dermoscopy survey investigating the prevalence, advantages and disadvantages of dermoscopy use among Australian dermatologists, *Australas J Dermatol*, 52, 14–18.

Vestergaard, M., Macaskill, P., Holt, P. & Menzies, S.W., 2008, Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting, *Br J Dermatol*, 159, 669–76.

Wang, S.Q., Dusza, S.W., Scope, A., Braun, R.P., Kopf, A.W. & Marghoob, A.A., 2008, Differences in dermoscopic images from nonpolarized dermoscope and polarized dermoscope influence the diagnostic accuracy and confidence level: a pilot study, *Dermatol Surg*, 34, 1389–95.

Zalaudek, I., Kittler, H., Marghoob, A.A., Balato, A., Blum, A., Dalle, S., Ferrara, G., Fink-Puches, R., Giorgio, C.M., Hofmann-Wellenhof, R., Malvehy, J., Moscarella, E., Puig, S., Scalvenzi, M., Thomas, L. & Argenziano, G., 2008, Time required for a complete skin examination with and without dermoscopy: a prospective, randomized multicenter study, *Arch Dermatol*, 144, 509–13.

2 Principles of dermoscopy and dermoscopic equipment

Steven Q. Wang, Ashfaq A. Marghoob, and Alon Scope

INTRODUCTION

Dermatoscopy, which is most commonly referred to daily as dermoscopy, uses a handheld microscope called a dermatoscope (or dermoscope) that is equipped with a magnification lens and a light source. This device allows the observer to examine the subsurface primary morphology of cutaneous lesions. In the hands of experienced users, dermoscopy can improve the clinician's diagnostic accuracy (Bafounta et al., 2001; Kittler et al., 2002) and confidence level (Benvenuto-Andrade et al., 2006) for both pigmented and nonpigmented skin lesions. Although unaided (naked) visual inspection of the skin allows the clinician to appreciate the gross morphologic features of lesions, such as their size, shape, colors, contours, and topography, dermoscopy allows the clinician to visualize structures below the level of the stratum corneum to the depth of the superficial dermis. In other words, dermoscopy has opened up a new dimension in the morphologic evaluation of skin lesions by revealing colors and structures that are normally not visible to the unaided eye.

Rona MacKie, in the 1970s, was one of the first clinicians to recognize the advantage of dermoscopy for the preoperative evaluation of equivocal pigmented skin lesions (MacKie, 1971; MacKie, 1972). Thereafter, many clinicians and researchers worldwide have studied it extensively, and a significant progress has made in defining dermoscopic patterns and structures of pigmented and nonpigmented skin lesions. Today, there remains little doubt that dermoscopy is a valuable clinical tool for the noninvasive, in vivo evaluation and diagnosis of cutaneous lesions.

PRINCIPLES OF NONPOLARIZED DERMOSCOPY

Dermoscopy provides additional information beyond that gleamed by evaluating the lesion through a simple magnifying lens. To understand how dermoscopy provides this information requires an understanding of the optical principles involved in dermoscopy, in particular, the interactions of light with the skin. Because the refractive index of the stratum corneum is higher than that of air, much of the incident light is reflected off the surface of the skin (Fig. 2.1); (Anderson & Parrish, 1981; Pan et al., 2008) this diffuse backscattered light overwhelms the retina, and thereby obscures the visualizing of light that is reflected from the deeper layers of the skin. Consequently, with naked-eye examination, we are mostly able to observe the morphologic features manifest on the surface layer of the skin (stratum corneum), and only minimally able to appreciate the colors and structures located in the deeper layers of the epidermis and the dermis.

The first handheld dermoscope introduced into clinical practice used a nonpolarized light source to illuminate the skin. Most nonpolarized dermoscopes (NPDs) today contain light-emitting diodes to provide illumination, and all NPDs are equipped with a 10× magnification lens (Fig. 2.2). Examining lesions with NPD necessitates direct contact of the dermoscope's glass plate with the skin, between which the presence of a liquid interface is required (ideally with refraction index equal to that of skin) (Fig. 2.3). This setup replaces the normal skin–air interface with a skin–liquid interface. Because there is a closer match of refractive indices within the skin–liquid–glass interface, light reflection is decreased, thereby minimizing glare, which in turn makes the stratum corneum appear more translucent. This optical setup permits the observer to see deeper structures in the skin (Fig. 2.4). It should now be obvious that when utilizing NPD it is imperative that air pockets (i.e., air bubbles) present between the dermoscope's glass plate, the liquid, and the skin be eliminated; such air pockets create a skin–air interface that will preclude the observer from visualizing structures below the stratum corneum.

Different immersion liquids can be used for dermoscopy, including water, mineral oil, alcohol or gel (i.e., ultrasound gel, antibacterial gel). In one study (Gewirtzman et al., 2003), 70% alcohol was reported to be the best immersion liquid since it yielded fewer air bubbles and provided clearer images. An added benefit of alcohol is the potential for it to reduce bacterial contamination, and thus it may be more hygienic as compared with other liquids (Stauffer et al., 2001). However, for examination of the nail apparatus, ultrasound or antibacterial gels are much superior to alcohol (Ronger et al., 2002; Kelly & Purcell, 2006), because the gel's viscosity prevents it from rolling off the convex nail surface. It is common to have air bubbles trapped in the gel and the bubbles can be distracting and may prevent the observer from getting a clear view of the lesion. In efforts to minimize the number of air bubbles in the gel it is best to store the gel bottles upside down, to avoid shaking the bottle, and to squeeze out a small amount of the gel before use so as to discard remnant dried gel.

PRINCIPLES OF POLARIZED DERMOSCOPY

Polarized dermoscopy (PD) units were introduced into the clinical arena in the year 2000 (Fig. 2.5). These handheld dermoscopes rely on a different set of optical principles from those described above for NPD. The PD devices use two polarizers to achieve cross-polarization. Under this condition, the polarizers allow the dermoscope to preferentially capture the backscattered light from the deeper layers of the skin (mechanism is explained in Fig. 2.6). The main advantages of the cross-polarized system are that it eliminates the necessity of a liquid interface and it does not require direct contact with the skin (Fig. 2.7). These innovations allow the examiners to scan lesions at a relatively rapid pace. Although PD does not require direct contact and a liquid interface, some PD devices do allow the user to opt between noncontact PD and contact PD, which can be used with or without the application of fluid onto the skin. In addition, dermoscopes that allow the user to toggle between PD and NPD are now available. When these "hybrid" dermoscopes are used for toggling between the PD and NPD modes, the dermoscope should be in direct contact with a liquid interface. If this is not done then the user will see dermoscopic structures only in the polarized mode; however, in the nonpolarized mode, no dermoscopic structures will be discernable and the observer will simply see a magnified clinical (not dermoscopic) image of the lesion.

POLARIZED VS. NONPOLARIZED DERMOSCOPY

For most pigmented and nonpigmented skin lesions, PD and NPD offer overall similar images. However, there are some important differences between the two types of dermoscopes (Table 2.1) (Agero et al., 2006; Benvenuto-Andrade et al., 2007; Wang et al., 2008).

In general, blue-white color (Fig. 2.8A, B) due to orthokeratosis or regression, and milia-like cyst (Fig. 2.9A, B) are more conspicuous under NPD. However, blood vessels (Fig. 2.10A, B), vascular blush due to increased blood volume (Fig. 2.11A, B), and white shiny areas (i.e., scar or chrysalis/crystalline) (Fig. 2.8A, B) are more conspicuous under PD. Besides the features mentioned above, there are also slight color differences between PD and NPD. The PD instrument displays the melanin pigment with varying and darker shades of brown and blue compared with NPD (Fig. 2.12). Although most of the aforementioned differences between PD and NPD are due mainly to the inherent properties of polarized *versus* nonpolarized light, some are due to the effects of pressure being placed (contact dermoscopy) or not being placed (noncontact dermoscopy) onto the skin surface (Figs. 2.10–2.12). As mentioned previously, NPD requires a liquid interface and contact with the skin. The pressure applied from the NPD scope against the skin can compress small blood vessels in a lesion, making it difficult to visualize them (Fig. 2.10); in fact, as little as 18 mmHg pressure is required to blanch out the

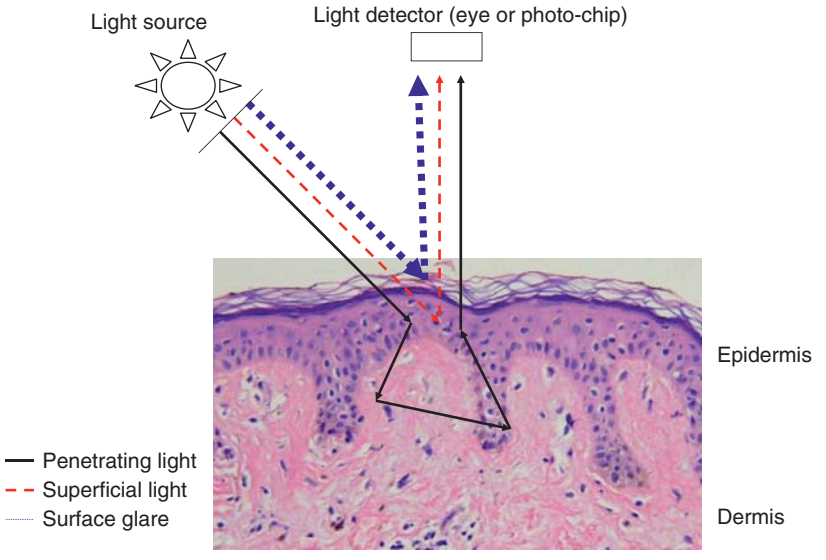

Figure 2.1 This is a schematic representation of optical properties of light without the use of dermoscopy. The arrows indicate the path of light through the skin. Some of the light is absorbed by the superficial layers of the epidermis and is scattered only slightly (thin red line) and some of the light penetrates more deeply and undergoes more scattering events (thin black line). However, most of the incident light is reflected off the stratum corneum (thick blue line); this surface glare overwhelms the retina, and thereby precludes the observer from visualizing the light reflected from the deeper layers of the skin (red and black lines). Thus, practically speaking, the clinical (nondermoscopic) examination of the skin with or without a magnifying lens only sees the light that is reflected from the skin surface (thick blue line), and thus most subsurface structures remain hidden from view.

Figure 2.2 The most frequently utilized nonpolarized contact dermoscopes are shown in this figure. From left to right these scopes are: Episcope (Welch Allyn; www.welchallyn.com); DermLite Fluid (3GEN, LLC; www.dermlite.com); Delta 20 (Heine; www.heine.com); DermoGenius (Biocam; www.dermogenius.com)

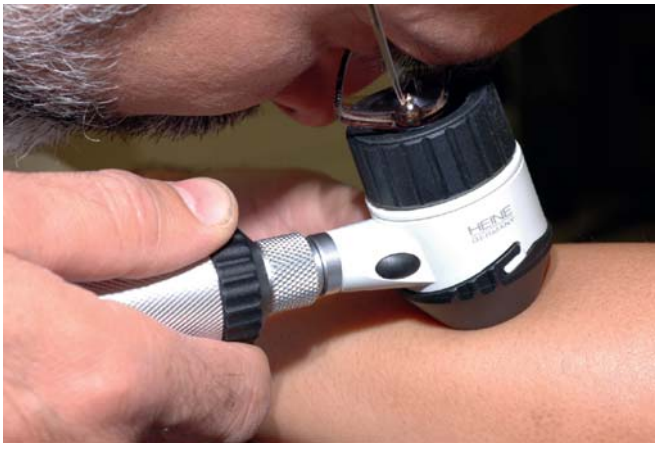

Figure 2.3 Physician examining the skin with a contact nonpolarized dermoscope.

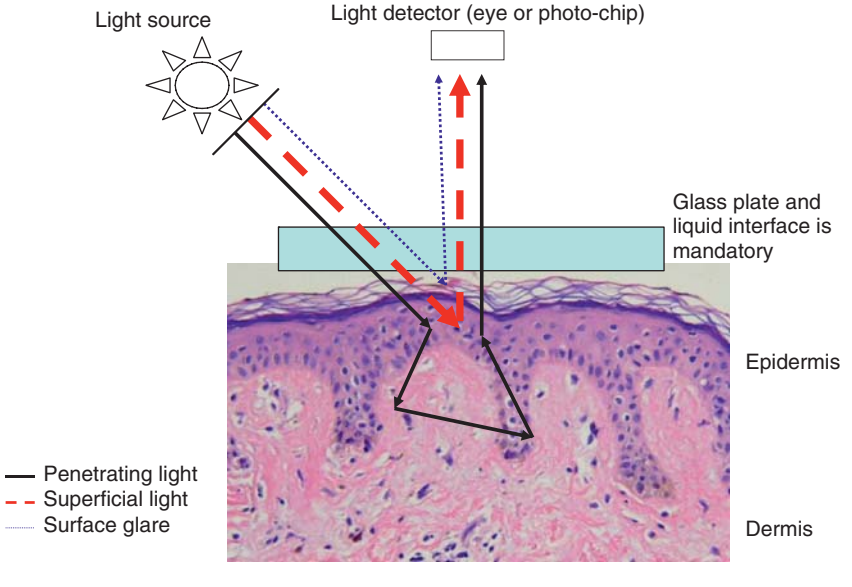

Figure 2.4 This is a schematic representation of optical properties of light during the use of contact NPD with a liquid interface. The arrows indicate the path of light through the skin. Most of the light is absorbed and reflected from the superficial layers of the epidermis after undergoing minimal scattering events (thick red line). Some of the light is reflected off the stratum corneum (thin blue line) but this surface glare is insufficient to interfere with the ability to visualize subsurface dermoscopic structures. Some of the light penetrates more deeply and is absorbed and reflected back after multiple scattering events (thin black line); however, the light from the deeper layer contributes only a small fraction to that detected with NPD, and most of the light reaching the retina is from the more superficial, minimally scattered light (thick red line). *Abbreviation*: NPD, nonpolarized dermoscopy.

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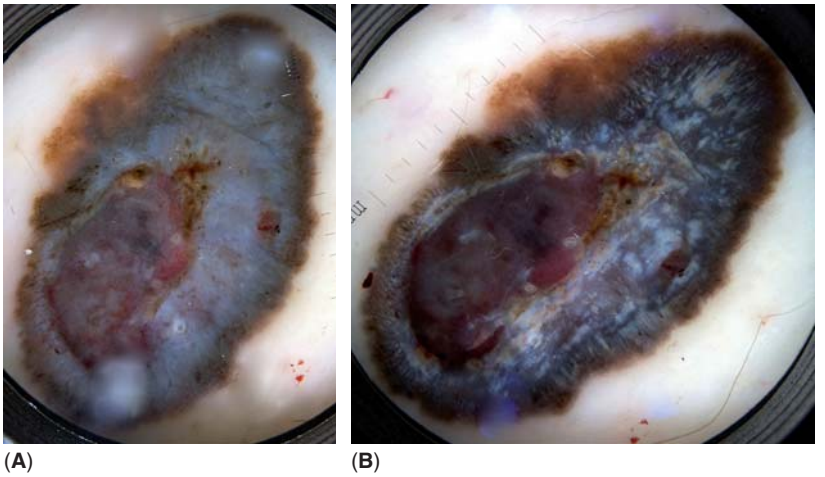
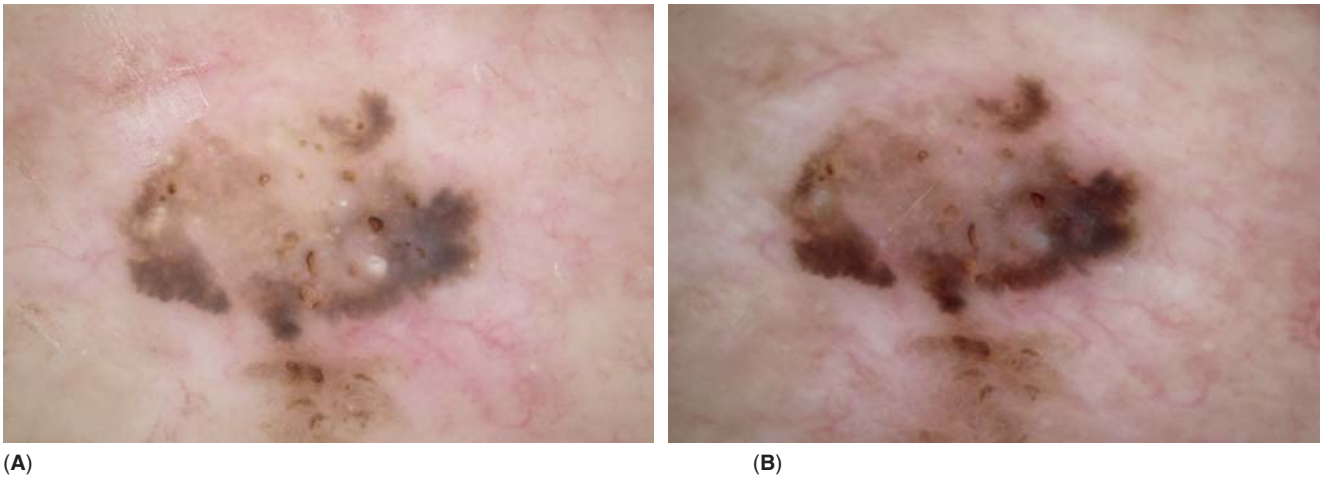


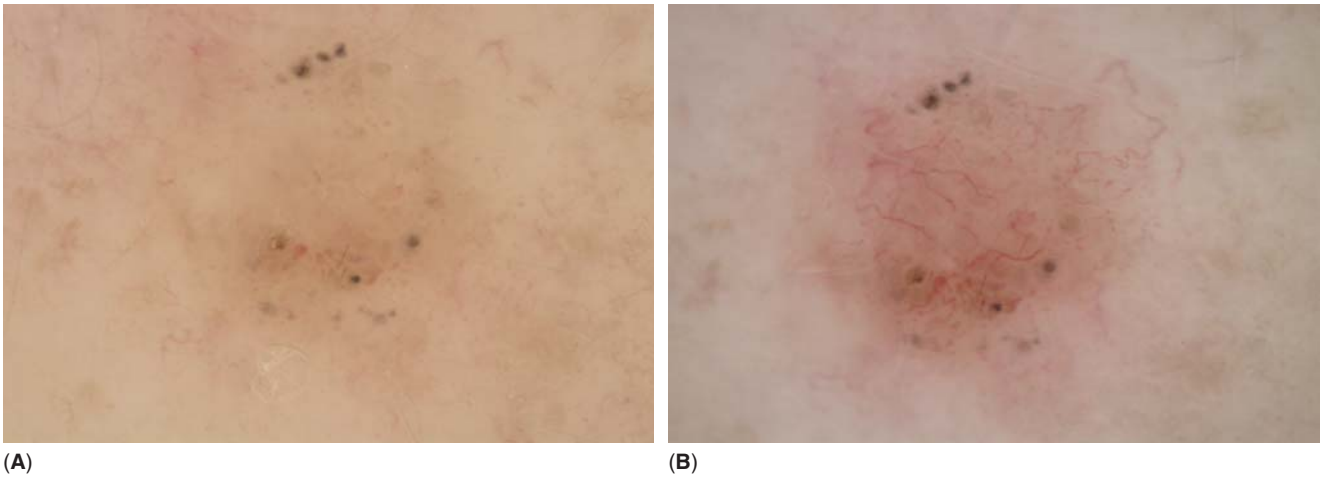
(**A**) (**B**)

Figure 2.8 Image was taken with (**A**) NPD and (**B**) PD. This is a melanoma 0.9 mm in thickness. Notice that the blue-white veil at the center of the lesion is more conspicuous under NPD and is difficult to appreciate with PD. However, linear white shiny streaks, known as chrysalis/crystalline structures can only be seen with PD. Blue white veil is due to orthokeratosis and will be seen with a device that preferentially images the superficial layers (NPD), whereas chrysalis/crystalline structures which are thought to correlate with altered collagen in the stroma, are only visible with a device that preferentially images deeper layers (PD). *Abbreviations*: PD, polarized dermoscopy; NPD, nonpolarized dermoscopy.



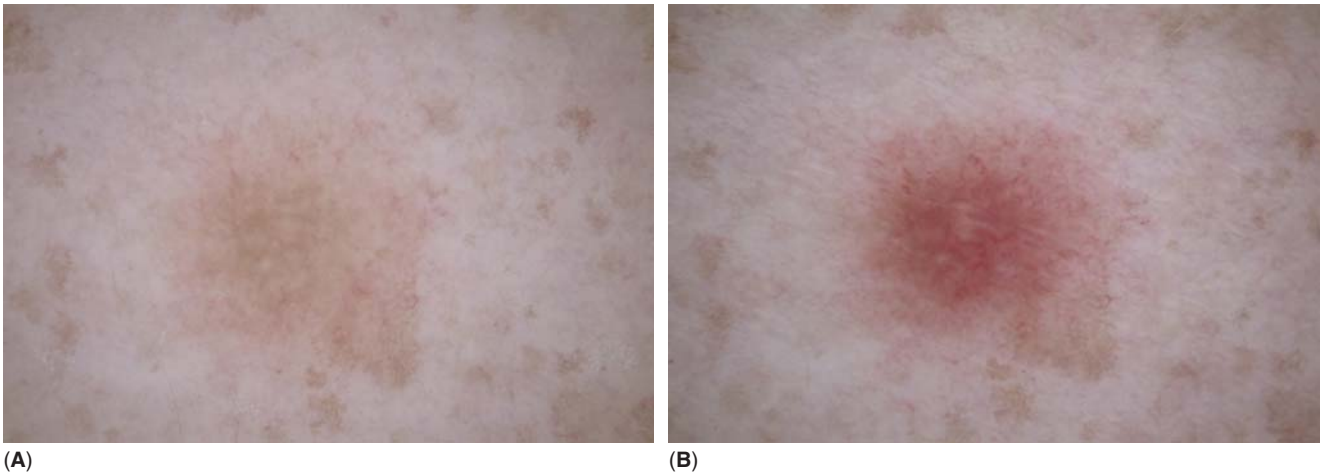
(**A**) (**B**)

Figure 2.9 Image was taken with (**A**) NPD and (**B**) PD. This is a seborrheic keratosis. Because milia-like cysts are not visible under PD, this lesion could be misdiagnosed as a melanoma. However, with NPD, the milia-like cysts are readily identifiable and the correct diagnosis can be rendered with ease. *Abbreviations*: PD, polarized dermoscopy; NPD, nonpolarized dermoscopy.



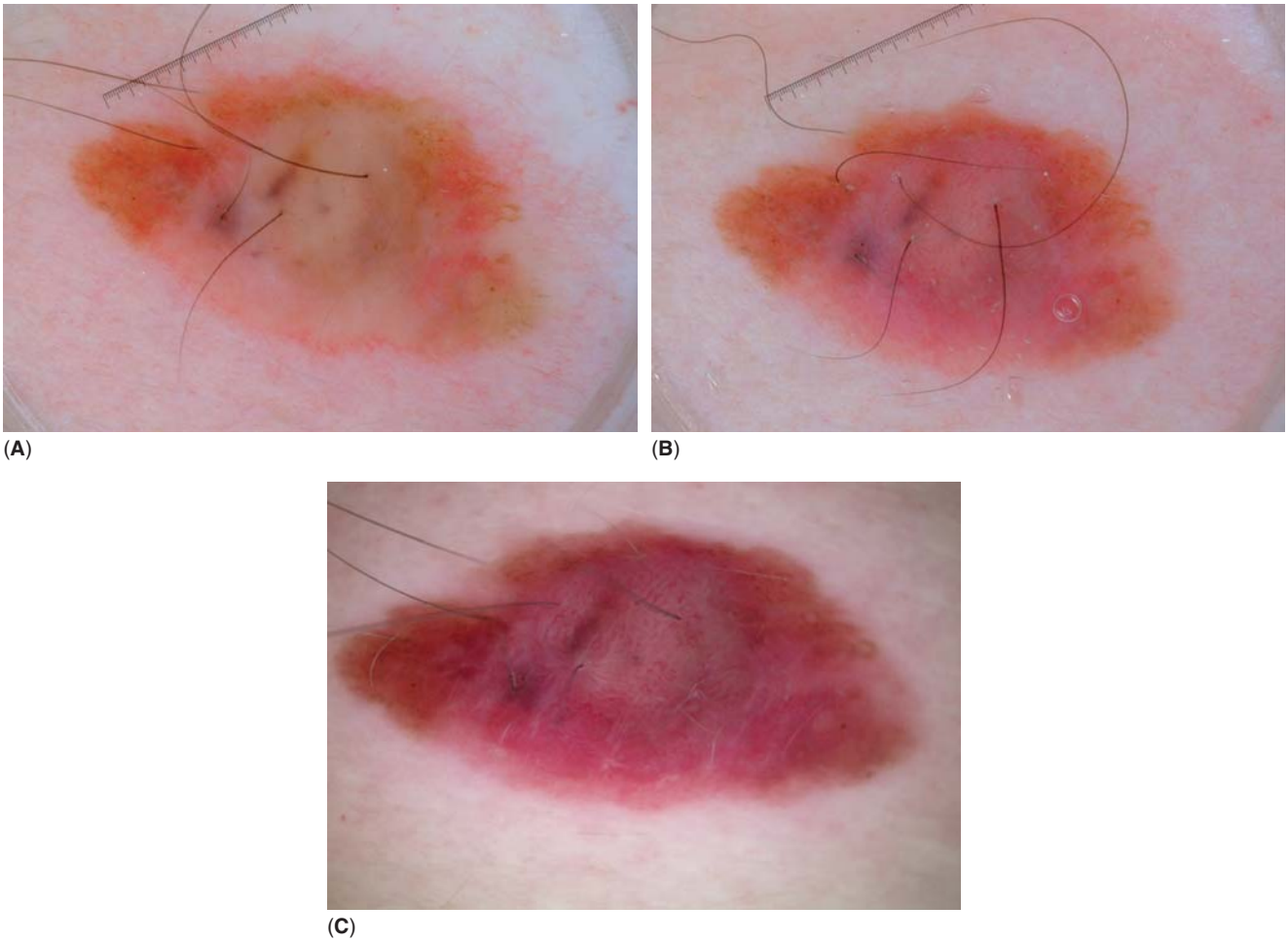
(**A**) (**B**)

Figure 2.10 Image was taken with (**A**) NPD and (**B**) PD. This is a basal cell carcinoma. Notice that the arborizing blood vessels are better seen with PD than with NPD. This is partially due to the compression of blood vessels during the examination with NPD and partially due to the enhanced ability to visualize deeper structures with PD. *Abbreviations*: PD, polarized dermoscopy; NPD, nonpolarized dermoscopy.



(**A**) (**B**)

Figure 2.11 Image was taken with (**A**) NPD and (**B**) PD. This is a melanoma 0.3 mm in thickness. Notice that the vascular blush (pink veil, due to vasodilation) is better seen with PD than with NPD. This is partially due to the compression of blood vessels during the examination with NPD and partially due to the enhanced ability to visualize blood and red colors with PD. *Abbreviations*: PD, polarized dermoscopy; NPD, nonpolarized dermoscopy.



(**A**) (**B**)

(**C**)

Figure 2.12 The three images are of the same melanoma 1.65 mm in thickness arising in a pre-existing nevus. Image (**A**) was captured with an NPD using alcohol as the liquid interface. Image (**B**) was captured using NPD and ultrasound gel as the liquid interface. Image (**C**) is taken with PD without any direct contact with the skin. These images highlight the effects of placing pressure on the lesion. PD without direct skin contact (*image C*) allows for the blood vessels and vascular blush to be most apparent. Using gel as the liquid interface during NPD allows the operator to apply less pressure on the lesion as compared with NPD when alcohol is used as the fluid interface. As can be seen in the figure, minimizing the pressure being applied onto the skin during NPD examination (*image B*) will greatly enhance the ability to visualize the blood vessels. Besides the effects of pressure, this case also highlights some of the inherent difference between nonpolarized and polarized light. Notice that chrysalis/crystalline structure can be seen in the PD image (*bottom*) but is not apparent in the two NPD images. *Abbreviations*: PD, polarized dermoscopy; NPD, nonpolarized dermoscopy.

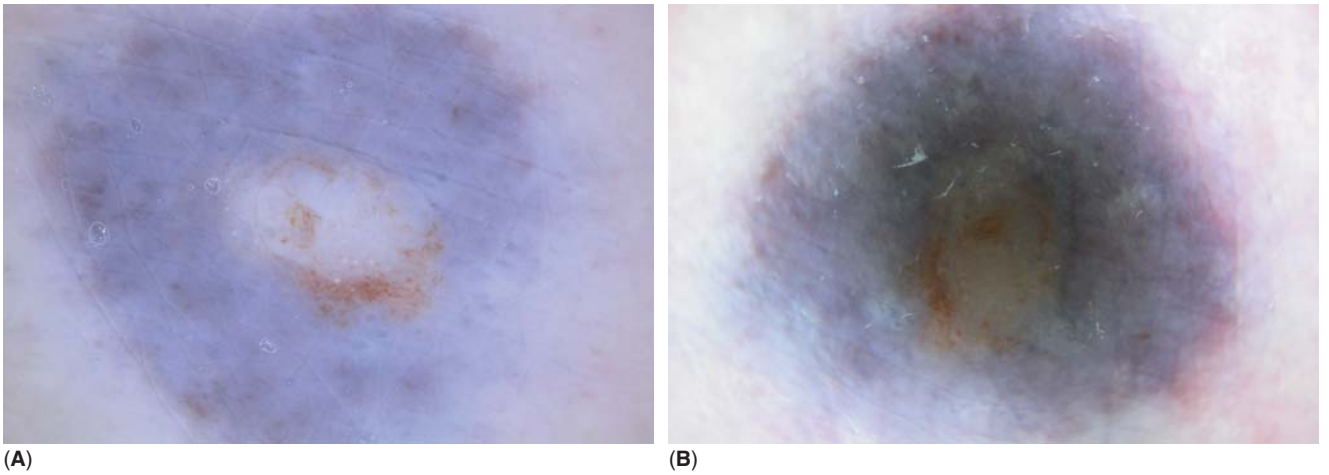


Figure 2.13 Image taken with (**A**) NPD and (**B**) PD. This is a combined blue nevus. Blue nevi can appear differently on NPD and PD. Under NPD, the lesion has a more homogeneous blue appearance, whereas under PD, the lesion displays varying shades of brown and blue. *Abbreviations*: PD, polarized dermoscopy; NPD, Nonpolarized dermoscopy.

Figure 2.14 Most handheld dermoscopes can be coupled to a camera via an adapter. In this image the handheld DermoGenius is attached to a Nikon camera and the handheld DermLite is attached to a Cannon camera.

Figure 2.15 Acquiring images through a dedicated dermoscopic camera lens tends to be less cumbersome. In addition, the image quality is usually better and more reproducible as compared to the image quality acquired with a handheld unit attached to a camera. The dedicated dermoscopic camera lenses shown in this figure are (1) EpiLume dermoscopy lens produced by Canfield is shown attached to a Nikon camera (*left*), (2) Heine Dermaphot lens is shown attached to a Minolta camera (*middle*), (3) DermLite Foto lens produced by 3GEN is shown attached to a Cannon camera (*right*).

blood volume within a lesion (Fig. 2.11). Since PD does not require direct skin contact, blood vessels and pink color are more evident under PD. Furthermore, polarized light must transverse a distance of between 0.06 and 0.1 mm of skin before sufficient amounts of polarized light changes its angle of polarization (randomization of polarization, Fig. 2.6), thereby allowing it to pass through the cross-polarizing filter thereby allowing it to reach our retina. In other words, unlike NPD, PD is "blind" from the skin surface to a depth of about 0.06–0.1 mm. This is the reason why milia-like cysts (horn pseudocysts in the epidermis) and blue-white veil (orthokeratosis), both due to superficial changes in the epidermis, are less conspicuous with PD (Figs. 2.8 and 2.9). Although PD is not ideal for evaluating the superficial layer of the skin, it does allow for improved visualization of deeper skin layers compared with NPD. This helps explain why melanin pigment can appear in varying shades of brown and blue (Tyndall effect) under PD (Fig. 2.13). It also helps explain why the blood vessel morphology is more conspicuous under PD (Fig. 2.10). In addition, polarized light rapidly randomizes its polarization when it encounters a birefringent structure, such as collagen. This property helps explain why scars and chrysalis/crystalline structures are more conspicuous under PD (Fig. 2.8) (Marghoob et al., 2009).

Although most lesions can be correctly diagnosed via either NPD or PD, one study demonstrated that the differences between PD and NPD may impact the diagnostic accuracy and diagnostic confidence level (Wang et al., 2008). For example, some seborrheic keratosis may be misdiagnosed with PD due to the inability to visualize the milia-like cysts with polarized light (Fig. 2.9B). However, the same seborrheic keratosis is likely to be easily diagnosed with NPD (Fig. 2.9A). As another example, some amelanotic or structureless melanomas may only be identifiable due to the presence of blood vessels, vascular blush, and/or chrysalis/crystalline structures. These structures are all easy to appreciate with PD and often difficult to impossible to visualize with NPD (Figs. 2.8 and 2.11). It is clear that PD and NPD provide complementary information. PD provides maximum sensitivity for detecting a cutaneous malignancy while NPD provides maximum specificity by correctly identifying lesions such as seborrheic keratosis. Thus, using both may provide the clinician with the highest diagnostic accuracy.

CAPTURING DERMOSCOPIC IMAGES

Many clinicians are inclined to document the dermoscopic appearance of lesions by capturing an image of the lesion with a camera. Fortunately, adapters are available for most handheld dermoscopes that permit coupling of the dermoscope to the camera (Fig. 2.14). In addition, dedicated dermoscopic camera lenses are also available and they tend to be less cumbersome to use as compared with handheld units attached to a camera (Fig. 2.15). These

Table 2.2 Dermoscopic Devices with the Added Features of Digital Image Capture and Analytic Algorithms

Device name[a]	Function	Company	Website
DB-Dermo Mips	ANN and "similarity" classifier	Biomips srl	www.skinlesions.net
DermoGenius Ultra	ABCD characteristics and Digital Standardized Dermatological Point Score (DSDP)	BIOCAM GmbH	www.biocam.de
Fotofinder Dermoscope	Comparison with a reference bank	TeachScreen Software	www.fotofinder.de
MicroDerm	DANAOS–ANN clasifier	VisioMED	www.visiomedag.com
MoleMate	Spectrophotometric intracutaneous analysis	Astron Clinica	www.astronclinica.com
Molemax III	ABCD and seven-point score	Derma Medical Systems	www.dermamedicalsystems.com
Solarscan	Comparison with a reference bank	Polartechnics	www.polartechnics.com.au

Clinical and dermoscopic digital image capture for all instruments. All dermoscopic images are taken with a liquid interface except DB-Dermo Mips, which uses polarized light. [a]Device names are registered trademarks. *Abbreviation:* ANN, artifical neural network.

dedicated lenses generally result in the easier acquisition of sharper and clearer images as compared with images acquired through handheld units. Lastly, numerous companies are now producing dermoscopic lenses that can easily be attached to iPhones (Fig. 2.5). The dermoscopic image quality acquired via the camera on a mobile phone device is on par with those taken via more traditional methods.

Most images captured today are digitally acquired. These images can easily be stored on hard drives, CDs, DVDs, and others. However, easy retrieval of relevant images may pose a challenge. Multiple image database programs are available that can facilitate in the process of organizing and retrieval of images. In addition, multiple systems are commercially available consisting of a dermoscopic imaging device, which is directly linked to a computer. These systems simplify the process of image acquisition, storage, organization, retrieval, and image viewing. Many of these systems have the added benefit of providing computer-based analytical algorithms to assist clinicians in managing skin lesions (Table 2.2).

CONCLUSIONS

1. Dermoscopy allows for the visualization of colors and structures present not only on the surface of the skin but also in the epidermis and dermis.
2. Correct interpretation of structures seen under dermoscopy can improve the clinician's diagnostic accuracy and confidence level for both pigmented and nonpigmented skin lesions.
3. There are differences between the images seen with nonpolarized and polarized dermoscopes. Both types of devices provide complementary information. In general, structures in the superficial epidermis (e.g., milia-like cysts) are more conspicuous with nonpolarized dermoscopes, and deeper structures (e.g., blood vessels, collagen) are more conspicuous with polarized devices.
4. To capture dermsocopic images, various imaging devices are available.

REFERENCES

Agero, A.L., Taliercio, S., Dusza, S.W., Salaro, C., Chu, P. & Marghoob, A.A., 2006, Conventional and polarized dermoscopy features of dermatofibroma. *Arch Dermatol*, 142, 1431–7.

Anderson, R.R. & Parrish, J.A., 1981, The optics of human skin. *J Invest Dermatol*, 77, 13–19.

Bafounta, M.L., Beauchet, A., Aegerter, P. & Saiag, P., 2001, Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. *Arch Dermatol*, 137, 1343–50.

Benvenuto-Andrade, C., Dusza, S.W., Agero, A.L., Scope, A., Rajadhyaksha, M., Halpern, A.C. & Marghoob, A.A., 2007, Differences between polarized light dermoscopy and immersion contact dermoscopy for the evaluation of skin lesions. *Arch Dermatol*, 143, 329–38.

Benvenuto-Andrade, C., Dusza, S.W., Hay, J.L., Agero, A.L., Halpern, A.C., Kopf, A.W. & Marghoob, A.A., 2006, Level of confidence in diagnosis: clinical examination versus dermoscopy examination. *Dermatol Surg*, 32, 738–44.

Gewirtzman, A.J., Saurat, J.H. & Braun, R.P., 2003, An evaluation of dermoscopy fluids and application techniques. *Br J Dermatol*, 149, 59–63.

Kelly, S.C. & Purcell, S.M., 2006, Prevention of nosocomial infection during dermoscopy? *Dermatol Surg*, 32, 552–5.

Kittler, H., Pehamberger, H., Wolff, K. & Binder, M., 2002, Diagnostic accuracy of dermoscopy. *Lancet Oncol*, 3, 159–65.

MacKie, R.M., 1971, An aid to the preoperative assessment of pigmented lesions of the skin. *Br J Dermatol*, 85, 232–8.

MacKie, R.M., 1972, Cutaneous microscopy in vivo as an aid to preoperative assessment of pigmented lesions of the skin. *Br J Plast Surg*, 25, 123–9.

Marghoob, A.A., Cowell, L., Kopf, A.W. & Scope, A., 2009, Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*, 145, 618.

Pan, Y., Gareau, D.S., Scope, A., Rajadhyaksha, M., Mullani, N.A. & Marghoob, A.A., 2008, Polarized and nonpolarized dermoscopy: the explanation for the observed differences. *Arch Dermatol*, 144, 828–9.

Ronger, S., Touzet, S., Ligeron, C., Balme, B., Viallard, A.M., Barrut, D., Colin, C. & Thomas, L., 2002, Dermoscopic examination of nail pigmentation. *Arch Dermatol*, 138, 1327–33.

Stauffer, F., Kittler, H., Forstinger, C. & Binder, M., 2001, The dermatoscope: a potential source of nosocomial infection? *Melanoma Res*, 11, 153–6.

Wang, S.Q., Dusza, S.W., Scope, A., Braun, R.P., Kopf, A.W. & Marghoob, A.A., 2008, Differences in dermoscopic images from nonpolarized dermoscope and polarized dermoscope influence the diagnostic accuracy and confidence level: a pilot study. *Dermatol Surg*, 34, 1389–95.

3 Histopathologic tissue correlations of dermoscopic structures

Ralph P. Braun, Alon Scope, Ashfaq A. Marghoob, Katrin Kerl, Harold S. Rabinovitz, and Josep Malvehy

Dermoscopy enables the visualization of structures and colors beneath the surface of the skin, which are not routinely discernible to the unaided eye. In essence, dermoscopy is a new method of gross histopathologic examination of the skin performed by clinicians, since structures and colors observed by dermoscopy have specific correlates on histopathologic examination. To make accurate diagnosis using dermoscopy, clinicians must learn the definition and histopathologic correlation of dermoscopic structures and colors.

What are the fundamental differences between dermoscopic and histopathologic evaluations?

Histopathologic evaluation is performed on vertical sections of tissue, allowing the assessment of the full depth of the lesion at scanning magnification and at cellular-level magnification. Histopathology is performed on paraffin-embedded tissue, allowing for special stains and immunohistochemical techniques that may assist in diagnosis.

Dermoscopic evaluation is based on a horizontal (*en face*) view of the entire lesion (Soyer et al., 2005; Ferrara, 2009). Dermoscopic structures and colors are two-dimensional surface projections of tissue structures (e.g., melanocytic nests and blood vessels) at different depths of the skin. While the dermoscopist can see the entire breadth of the lesion in the horizontal plane, the structure and colors seen on dermoscopy are generally limited in depth to the papillary dermis (Braun et al., 2003). Furthermore, dermoscopy does not allow for evaluation of the lesion at a cellular level. However, since dermoscopy is a noninvasive procedure, it does allow for the ability to sequentially monitor lesions, which in turn may provide information regarding the lesion's biology and growth dynamics.

Using dermoscopy, we can identify "colors" and "structures" that are not perceived by the unaided eye. Integrating the observations of dermoscopic colors and structures allows for making repeatable inferences regarding the tissue morphology of the lesion on the histology level (Table 3.1) (Anderson & Parrish, 1981).

DERMOSCOPY COLORS

Colors in skin lesions can provide important morphologic information (Fig. 3.1) Melanin is the main chromophore in pigmented skin lesions. Depending on the anatomic location and concentration of melanin in the skin, the colors perceived on dermoscopy range from black to blue (i.e., Tyndall effect, Fig. 3.2) (Anderson & Parrish, 1981; Reisfeld, 2000). If melanin is located in the stratum corneum or immediately beneath it, the lesion would appear black on dermoscopy. Melanin at the dermoepidermal junction (DEJ) would be perceived as light brown to dark brown, depending on its density. Melanin in the dermis results in shades of blue to gray. Thus, the colors seen on dermoscopy allow the clinician to predict the anatomic location of the cells that contain melanin (e.g., melanocytes, keratinocytes, and melanophages). Other important determinants of lesion color include hemoglobin in red blood cells (pink to red colors) and collagen fibers in the dermis (white color).

DERMOSCOPY STRUCTURES

Pigment Network

The pigment network consists of a grid of intersecting pigmented "lines" forming a honeycomb pattern (Fig. 3.3). The anatomic basis of the pigment network is melanin in keratinocytes or in melanocytes along the DEJ, representing the way the rete ridge pattern of the epidermis appears when viewed in the horizontal plane (Fig. 3.4). The less-pigmented "holes" of the network correspond to tips of the dermal papillae and the overlying suprapapillary plates of the epidermis. A wide diameter of dermal papillae would correspond dermoscopically to wider network "holes," whereas narrow dermal papillae would result in a denser sieve of the grid.

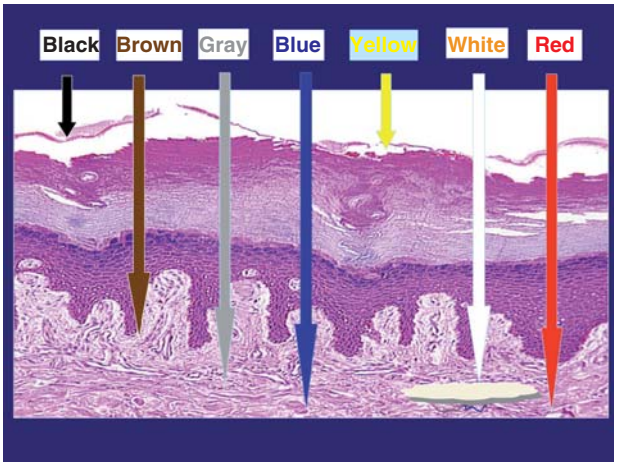


Figure 3.1 The quantity and location of melanin, blood vessels, vascular volume, keratinocytes, and collagen all contribute to the colors seen under dermoscopy. The stratum corneum, devoid of blood and melanin, appears yellow. In addition, areas with sebaceous differentiation can also manifest a yellow hue. Blood vessels and vascular volume are responsible for the red and pink hues. White color is due to depigmentation, fibrosis, alterations in the collagen matrix, or due to keratin within cysts. Melanin appears black when located in the stratum corneum, brown when located at the dermoepidermal junction, gray when located in the papillary dermis, and blue when located in the deeper dermis. Melanin, when present in multiple layers of the skin can also appear black. In addition, a jet black color is usually due to congealed blood and orange hues are due to serum present in erosions or superficial ulcerations.

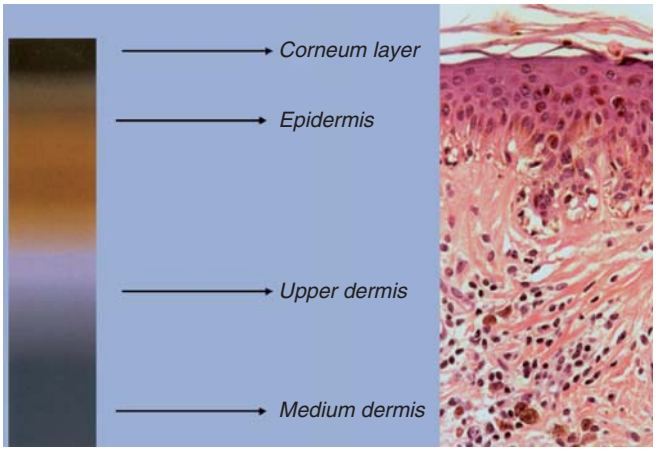


Figure 3.2 Colors in dermoscopy depending on the location of melanin in the skin.

Table 3.1 Dermoscopic Structures and their Histopathologic Correlates

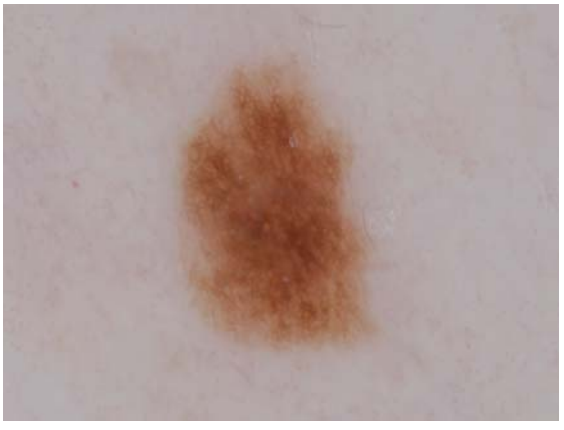
Dermoscopic structures	Definition	Histopathologic correlation	Significance
Pigment network (reticulation)	Grid-like or honeycomb pattern consisting of intersecting pigmented "lines" and hypopigmented "holes"	Melanin in keratinocytes and/or melanocytes along the epidermal rete ridges	The presence of a network, with few exceptions (e.g., dermatofibroma, lentigo, accessory nipple), indicates that the lesion is of melanocytic origin. The typical network is associated with nevi and an atypical network is associated with melanoma and dysplastic nevi
Pseudonetwork	In facial lesions, diffuse pigmentation is interrupted by nonpigmented adnexal openings, giving the appearance of a network	Pigment in the epidermis or dermis interrupted by follicular and adnexal openings on the face	This pattern can be seen in melanocytic and nonmelanocytic pigmented lesions of the face
Structureless areas	Areas devoid of dermoscopic structures including regression structures. These areas are usually hypopigmented compared with the surrounding lesion, but not in comparison to the surrounding normal skin. (N.B.: If the area is uniformly dark, it is referred to as a "blotch" – see below)	Flattening of the rete ridge pattern and/or decrease in concentration of eumelanin with/without the presence of pagetoid cells. It may also simply be due to a loss of contrast between the holes and lines of the network	In nevi it is found within the nevus. In melanoma it tends to be found at the periphery of the lesion
Blotches	Dark brown to black, usually homogenous areas of pigment that obscures the ability to visualize underlying structures	Aggregates of melanin in the stratum corneum, epidermis, and upper dermis	In nevi the blotch is homogenous and located toward the center of the lesion. In melanoma the blotches tend to be heterogenous, displaying multiple hues, and located off center
Dots	Small, round structures <0.1 mm in diameter that may be black, brown, gray, or bluish	Aggregates of melanocytes or melanin granules. Black dots represent pigment in the upper epidermis or stratum corneum. Brown dots represent pigment at the dermoepidermal junction or in the spinous layer. Gray-blue dots represent pigment in the papillary dermis (see below – peppering)	Dots in nevi tend to be located toward the center of the lesion and/or overlie the network lines. In melanoma the dots are not associated with the network and/or are located toward the periphery of the lesion
Peppering or granularity or blue-white veil over flat (macular) areas	Tiny, blue-gray granules	Melanin deposited as intracellular (mostly within melanophages) or extracellular particles in the upper dermis	This is a sign of regression and can be seen in melanocytic and nonmelanocytic lesions, such as lichen planus-like keratosis. In nevi the area of regression usually encompasses <10% of the surface area of the lesion. In melanoma, it tends to encompass >50% of the surface area
Globules	Round to oval structures that may be brown, black, blue-gray, or red with diameters >0.1 mm	Nests of melanocytes in the dermis	The presence of aggregated globules (i.e., 3 or more) indicates that the lesion is of melanocytic origin. In nevi the globules tend to be of similar size, shape, and color, distributed in a symmetric manner. In melanoma, the globules are of different shape, size, and color, distributed in a random manner
Streaks (pseudopods, radial streaming)	Radially arranged, linear projections of dark pigment (brown to black) at the periphery of the lesion that eminate from the tumor and radiate towards normal skin	Confluent junctional nests of melanocytes	The presence of a peripheral streaks indicates that the lesion is of melanocytic origin. In Spitz nevi, streaks are arranged circumferentially around the entire perimeter of the lesion. In melanoma, the streaks are located focally at the perimeter

(*Continued*)

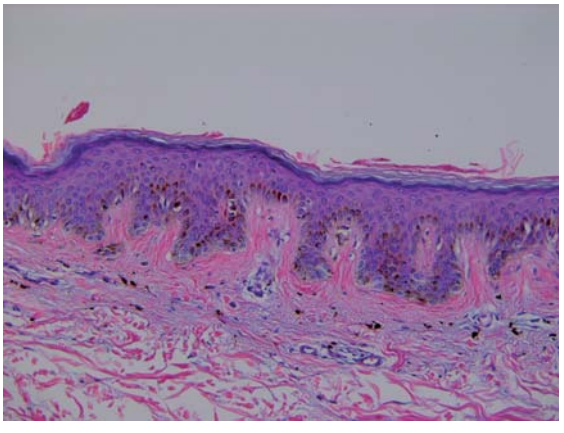
Table 3.1 (Continued) Dermoscopic Structures and their Histopathologic Correlates

Dermoscopic structures	Definition	Histopathologic correlation	Significance
Negative pigment network	Serpiginous interconnecting hypopigmented lines that surround irregularly shaped brown structures that resemble elongated and curvilinear globular structures	Speculation is that it corresponds with thin elongated rete ridges that are accompanied by large melanocytic nests within widened papillary dermis. However, it may also be due to bridging of rete ridges or due to abnormally shaped melanocytic nests	The presence of a negative network is another indication that the lesion is of melanocytic origin. Although it may be seen in congenital nevi, it is most often associated with Spitz nevi and melanoma
Chrysalis/crystalline	Consist of white shiny linear streaks that are seen only with polarized dermoscopy. These white streaks are oriented parallel, and sometimes also orthogonal (perpendicular) to each other	Speculation is that they correlate histopathologically with increased or altered collagen in the superficial dermis (fibrosis)	Chrysalis structures can be seen in scars, dermatofibromas, basal cell carcinomas, and lichen-planus like keratosis. When seen in a melanocytic lesion the differential diagnosis is usually between melanomas and Spitz nevi
Regression structures (also termed blue-white veil over flat/macular areas)	White, scar-like depigmentation (lighter than the surrounding skin, and appears shiny white under polarized dermoscopy) often combined with or adjacent to blue-gray areas or peppering	Scar-like changes: thickened fibrotic papillary dermis, sparse lymphocytic infiltrates, and variable numbers of melanophages	The presence of regression structures should alert the observer to the possibility that the lesion is a melanoma. Other lesions that reveal regression structures include lichen-planus like keratosis and, less commonly, nevi
Blue-white veil over palpable/raised areas	Irregular, confluent blue pigmentation with an overlying white "ground glass" haze	Aggregation of heavily pigmented melanocytes and/or melanophages in the dermis in combination with compact orthokeratosis of the stratum corneum and acanthosis (thickened epidermis)	In melanoma the blue-white veil is heterogeneous, prominent, and asymmetrically placed. In nevi it tends to be homogenous with a light hue, located toward the center of the lesion. It is found focally within melanoma and nevi. However, in blue nevi it encompasses the entire surface of the lesion and has a steel blue homogenous hue. This structure can also be seen in seborrheic keratoses and pigmented basal cell carcinomas.
Vascular structures	Pink hue (milky red areas) and isolated blood vessels with varying morphologies	Dilated blood vessels in the papillary dermis or an increase in the number of blood vessels	May be due to an increased vascular volume (vascular blush) or neoangiogenesis
Milia-like cysts	Round whitish or yellowish structures that shine brightly (like "stars in the sky") under nonpolarized dermoscopy	Intraepidermal keratin cysts	Usually associated with seborrheic keratosis but can, on occasion, be seen in melanoma and congenital nevi
Comedo-like openings	"Blackhead"-like plugs on the surface of the lesion	Concave clefts in the surface of the epidermis, often filled with keratin	Usually associated with seborrheic keratosis but can be seen in nevi that have a mamillated surface
Ridges and fissures	Cerebriform surface resulting in gyri (ridges) and sulci (fissures)	Wedge-shaped clefts of the surface of the epidermis often filled with keratin	This feature is associated with seborrheic keratosis
Fingerprint-like structures	Thin light brown lines that do not interconnect to form a meshwork pattern	Probably represent thin, elongated epidermal ridges	Feature of lentigo or early seborrheic keratosis
Moth-eaten border	Concave invaginations of the lesion border	Not available	Feature associated with a solar lentigo
Leaf-like areas	Brown to gray-blue discrete bulbous structures that often create shapes that resembles a leaf	Large, complex nodules of pigmented basal cell carcinoma in the upper dermis. These nodules are often closely associated with the undersurface of the epidermis.	Highly specific for basal cell carcinoma
Spoke-wheel-like structures	Well-circumscribed brown to gray-blue-brown radial projections meeting at a darker brown central hub	Pigmented aggregates of basal cell carcinoma that emanate from the undersurface of the epidermis with multiple projects into the dermis	Highly specific for basal cell carcinoma
Large blue-gray ovoid nests	Large, well-circumscribed areas, larger than globules	Large nests of basal cell tumor in the dermis	In the absence of a network these structures are highly specific for basal cell carcinoma
Multiple blue-gray non-aggregated globules	Round well-circumscribed structures that resemble small ovoid nests	Small nests of basal cell tumor in the dermis	In the absence of a pigment network it suggests the diagnosis of basal-cell carcinoma
Lacunae	Red, maroon, or black lagoons	Dilated vascular spaces	Seen in angiomas and angiokeratomas

▲ **Figure 3.3a** Clinical image of a junctional nevus.



◀ **Figure 3.3b** Dermoscopy shows a regular homogenous honeycomb-like pigment network thinning out at the periphery.



◀ **Figure 3.3c** Histology shows the rete ridge pattern. There is more pigment per unit area overlying the rete ridge and this results in the dermoscopic observation of network lines. There is less pigment per unit area overlying the supra-papillary plate and this corresponds to the dermoscopic holes in the network (Fig. 3.4).

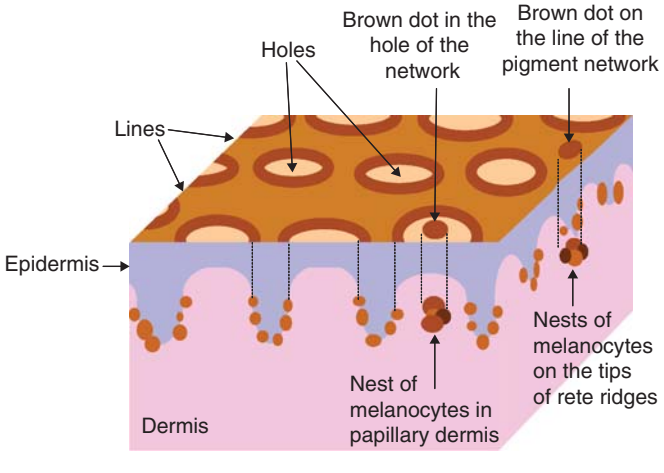


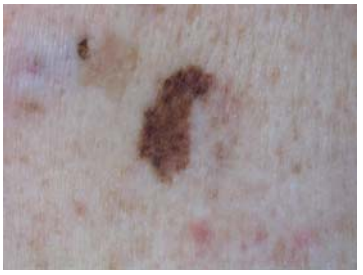
Figure 3.4 Schematic representation of the normal pigment network. The lines of the network reflect melanin along the rete ridges, and the holes correspond to the tips of dermal papillae and the overlying suprapapillary plate. The width of the network lines reflects the width of the rete ridges (Pehamberger et al., 1993; Pehamberger et al., 1987; Steiner et al., 1987). Brown dots on the network correspond to melanocytic nest at the tip of rete ridges. Brown dots in the hole of the network correspond to small nevomelanocytic nests situated in the papillary dermis. (Menzies, 2009; Menzies et al., 1996b; Menzies et al., 1996a).

The pigment network in melanocytic lesions is further characterized as typical or atypical (Argenziano et al., 1998):

(a) The typical network is regularly meshed and composed of lines that are relatively uniform in width and homogenous in color; the lines often become gradually thinner and fainter in pigmentation at the lesion's periphery (Fig. 3.3). On histopathology, the lines of the typical network correspond to pigment in rete ridges. That are relatively uniform in width and equidistant from each other (Fig. 3.3). The typical network usually corresponds to the junctional component of a nevus. However, reticulation can also be seen in darkly pigmented normal skin and heavily pigmented rete ridges as encountered in dermatofibromas (Zaballos et al., 2008; Puig et al., 2005; Arpaia et al., 2005).

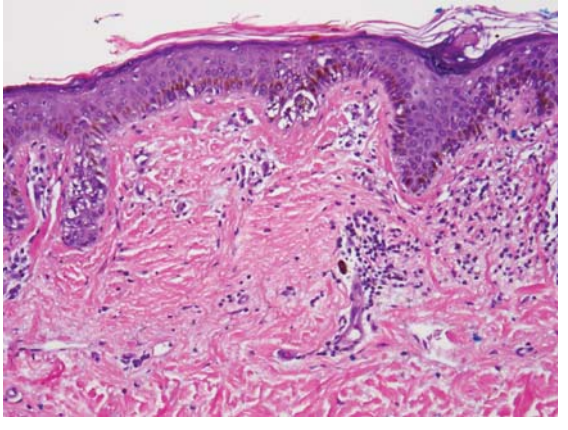
(b) The atypical network is irregularly meshed with lines that vary in width and degree of pigmentation and with "holes" that are heterogeneous in area and shape (Fig. 3.5A, B). An atypical network shows foci with broader and darker pigmented lines; the network often ends abruptly at the lesion's periphery. An atypical network within a lesion may also appear perturbed and broken up, a finding referred to as "branched streaks" (Fig. 3.6A, B). On histolopathology, the irregular lines of an atypical network correspond to variation in the width, length, and spacing of the rete ridges due to variation in the size, spacing, and tendency to confluence of nests of melanocytes (Fig. 3.5C). Rete ridges that are elongated and widened by larger junctional nests of melanocytes would appear as darker and wider lines on dermoscopy. The atypical network is often seen in melanoma and dysplastic nevi.

The anatomy of the rete ridge pattern on the palms, soles, and face differs from that of nonglabrous skin. Accordingly, the pigment network is usually absent in these locations and is replaced by a pseudonetwork pattern on the face (chap. 9c) (Schiffner et al., 2000) and a parallel pigment pattern on the palms and soles (chap. 9a) (Saida et al., 2004). If the rete ridges on nonglabrous skin are truncated and/or contain less melanin pigment, the pigment network may not be visible. Areas within a lesion that are devoid of any network or other structures, such as globules or regression structures, are called "structureless areas."



▲ **Figure 3.5a** Clinical image of an atypical melanocytic nevus.

◀ **Figure 3.5b** The dermoscopic appearance of this lesion reveals an atypical network.



◀ **Figure 3.5c** The atypical network corresponds histologically to melanin along rete ridges that vary in size, amount of melanin, and spacing. These architectural changes explain the atypical pigment network as seen in dermoscopy.

▲ **Figure 3.6a** Clinical image of an atypical mole.

◀ **Figure 3.6b** Dermoscopy showing an irregular network, which is irregularly meshed and fragmented creating branched streaks within the lesion. N.B., branched streaks differ from streaks. Branched streaks consist of broken-up network fragments within the lesion. Streaks consist of radial extensions or pseudopods at the periphery of the lesion that extend from the tumor towards normal skin. This lesion was biopsied and was a dysplastic nevus.

Structureless Areas

Structureless areas are defined as areas with a size that is at least 10% of the lesion's surface area and are devoid of any discernible structures, such as globules, network, or regression structures (i.e., scars, peppering, granularity, or blue-white veil over flat areas). They are hypopigmented compared with the rest of the lesion; however, they manifest the same or slightly more pigment compared with the surrounding normal skin (N.B.: structureless areas that are hyperpigmented are called blotches) (Stolz et al., 2002a; Stolz et al., 2002b). Focal structureless areas within a lesion are a common finding in nevi (Fig. 3.7). However, focal tan to light brown structureless areas at the periphery of a melanocytic lesion is commonly associated with melanoma (Annessi et al., 2007) (Fig. 3.8). Peripherally located structureless areas in melanoma tend to have a light brown to fawn color and tend to end abruptly at the edge of a lesion. Histologically, these areas are characterized by flattening of the DEJ (loss of the undulating pattern of rete ridges and dermal papillae) (Stolz et al., 2002a) and scattering of atypical melanocytes in suprabasal epidermal layers (i.e., pagetoid cells) (Fig. 3.8C).

Blotches

A blotch is defined as an area with a size that is at least 10% of the lesion's surface area and is heavily pigmented (Fig. 3.9) (Yadav et al., 1993; Soyer et al., 2000). In a blotch the melanin pigment is often present throughout the skin, including the stratum corneum, epidermis, and the dermis (Fig. 3.9C). The dark pigment in a blotch visually obscures the ability to discern any underlying structures.

Blotches can be regular or irregular (Argenziano et al., 1998). Regular blotches are defined as those that display symmetry, regular borders, homogenous dark hue, and are located within the center of the lesion (Fig. 3.9A). A pigment network often surrounds a regular blotch. Regular blotches are associated with nevi.

Irregular blotches are defined as those that are asymmetric, have irregular contours, are located off center, and/or display multiple dark hues (i.e., heterogenous dark hues). Irregular blotches are associated with melanoma.

Occasionally, a blotch-like structure can be seen in "activated" nevi. This structure is due to heavy concentrations of melanin in the stratum corneum; called a black lamella or pseudoblotch. Because the pigment is present in the stratum corneum, it can easily be stripped off using a tape-stripping procedure, thereby revealing underlying structures (Guillod et al., 1997) (Fig. 3.10).

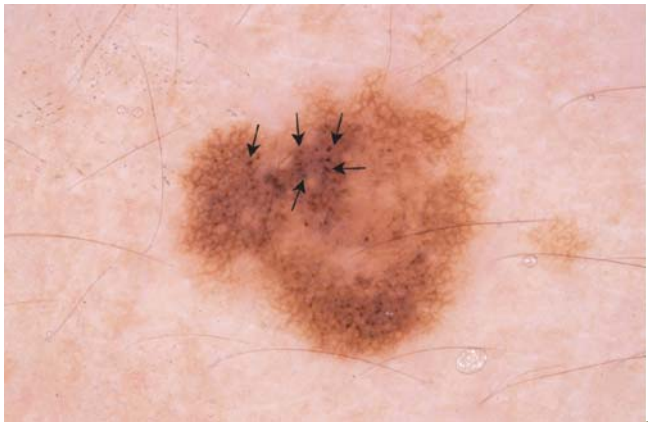
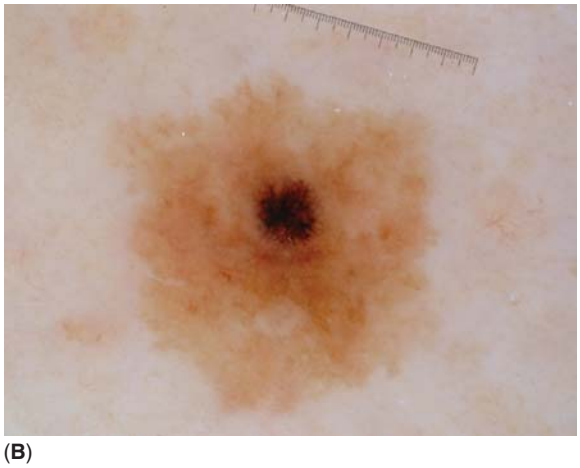


Figure 3.7 Dermoscopy image of a compound nevus with a regular pigment network in the periphery and a central structureless area and some black dots in the upper part of the lesion (*arrows*).

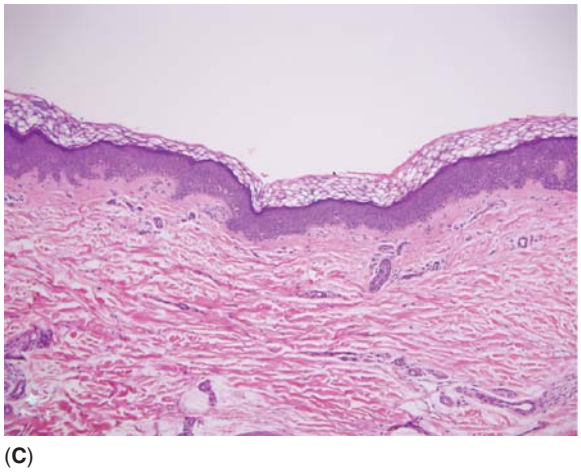
Dots

Dots are small, round structures of less than 0.1 mm in diameter that have a red color when corresponding to blood vessels (chap. 10) (Soyer et al., 2000; Yadav et al., 1993); however, when due to melanin, their color ranges from black, brown, to blue-gray depending on the depth and concentration of the melanin in the skin (Tyndall effect) (Menzies, 2009). Black dots are often due to melanin pigment accumulation in the stratum corneum (Fig. 3.11), but can also be due to vertical stacking of pigment within the

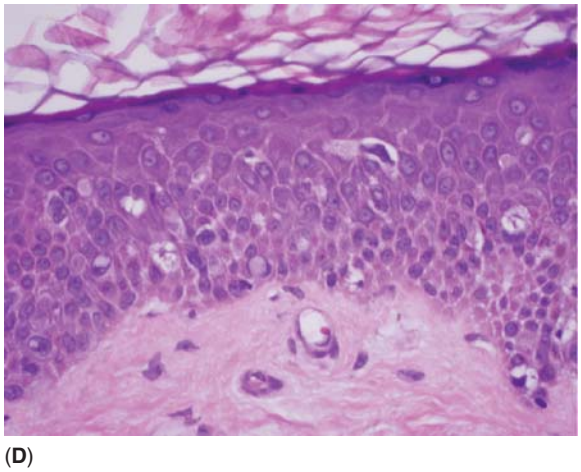
Figure 3.8a Clinical image of a thin melanoma.



(**B**)



(**C**)

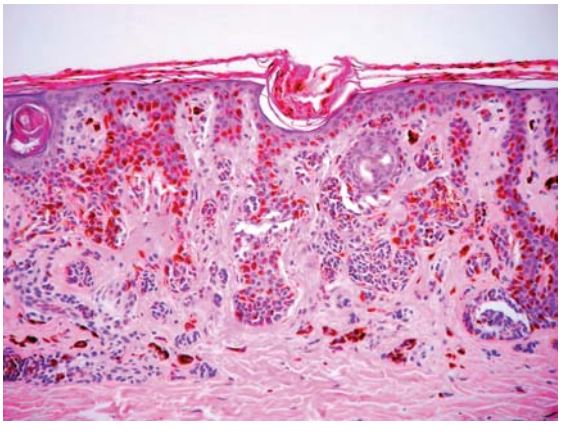


(**D**)

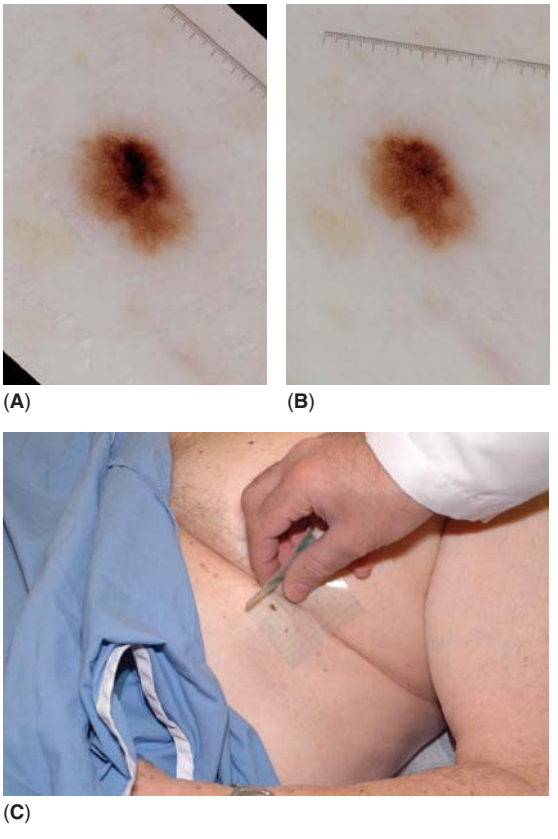
Figure 3.8 (**B**) With dermoscopy one can appreciate the presence of light brown structureless areas. The presence of tan structureless areas at the periphery of a melanocytic lesion is associated with an increased odds ratio for melanoma. (**C** and **D**) Histology image corresponding to the peripheral structureless area showing flattening of the rete ridges with pagetoid spread of melanocytes in the suprabasal epidermis (**C**, 10× original magnification, hematoxylin and eosin stain; **D**, 40× magnification).

▲ **Figure 3.9a** Clinical image of a lesion.

◀ **Figure 3.9b** Dermoscopy shows a dark central hyper-pigmentation area (blotch) that is obscuring the ability to visualize any underlying structures.



◀ **Figure 3.9c** Histology image showing melanin pigment in the stratum corneum, epidermis, and dermis.



(**A**) (**B**)

(**C**)

Figure 3.10 (**A**) This melanocytic lesion appears to have an off center located blotch, making it suspicious for melanoma. (**C**) However, simple tape-stripping procedure discloses that the presumed blotch is actually a black lamella. After removal of the black lamella the underlying typical network becomes apparent (**B**); thus obviating the need for a biopsy of this benign reticulated nevus). The black lamella will usually reappear 3–12 months after the tape-stripping procedure.

epidermis or due to heavy aggregates of melanin in small clusters of melanocytes or keratinocytes located in the upper layers of the epidermis (just below the stratum corneum). Black dots that are located in the stratum corneum are usually found overlying the gridlines of the network and they can easily be tape stripped off the skin (Fig. 3.12) (Guillod et al., 1997). Brown dots are often associated with focal melanin accumulations at the DEJ or spinous layer and they usually correspond histologically to small junctional melanocytic nests (Fig. 3.13). The dots, resulting from nevus nests located at the tips of rete ridges, tend to be situated overlying the network lines (Fig. 3.14) (Puppin et al., 1993). Less frequently, brown dots correspond to melanocytic nests located in the skin below the stratum corneum or even within the stratum corneum (Fig. 3.13). The nests present within the stratum corneum are probably in the process of being extruded from the skin via transelimination (Fig. 3.13C). Brown dots corresponding to small melanocytic nests situated in the papillary dermis appear as dots situated within the holes of the network (Fig. 3.15). These so-called target network with dots/globules or halo dots/globules are a common finding in congenital melanocytic nevi (Fig. 3.15). Although on rare occasions brown dots can be tape stripped off the skin, most brown dots cannot be removed via tapestripping (Guillod et al., 1997; Krischer et al., 1997).

Black or brown dots may appear after acute ultraviolet exposure; however, these dots tend to disappear over time (Dobrosavljevic et al., 2009; Tronnier et al., 2000; Hofmann-Wellenhof et al., 1998; Hofmann-Wellenhof et al., 1997). It is interesting to note that many non–ultraviolet-induced dots that are successfully tape stripped off the skin reappear with time.

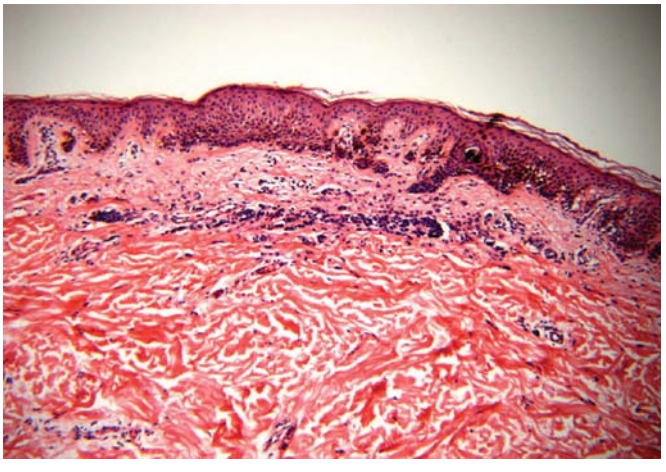
Gray-blue dots (also called granules or peppering) are due to fine melanin particles within melanophages or as extracellular "dust" in the superficial dermis (Braun et al., 2007); a feature associated with regression (Fig. 3.16).

Globules

Globules are symmetrical, round to oval, well-demarcated structures with a diameter that is larger than 0.1 mm (Fig. 3.17A, B). They usually correspond to nests of pigmented benign or malignant melanocytes situated in

▲ **Figure 3.11a** Clinical image of junctional nevus.

◀ **Figure 3.11b** Dermoscopy of this junctional nevus reveals multiple black dots overlying the pigment network.



◀ **Figure 3.11c** Histology shows accumulations of melanin pigment within the stratum corneum.

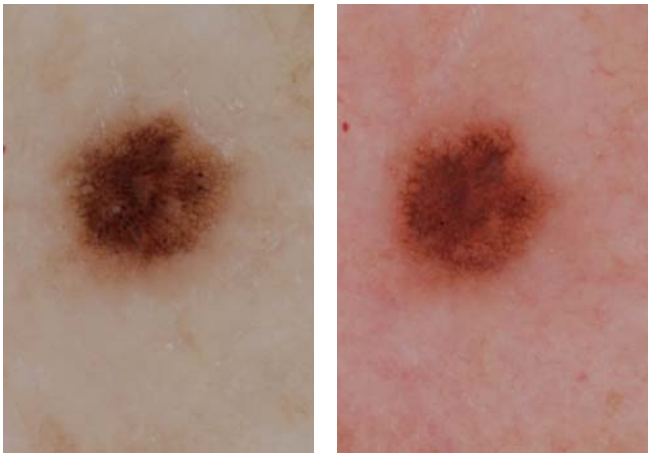


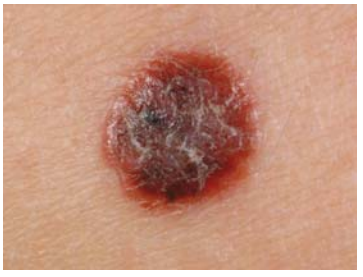
Figure 3.12 Nevus with multiple black dots (*left*). Same lesion after tape stripping shows that the majority of the dots have been removed and are no longer visible after tape-stripping (*right*).

the lower epidermis, at the DEJ, or in the papillary dermis (Fig. 3.17C, D). On occasion globules may correspond to large clumps of melanin, melanophages, or pigmented milia cysts. Similar to dots, the color of globules may be brown, black, blue-gray, or red. The significance of these colors is the same as was discussed for dots above.

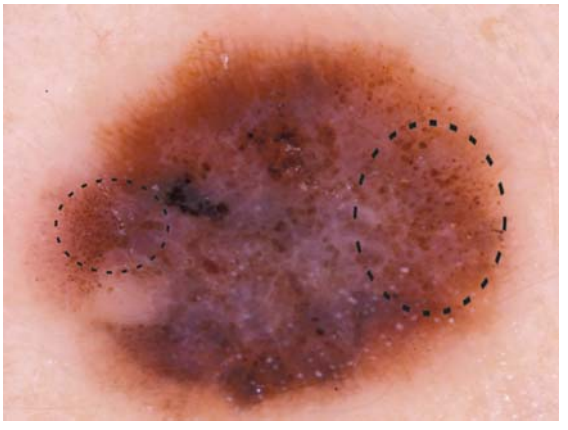
Both dots and globules may occur in nevi as well as in melanoma. In nevi, the globules are uniform in size, shape, and color (mostly brown), and evenly distributed in the lesion, being mostly present at its center surrounded by a network, or circumferentially along the entire perimeter of the nevus, or uniformly distributed throughout the nevus (Fig. 3.18). Dots in nevi are usually brown in color and overlie the pigment network lines. In contrast, in melanomas, globules and dots vary in size, shape, and color, are unevenly distributed in the lesion, and are frequently found focally at the periphery of lesions (Fig. 3.13). Because both dots and globules frequently correlate with nests of melanocytes, they are often described for simplicity and reproducibility as a combined term "dot's and globules" (Fig. 3.13).

Streaks

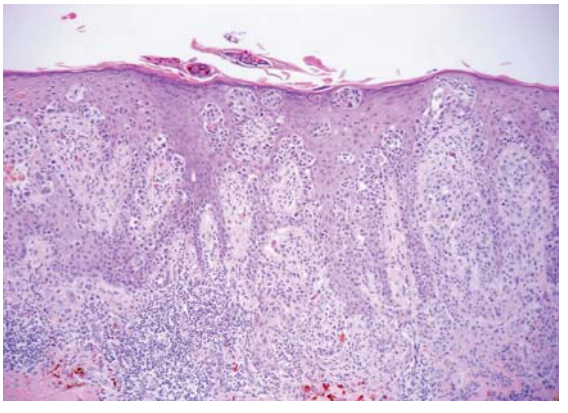
Streaks are linear pigmented projections seen at the periphery of lesions. Both pseudopods (streaks with bulbous projections at their tips) (Fig. 3.19) and radial streaming (streaks without bulbous projections at their tips) (Fig. 3.20) are considered to be streaks (Soyer et al., 2001; Ferrara et al., 2002; Argenziano et al., 1998; Argenziano et al., 2003). Streaks in melanoma are usually observed only focally and asymmetrically at the lesion's periphery and reflect the radial growth phase of the tumor. On the other hand, streaks that are distributed symmetrically around the entire perimeter of the lesion are seen mostly in pigmented spindle cell nevi (Spitz or Reed) (Argenziano et al., 2001; Peris et al., 2002; Ferrara et al., 2005; Marchell et al., 2005). Histologically, streaks represent confluent junctional nests of melanocytes (Figs. 3.20 and 3.21).



▲ **Figure 3.13a** Clinical image of a superficially spreading melanoma (Breslow 1.1 mm Clark III).



◀ **Figure 3.13b** Dermoscopy shows multiple dots and globules (area enclosed by dashed oval) varying in size and irregularly distributed throughout the lesion.



◀ **Figure 3.13c** Histology shows nested melanocytes in stratum corneum and in the epidermis, resulting in dots and globules as seen under dermoscopy.

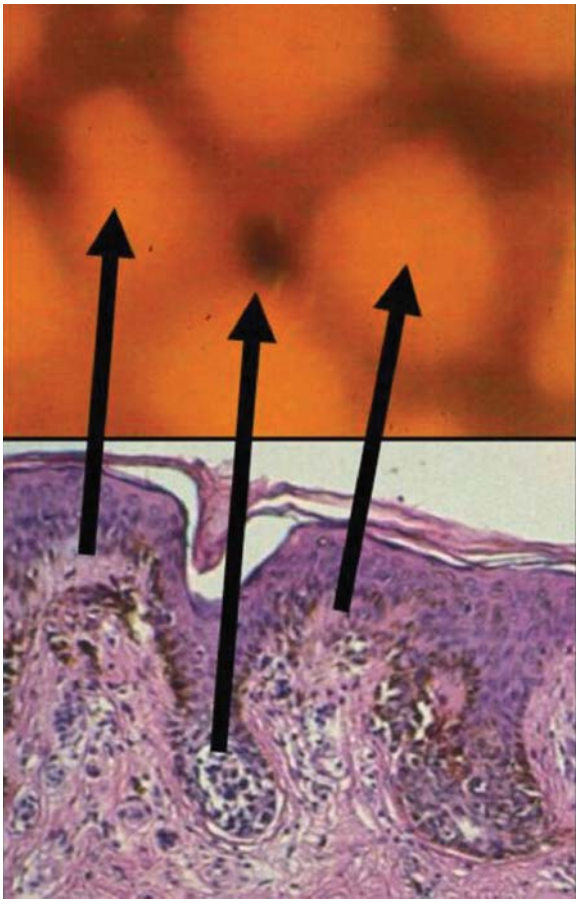


Figure 3.14 This shows the correlation between dermoscopy and histology: dots, resulting from nevus nests located at the tips of rete ridge, will appear to be situated overlying the network lines.

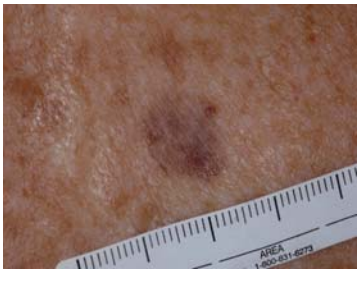
Pseudopods are finger-like projections of dark pigment (brown to black) at the periphery of the lesion. They have small knobs at their tips, and are connected to either a central pigment network or central pigmented blotch. To be considered pseudopods the bulbous knobs must have a maximum diameter that is larger than the network from which it originates (Fig. 3.22). Menzies and colleagues found pseudopods to be one of the most specific features of superficially spreading melanoma (Menzies et al., 1995; Menzies et al., 1996a; Menzies et al., 1996b). On histopathology, pseudopods correspond to junctional confluent nests of melanocytes at the periphery of the lesion (Fig. 3.23). Confluence of nests is also a criterion in histopathology, typical for dysplastic nevi or malignant melanoma. Fig. 3.22 depicts a schematic drawing of a pseudopod: depending on which area of the pseudopod is sectioned on histology, the pathologist will see this structure either as a circular cluster of cells of varying diameters or as an oval-shaped cluster of cells. Only if the pathology section passes exactly through the longitudinal axis of a pseudopod will the pathologist be able to recognize this structure as an elongated tubular cluster of cells. Needless to say, the statistical probability of this happening is very low unless of course the pathologist uses dermoscopy at the grossing table to orient and oversee the step sectioning process (Scope et al., 2007).

On occasion, peripheral globules and pseudopods can look similar to each other at first glance. However, with peripheral globules one will observe a small clear space separating the globule from the main tumor mass (Fig. 3.24) (Menzies et al., 1995; Menzies et al., 1996b). These peripheral globules are presumed to correspond to junctional melanocytic nests at the tips of rete ridges and they are usually associated with growing/enlarging nevi. In contrast, pseudopods emanate from, and are directly connected to, the main tumor mass through a stalk.

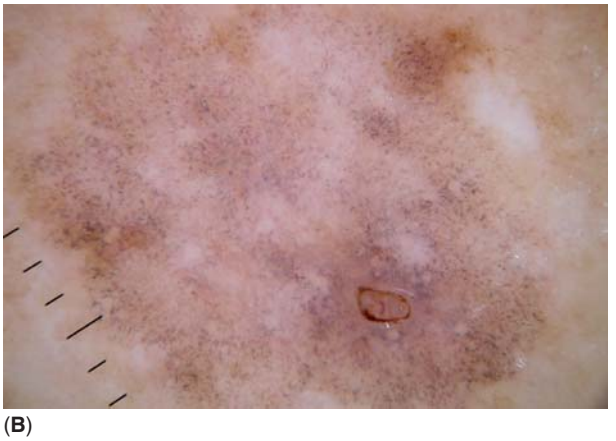
Radial streaming appears as radial parallel linear extensions at the periphery of the lesion (Fig. 3.20). On histopathology, radial streaming also correlates with confluent junctional nests of pigmented melanocytes.

▲ **Figure 3.15a** Clinical image of a small congenital melanocytic nevus.

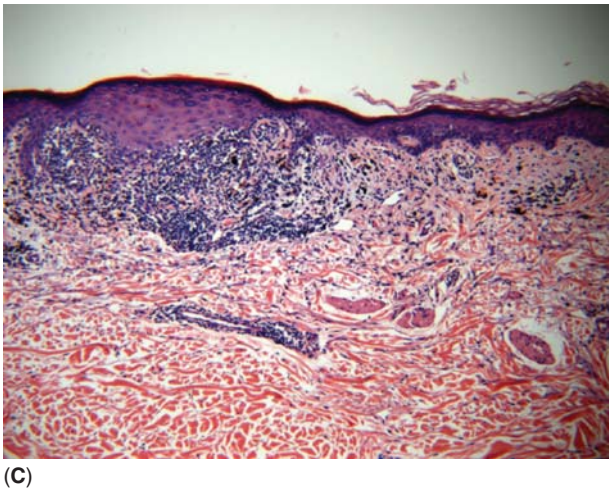
◀ **Figure 3.15b** Dermoscopy of this congenital nevus shows brown dots/globules in the center (hole) of the network. This target network is a common finding in nevi with congenital features.



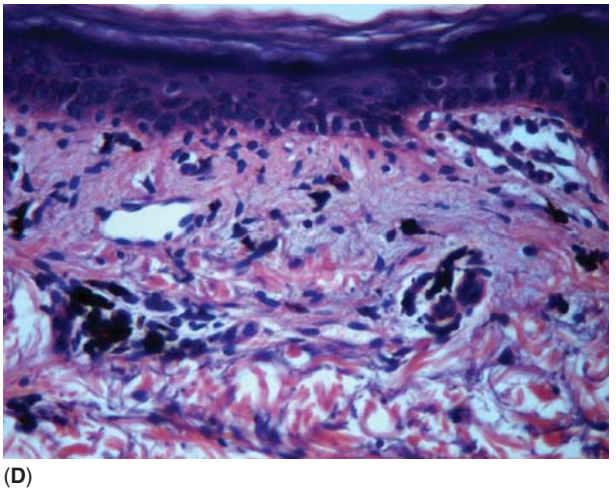
▲ **Figure 3.16a** Clinical image of lichen planus-like keratosis.



(**B**)



(**C**)



(**D**)

Figure 3.16 (**B**) Dermoscopy reveals multiple blue-gray dots and granules (also called "granularity") throughout the lesion. (**C&D**) On histopathology the granularity correlates with melanophages and free melanin in the dermis.

Negative Pigment Network

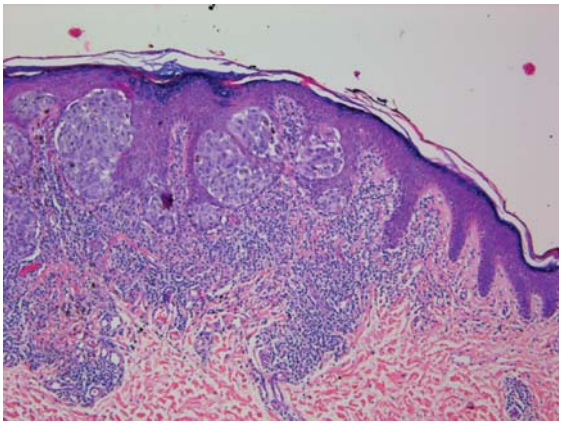
The "negative" of the pigmented network (also known as reverse or inverse network) consists of relatively lighter areas comprising the apparent grid of the network and relatively darker areas filling the apparent "holes" (Fig. 3.25). The lighter grid lines tend to be serpiginous and the darker areas, when viewed in isolation, resemble elongated tubular or curved globules (Fig. 3.26A, B). Histopathologically, the negative network appears to correspond to thin elongated rete ridges accompanied by large melanocytic nests within a widened papillary dermis (Fig. 3.26C) or to bridging of rete ridges (Fig. 3.27). Although the negative network is highly specific for melanoma (95% specific), it can also be found in some Spitz nevi and rarely in other nevi, such as congenital nevi. In congenital nevi, the negative pigmented network is usually diffuse and symmetrical in its distribution. In contrast, the negative pigmented network seen in melanoma is often focal and asymmetrically distributed.

Chrysalis/Crystalline

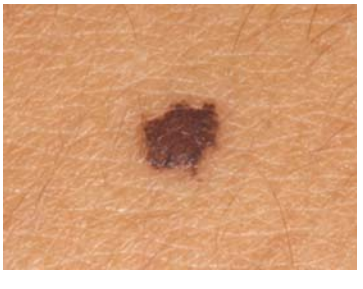
Chrysalis structures, also know as crystalline structures, are white shiny linear streaks that are seen under polarized dermoscopy, but not under nonpolarized dermoscopy (Fig. 3.28) (Marghoob et al., 2009). The white streaks are oriented parallel, and sometimes also orthogonal (perpendicular) to each other. Chrysalis structures can be seen in scars, dermatofibromas, basal cell carcinomas,

▲ **Figure 3.17a** Clinical image of a Spitz nevus.

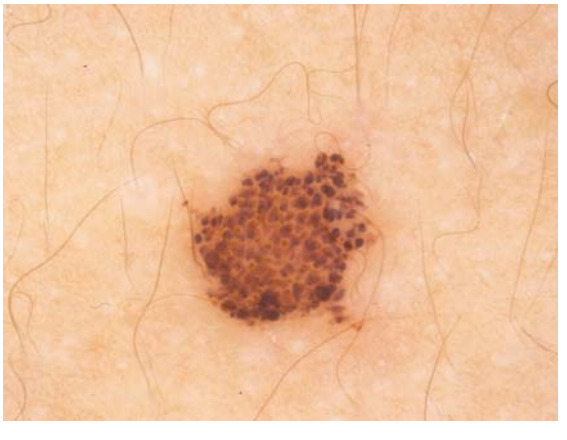
◀ **Figure 3.17b** Dermoscopy reveals a Spitz nevus with a globular pattern. The globules display different sizes, shapes and colors, including browns, black, and blue-gray.



◀ **Figure 3.17c** The globules correlate with nests of melanocytes in the dermis. The different colors of the globules is a function of the degree of melanization and depth within the dermis they are located (Tyndall effect).



▲ **Figure 3.18a** Clinical image of a small compound nevus.



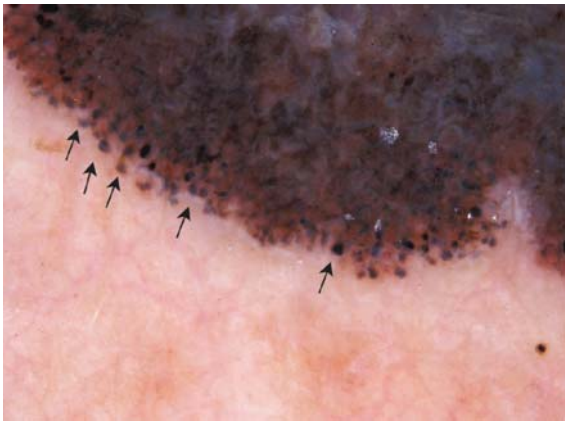
◀ **Figure 3.18b** Dermoscopy shows the lesion has a globular architecture. These globules correspond to nevomelanocytic nests in the dermis.

and also in melanomas and Spitz nevi (Marghoob et al., 2009; Balagula et al., 2011). These structures correlate histopathologically with altered collagen in the dermis (fibrosis) (Fig. 3.29). The birefringent properties of collagen bundles causes rapid randomization of polarized light and this is, why collagen appears bright white and more conspicuous under polarized dermoscopy.

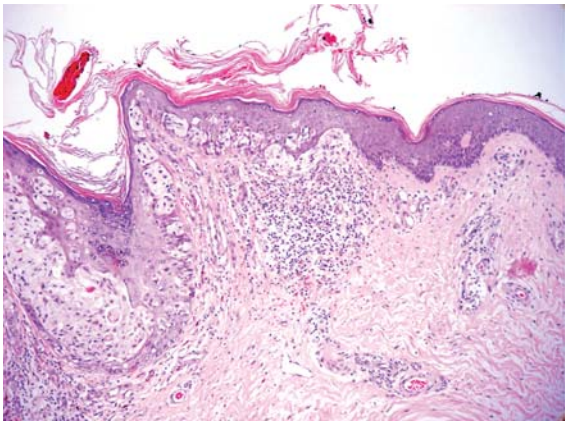
Regression Structures

Regression structures appear dermoscopically as white scar-like depigmentation (lighter than the surrounding skin) and/or "peppering" (speckled multiple blue-gray granules) (Braun et al., 2007). On histopathology fully evolved regression shows fibrosis and melanosis (infiltrate of melanophages) (Braun et al., 2007; Yadav et al., 1993; Massi et al., 2001; Soyer et al., 2000), and sparse lymphocytic infiltrates. The normal undulating DEJ pattern formed by rete ridges and dermal papillae is attenuated to completely flattened. Regression structures consisting of both scar like depigmentation and peppering (granularity) should raise suspicion for melanoma. Regression structures consisting of only peppering can be seen in melanoma, lichen planus like keratosis and nevi. In lichen planus like keratosis the

▲ **Figure 3.19a** Clinical image of a large superficial spreading melanoma 8 cm in diameter (Breslow 1.7 mm Clark III). The boxed-in area is highlighted in figure 3.19b.

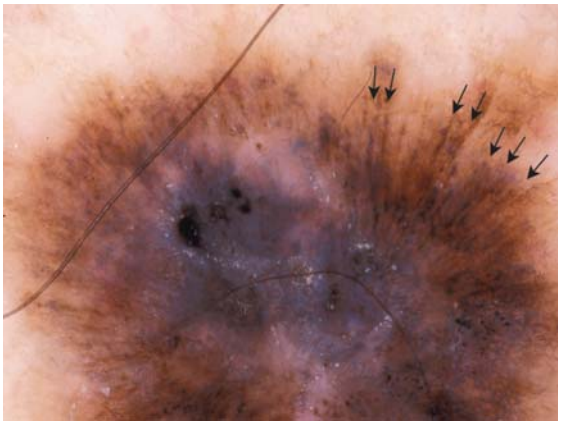


◀ **Figure 3.19b** Dermoscopy shows multiple pseudopods at the periphery



◀ **Figure 3.19c** The pseudopods correlate on histology to junctional confluent radial nests of melanocytes.

▲ **Figure 3.20a** Clinical image of a superficial spreading melanoma (Breslow 0.9 mm Clark III).



◀ **Figure 3.20b** Dermoscopy shows radial streaming (*arrows*) in the upper right portion of the lesion.

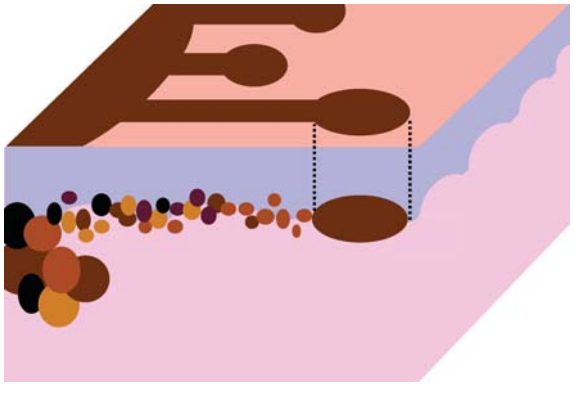
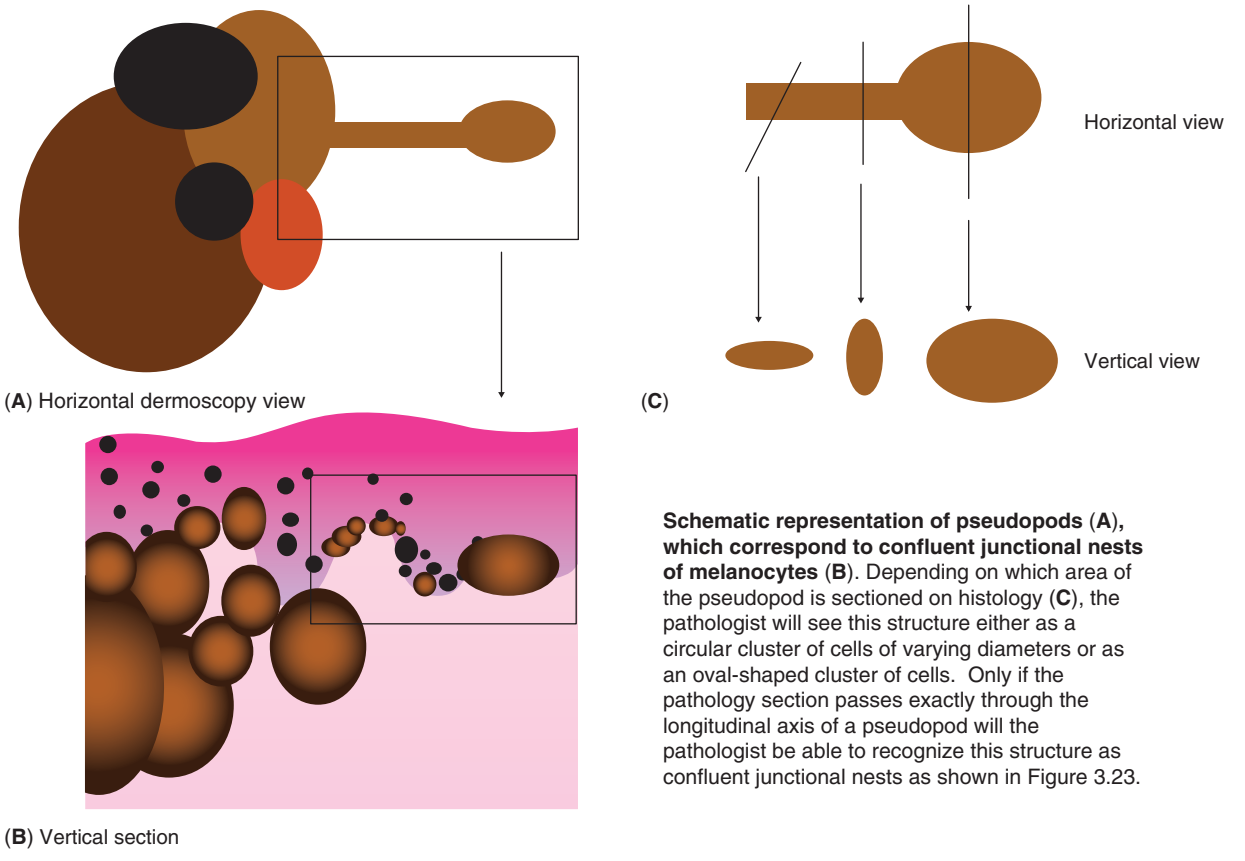


Figure 3.21 Schematic drawing of a pseudopod, showing horizontal confluent nests of melanocytes.

granularity tends to be coarse and diffusely distributed. In melanocytic lesions the granularity tends to be finer and focally distributed.

White scar-like depigmentation corresponds to a white discoloration of the lesion, which is lighter than the surrounding normal skin (Fig. 3.30). On histopathology, this dermoscopic structure correlates with fibrosis.

Granularity (also known as "peppering") is defined as accumulation of multiple very small (<0.1 mm), nondescript, blue-grey dots (Fig. 3.30A, B) (Braun et al., 2007; Zalaudek et al., 2004). If a large area shows dense, confluent granularity, it is difficult to distinguish from blue-white veil, however, clinically, granularity often is seen in macular portions of the lesion, while blue-white veil in palpable areas (Fig. 3.31). Histopathologically, granularity correlates with melanin in the superficial dermis, either as fine melanin particles in melanophages or extracellular "dust-like" particles (Fig. 3.30C). When granularity is encountered in nevi it tends to encompass less than 10% of the lesion's surface area. In contrast, in melanoma the granularity often encompasses more than 50% of the lesion's surface area.



Schematic representation of pseudopods (A), which correspond to confluent junctional nests of melanocytes (B). Depending on which area of the pseudopod is sectioned on histology (**C**), the pathologist will see this structure either as a circular cluster of cells of varying diameters or as an oval-shaped cluster of cells. Only if the pathology section passes exactly through the longitudinal axis of a pseudopod will the pathologist be able to recognize this structure as confluent junctional nests as shown in Figure 3.23.

Figure 3.22 Depending on how the histology vertical section passes through a pseudopod, the pathologist may see different sized and shaped nests at the peropheray instead of confluent junctional nests as seen in figure 3.23.

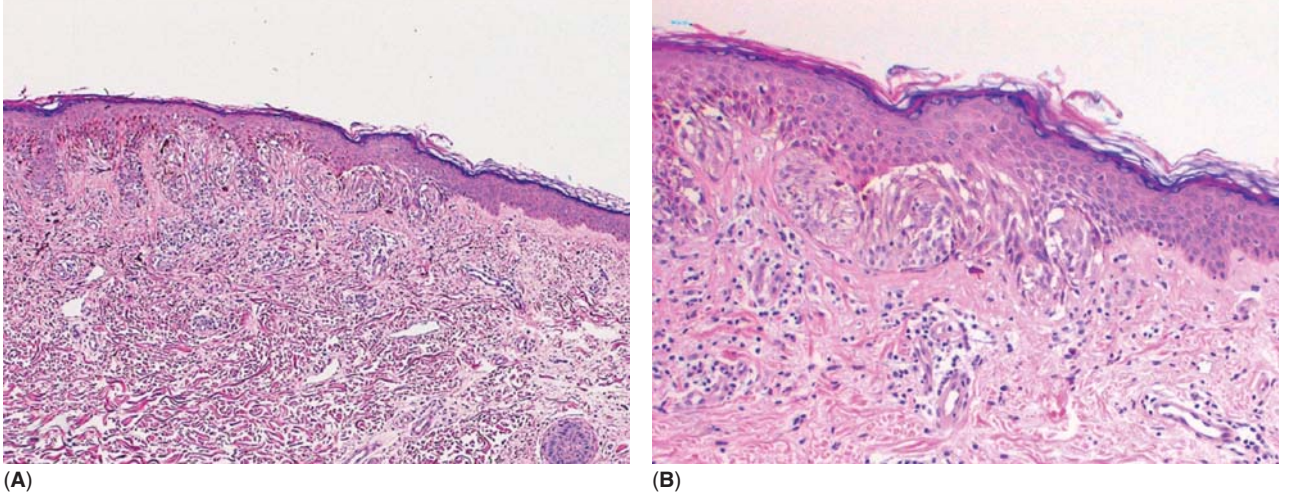


Figure 3.23 Histology of a pseudopod at different sections, showing confluent junctional nests of melanocytes.

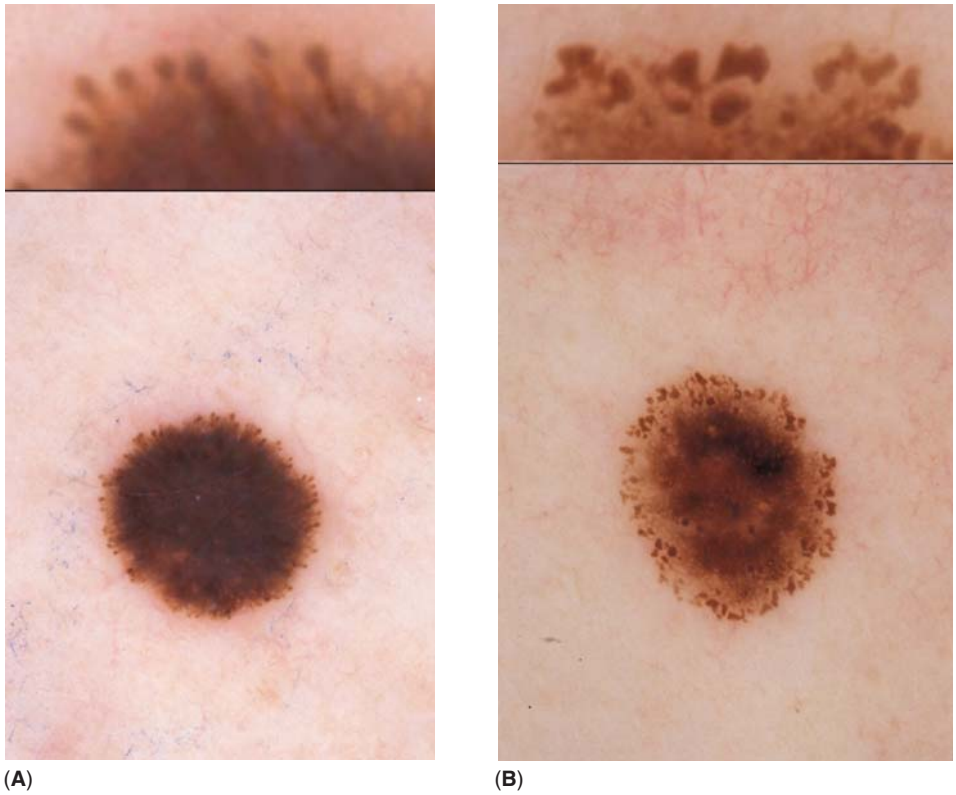
Blue-White Veil

Blue-white veil is confluent blue pigmentation with an overlying white "ground-glass" haze (Menzies et al., 2003). In melanoma, the blue-white veil does not occupy the entire surface area of the lesion, but rather is present as a focal, ill-defined area (Fig. 3.31A, B). Histopathologically, this dermoscopic structure corresponds to an aggregation of heavily pigmented cells (melanocytes and/or melanophages) or melanin in the dermis (blue color) in combination with compact orthokeratosis (Fig. 3.31C) (Yadav et al., 1993; Soyer et al., 2000).

At times, it is difficult to distinguish between regression structures (namely melanosis) and blue-white veil by dermoscopy because both structures display blue-white color. However, examining the lesion without dermoscopy can help differentiate between blue-white color due to regression versus due to deep melanocytes. In regression the surface contour will be flat (macular) and in blue-white veil the surface will be raised and palpable.

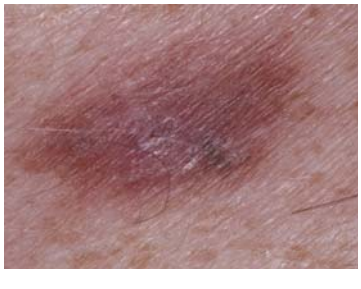
In melanoma the blue-white veil is nonuniform in color and is present focally within the lesion. In contrast, the blue-white veil has a uniform

Pseudopods

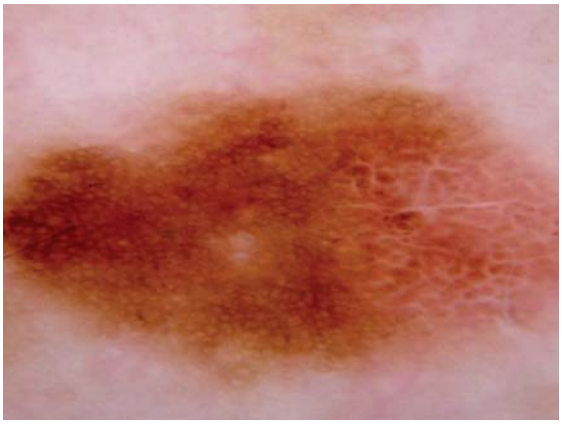


(**A**) (**B**)

Figure 3.24 (**A**) Reed nevus with a homogenous architecture in the center and pseudopods distributed symmetrically along its entire perimeter. Pseudopods (streaks) have a stalk that directly connects to the main tumor body. (**B**) Dysplastic nevus showing a peripheral rim of globules. The globules are not directly connected to the lesion; there is an intervening gap between the main tumor body and the peripheral globule.



▲ **Figure 3.25a** Clinical image of a melanoma



◀ **Figure 3.25b** Dermoscopy shows a pigmented lesion with a reticular architecture on the left side and a negative pigment network on the right side.

steel-blue color in blue nevi (Fig. 3.32) and it occupies the entire surface area of the lesion.

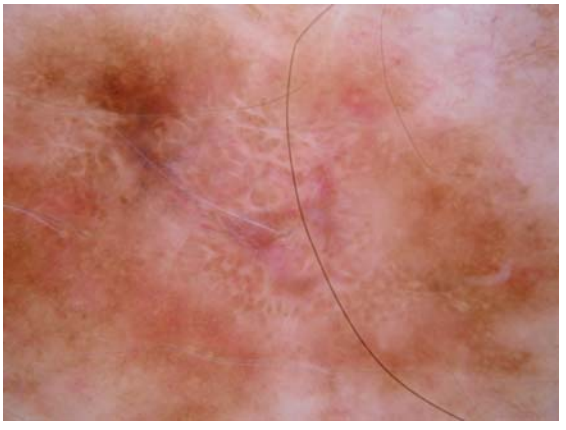
Vascular Structures

In recent years, more attention has been given to the vascular patterns of pigmented and nonpigmented lesions (Fig. 3.33) (Argenziano et al., 2004; Menzies et al., 2008). The increased availability of dermoscopes using polarized light allow for the inspection of a lesion without the need to contact the lesion. This prevents blood vessel compression, which in part helps in making the blood vessel morphology more conspicuous. A detailed description of blood vessel morphology can be found at chapter 12.

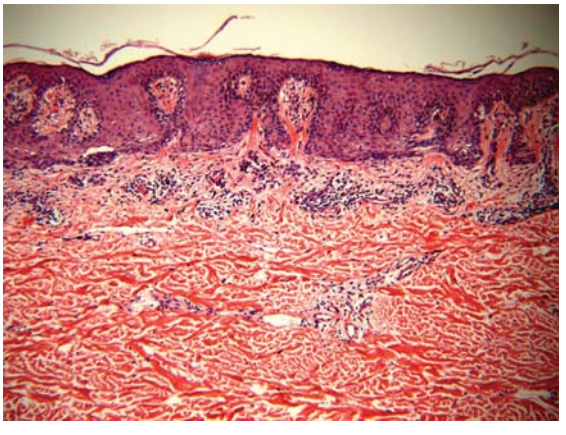
Milia-like Cysts

Milia-like cysts are round whitish or yellowish structures that are commonly, but not exclusively, seen in seborrheic keratosis (Fig. 3.34A, B) (Braun et al., 2002). They can also be seen in melanocytic nevi, especially those with a congenital pattern. Sometimes milia-like cysts are pigmented and resemble globules. Milia-like cysts correspond to intraepidermal keratin horn pseudocysts (Fig. 3.34C).

▲ **Figure 3.26a** Clinical image of a melanoma.



◀ **Figure 3.26b** Dermoscopy image of a melanoma with a negative pigment network.



◀ **Figure 3.26c** Histopathologically, the negative network appears to correspond to elongated rete ridges accompanied by large melanocytic nests within a widened papillary dermis or to bridging of adjacent rete ridges.

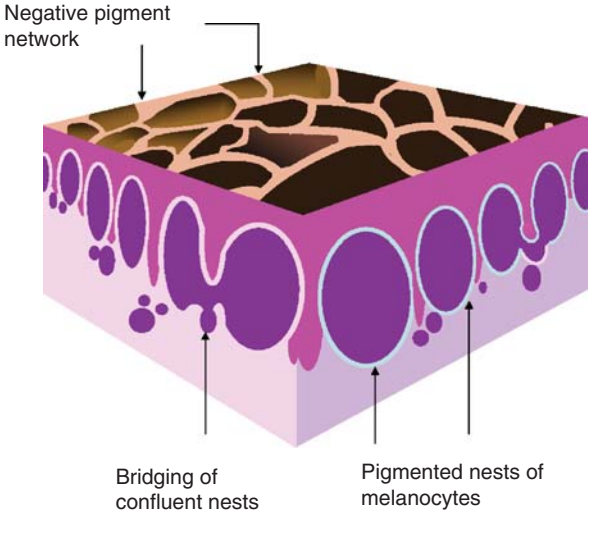


Figure 3.27 Schematic drawing of a negative pigment network.

Comedo-like Openings (Crypts, Pseudofollicular Openings)
Comedo-like openings are commonly seen in seborrheic keratosis and rarely in melanocytic nevi with a congenital pattern, such as papillomatous nevi (Braun et al., 2002). They appear on dermoscopy as dark roundish structures, and clinically, can be appreciated as surface invaginations. Histopathologically, comedo-like openings correspond to the concave, keratin-filled, invaginations of the epidermis (Fig. 3.34C).

Fissures and Ridges ("Brain-like or Cerebriform Appearance")
Fissures (invaginations or sulci) are commonly seen in seborrheic keratosis and may also be seen in melanocytic nevi with congenital pattern. In essence, fissures are linear grooves in the epidermis and, like comedo-like openings, correspond to surface invaginations. A pattern that resembles "brain-like appearance" or cerebriform appearance is created, with the grooves resembling "sulci" and the intervening ridges resembling surface "gyri" (Fig. 3.35). Fissures correspond histopathologically to wedge-shaped, keratin-filled invaginations of the epidermis (Braun et al., 2002).

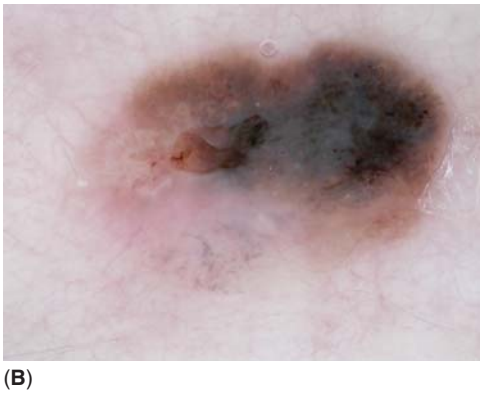
Fingerprint-like Structures
Some flat seborrheic keratoses (also known as solar lentigines) can show tiny ridges running in parallel and producing a pattern that is reminiscent of fingerprints (Fig. 3.36A, B) (Braun et al., 2002).

Moth-eaten Border
Some flat seborrheic keratoses have concave borders so that the pigment ends with curved to semi-circular indentations, which has been compared to a moth-eaten garment (Fig. 3.36A, B) (Menzies et al., 2003).

Leaf-like Areas
Leaf-like areas are seen as brown to gray-blue discrete bulbous blobs that often form a pattern shaped like a leaf (Fig. 3.37A, B) (Pehamberger et al., 1987; Menzies, 2002; Menzies et al., 2000). They can sometimes appear as tan, broad, and fuzzy streaks at the periphery of a lesion. In the absence of a pigment network, they are highly suggestive of pigmented basal cell carcinomas. Histopathologically, they represent dermal nodular aggregates of pigmented basal cell carcinoma (Fig. 3.37C).

Spoke-wheel-like Structures
Spoke-wheel-like structures are well-circumscribed brown to gray-blue–brown radial projections that radiate out from a dark brown central hub

▼ **Figure 3.28a** Clinical image of a melanoma.

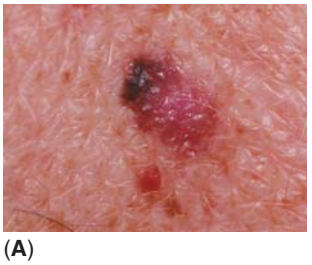


(**B**)

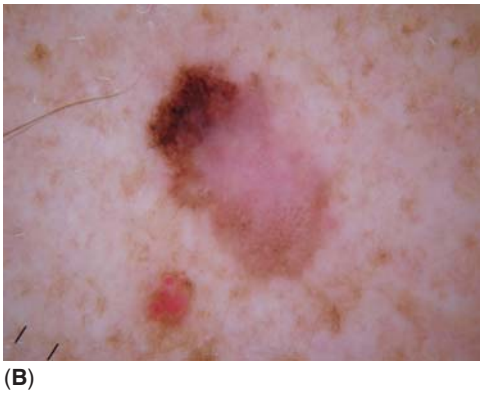
(**C**)

Figure 3.28 (**B**) nonpolarized dermoscopy image reveals a conspicuous blue-white veil. Notice that this blue-white veil becomes less obvious in polarized dermoscopy. (**C**) polarized light dermoscopy image showing multiple chrysalis/crystalline-like structures. Notice that the crystalline structure can only be seen in polarized dermoscopy. It is not visible with non-polarized dermoscopy.

▼ **Figure 3.29a** Clinical picture of a melanoma.

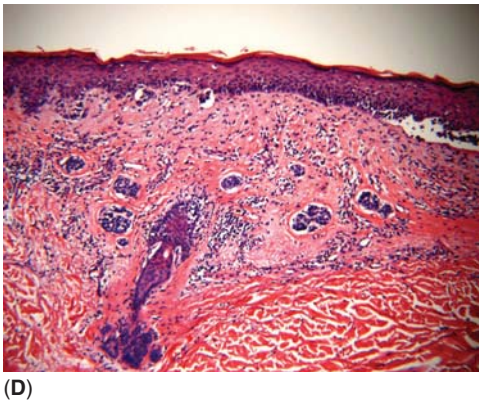


(**A**)



(**B**)

(**C**)



(**D**)

Figure 3.29 (**B**) nonpolarized dermoscopy; (**C**) polarized light dermoscopy. Chrysalis-like structures are only seen in polarized mode. (**D**) Histology shows stromal changes.

(Fig. 3.38A, B). Sometimes the radial projections are not visible and instead one sees a concentric globule consisting of a round structure with a central darker hub, which is surrounded by a brown halo of pigment (Menzies, 2002; Menzies et al., 2000). In the absence of a pigment network, spoke-wheels are highly suggestive of basal cell carcinoma. Histopathologically, they correspond to the nests of basal cell carcinoma emanating from the undersurface of the epidermis; a common finding is superficial basal cell carcinoma (Fig. 3.38C).

Large Blue-Gray Ovoid Nests

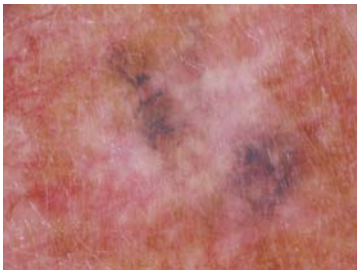
Ovoid nests are large, discrete, and well-circumscribed, pigmented ovoid areas, larger than globules (Fig. 3.39). When a network is absent, ovoid nests are highly suggestive of basal cell carcinoma. Ovoid nests correspond on histopathology to dermal aggregates of pigmented basal cell carcinoma (Menzies, 2002; Menzies et al., 2000).

Multiple Blue-Gray Non-aggregated Dots and Globules

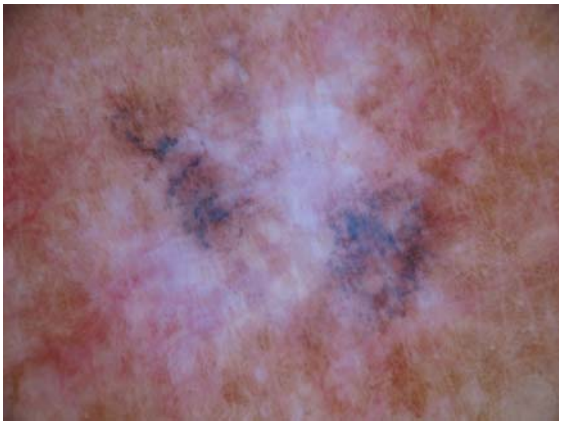
Multiple blue-gray dots and globules are round, discrete, and well-circumscribed structures that, in the absence of a pigment network, are highly suggestive of a basal cell carcinoma (Fig. 3.40). These dots and globules usually do not form aggregates as seen in melanocytic lesions. They correlate with dermal aggregates of pigmented basal cell carcinoma and are similar to ovoid nests, but smaller (Menzies et al., 2000; Menzies, 2002).

Lacunae

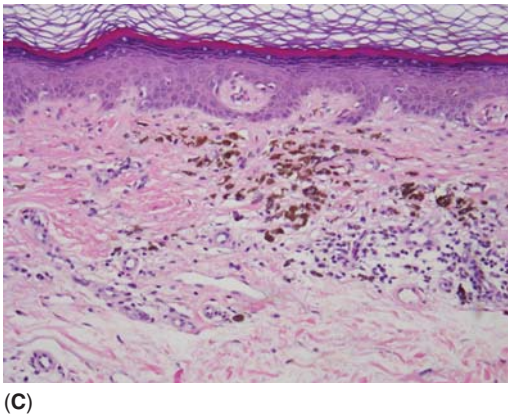
Lacunae are defined as multiple, clustered, well-demarcated, red to maroon to blue blobs with a round to oval shape (Fig. 3.41). If the lacunae are blue-black in color, then the lesion may be an angiokeratoma (Fig. 3.42) (Zaballos et al., 2007; Wolf, 2002). The lacunae correspond to cavernous dilated blood vessels (Fig. 3.42C).



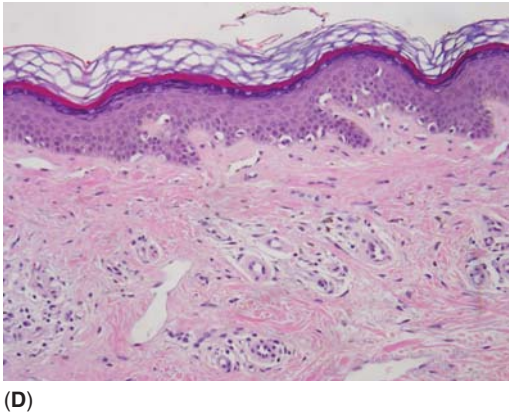
▲ **Figure 3.30a** Clinical image of a melanoma showing white scar-like depigmentation, which is lighter than the surrounding skin.



◀ **Figure 3.30b** Dermoscopy image reveals regression structures consisting of both scar like depigmentation and peppering (granularity).

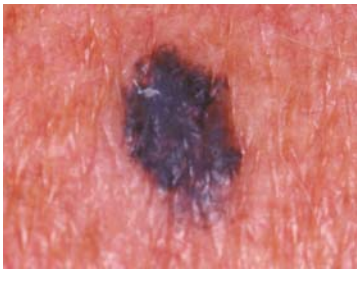


(**C**)

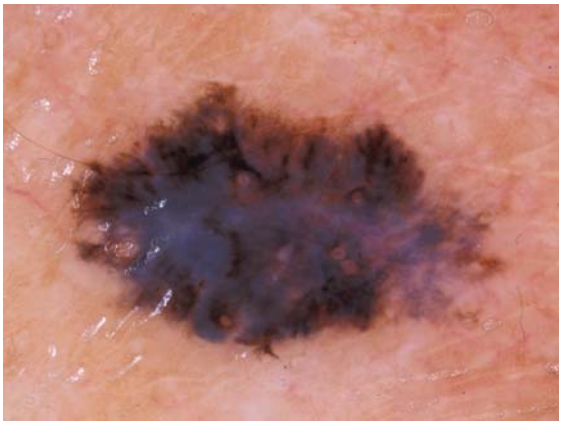


(**D**)

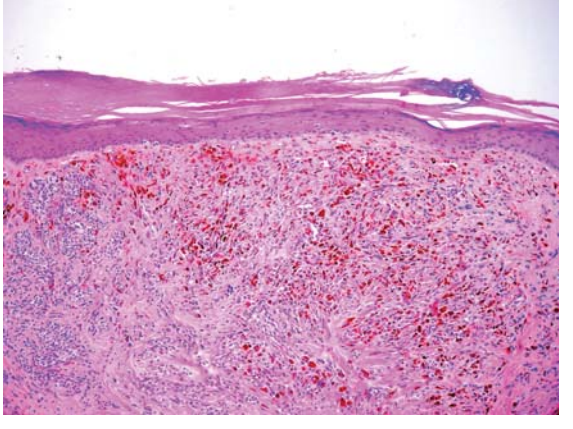
◀ **Figure 3.30** The histology (**C**) and (**D**) show fibrosis and melanosis.



▲ **Figure 3.31a** Clinical image of a superficial spreading melanoma (Breslow 0.3 mm Clark III).



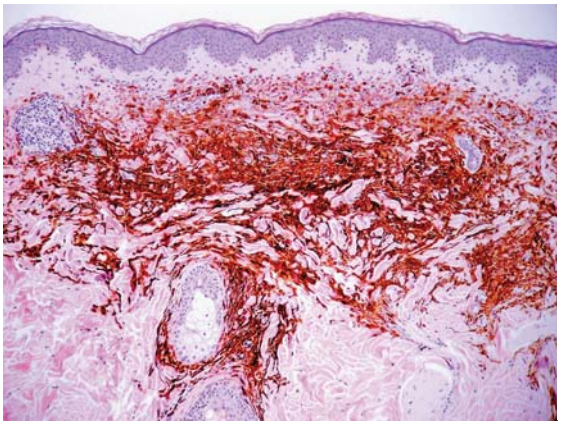
◀ **Figure 3.31b** Dermoscopy shows a central blue-white veil.



◀ **Figure 3.31c** Histology shows aggregation of heavily pigmented cells in the dermis in association with compact orthokeratosis.

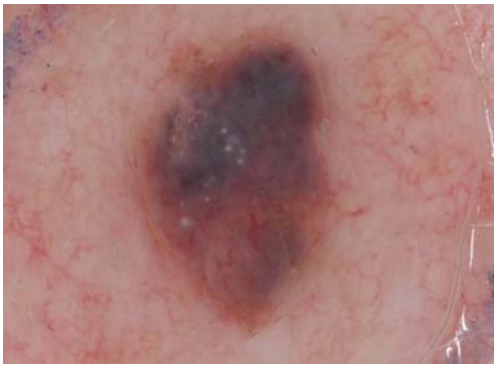
Figure 3.32a Clinical image of a blue nevus.

◀ **Figure 3.32b** Dermoscopy shows a homogenous blue-white veil encompassing the entire surface area of the lesion.

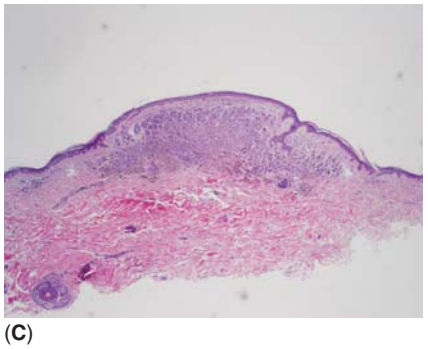


◀ **Figure 3.32c** Histology shows dendritic spindle-shaped cells in the dermis.

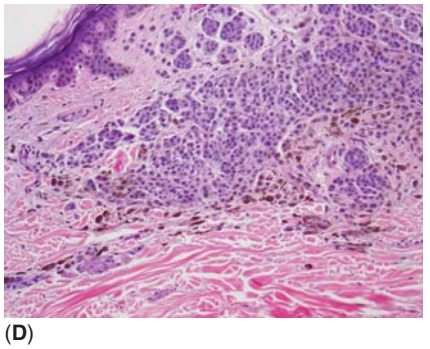
▼ **Figure 3.33a** Clinical image of an unusual intradermal nevus.



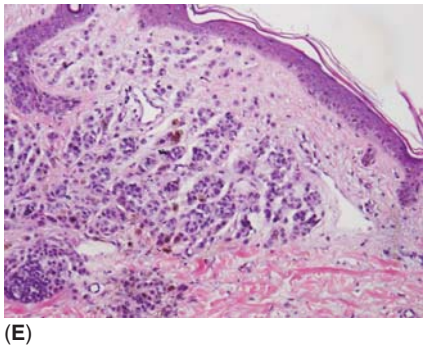
◀**Figure 3.33b** Dermoscopic reveals a melanocytic lesion that has atypical blood vessels. Melanoma should be considered in the differential of all melanocytic lesions manifesting such irregular vessels.



(**C**)



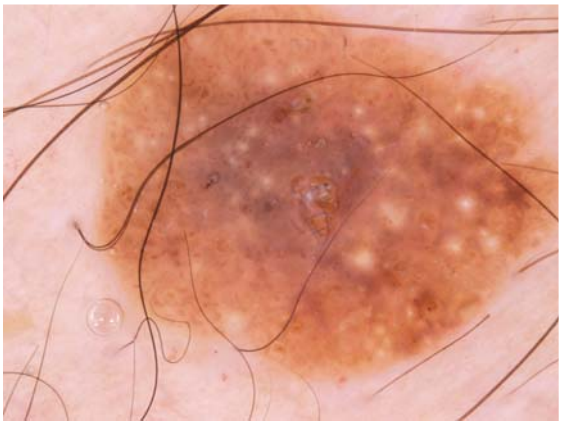
(**D**)



(**E**)

Figure 3.33 (C–E) Histologic of this lesion revealed an intradermal nevus with blood vessels in the lower part of the lesion. This nevus also was associated with some small milia-like cysts.

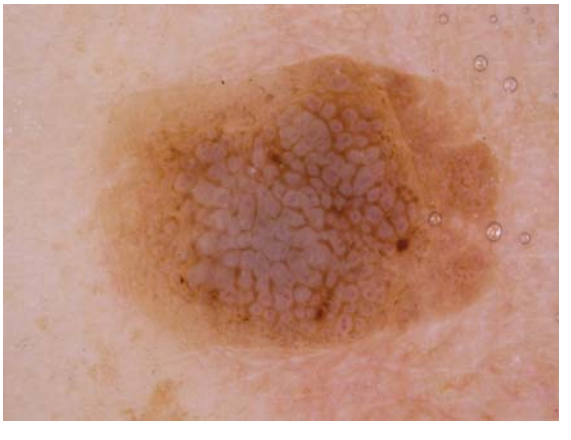
▲ **Figure 3.34a** Clinical image of a pigmented seborrheic keratosis.



◀ **Figure 3.34b** Dermoscopy shows multiple milia-like cysts, comedo-like openings and some fissures (sulci).

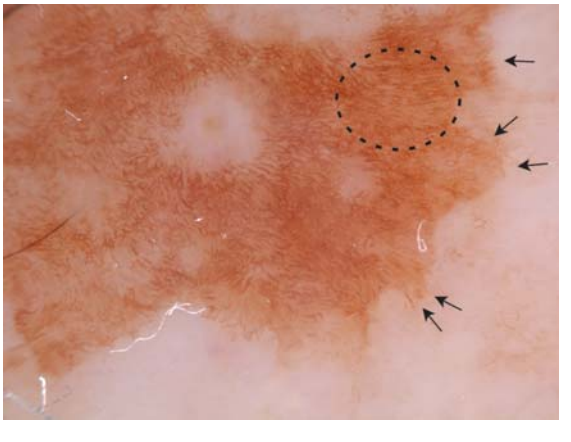
◀ **Figure 3.34c** Histology reveals numerous milia-like cysts and comedo-like openings.

▲ **Figure 3.35a** Clinical image of a seborrheic keratosis.



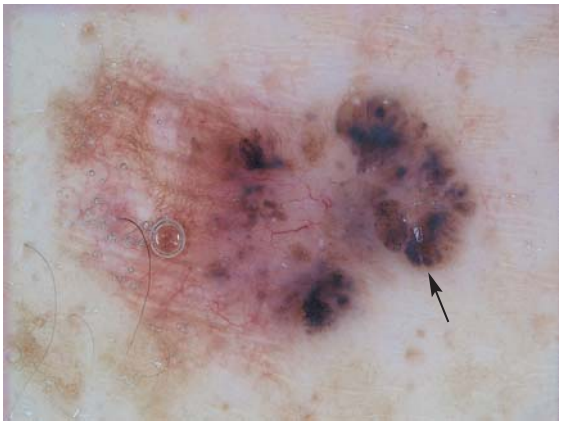
◀ **Figure 3.35b** Dermoscopy shows multiple gyri and sulci creating a brain-like appearance to the lesion. Hairpin blood vessels on the gyri can also be seen.

▲ **Figure 3.36a** Clinical image of an early flat seborrheic keratosis.

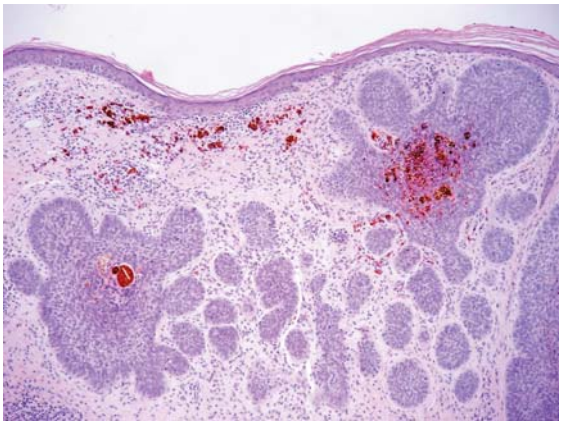


◀ **Figure 3.36b** Dermoscopy shows multiple parallel lines resembling finger-prints (dotted area) and a moth-eaten border (*arrows*) at the periphery.

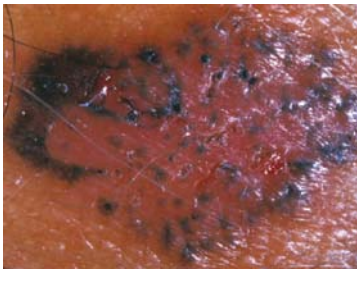
▲ **Figure 3.37a** Clinical image of a pigmented basal cell carcinoma.



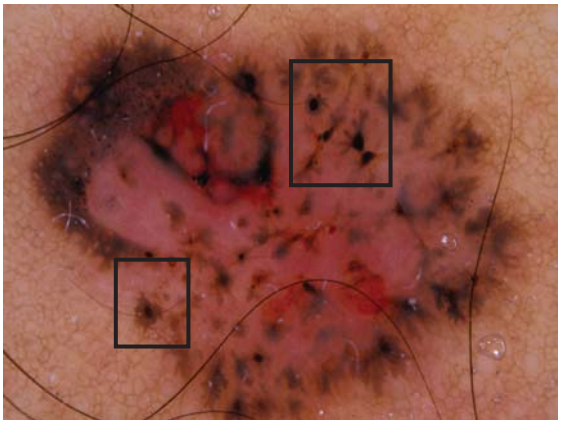
◀ **Figure 3.37b** Dermoscopy shows leaf-like areas (*arrow*).



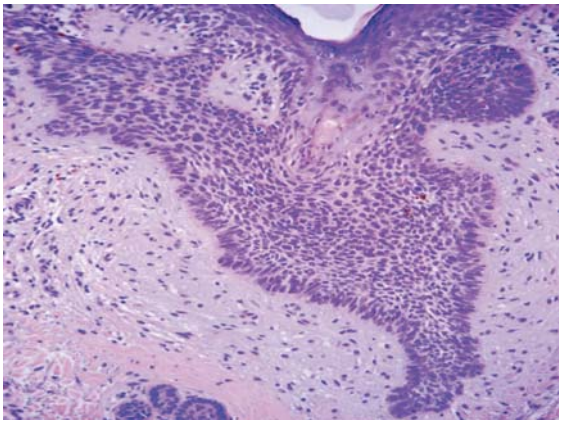
◀ **Figure 3.37c** Histology shows nests of pigmented epithelial nodules of basal cell carcinoma.



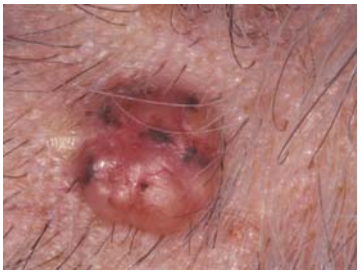
▲ **Figure 3.38a** Clinical image of a pigmented basal cell carcinoma.



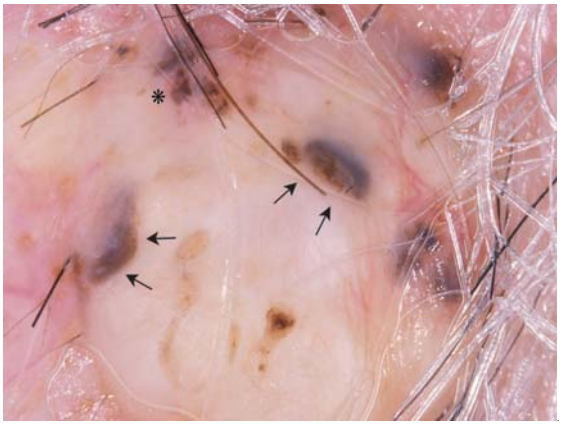
◀ **Figure 3.38b** Dermoscopy shows multiple spoke-wheel-like structures (*squares*).



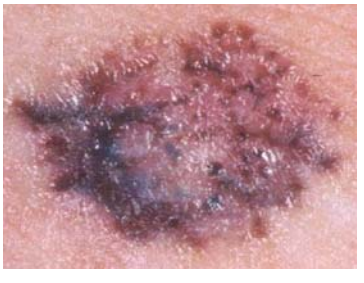
◀ **Figure 3.38c** Histology image of a spoke-wheel area corresponding to nests of basal cell carcinoma radiating off the undersurface of the epidermis.



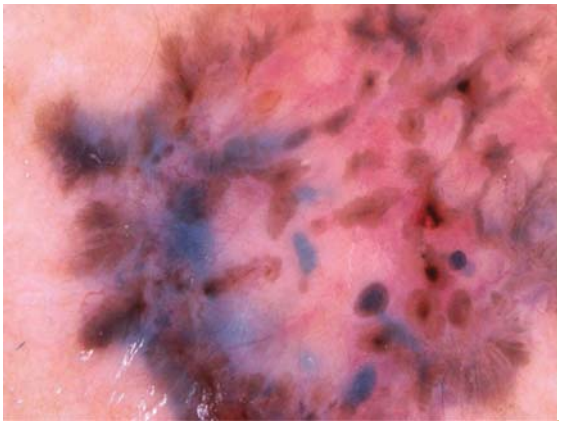
▲ **Figure 3.39a** Clinical image of a nodular pigmented basal cell carcinoma.



◀ **Figure 3.39b** Dermoscopy shows multiple blue-gray ovoid nests (*arrows*).

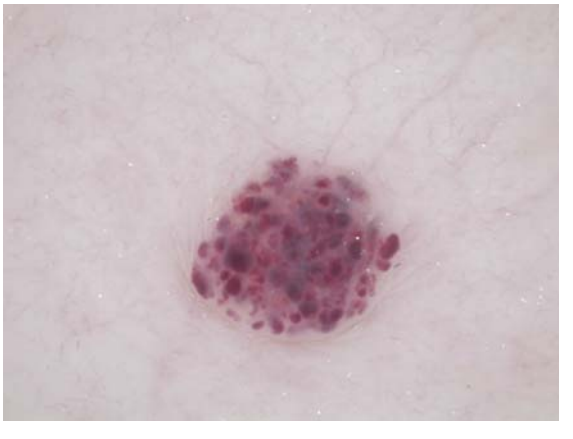


▲ **Figure 3.40a** Clinical image of a pigmented basal cell carcinoma.



◀ **Figure 3.40b** Dermoscopy shows multiple blue-gray globules.

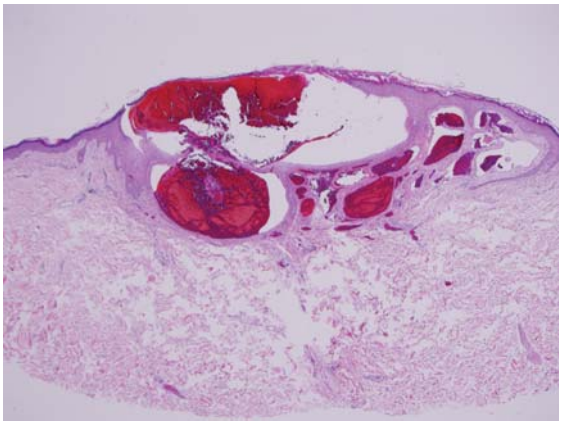
▲ **Figure 3.41a** Clinical image of an angioma.



◀ **Figure 3.41b** Dermoscopy shows multiple well-demarcated lacunae.

▲ **Figure 3.42a** Clinical image of an angiokeratoma.

◀ **Figure 3.42b** Dermoscopy image of angiokeratoma showing blue black lacunae.



◀ **Figure 3.42c** Histology shows large, dilated cavernous blood vessels.

REFERENCES

Anderson, R.R. & Parrish, J.A. 1981 The optics of human skin. *J Invest Dermatol*, 77, 13–19.

Annessi, G., Bono, R., Sampogna, F., Faraggiana, T. & Abeni, D. 2007, Sensitivity, specificity, and diagnostic accuracy of three dermoscopic algorithmic methods in the diagnosis of doubtful melanocytic lesions: the importance of light brown structureless areas in differentiating atypical melanocytic nevi from thin melanomas. *J Am Acad Dermatol*, 56, 759–67.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Soyer, H.P., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Argenziano, G., Soyer, H.P., Ferrara, G., et al., 2001, Superficial black network: an additional dermoscopic clue for the diagnosis of pigmented spindle and/or epithelioid cell nevus. *Dermatology*, 203, 333–5.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Arpaia, N., Cassano, N. & Vena, G. A., 2005 Dermoscopic patterns of dermatofibroma. *Dermatol Surg*, 31, 1336–9.

Balagula, Y., Braun, R.P., Rabinovitz, H.S., et al., 2011, The significance of crystalline/chrysalis structures in the diagnosis of melanocytic and nonmelanocytic lesions. *J Am Acad Dermatol* [Epub ahead of print].

Braun, R.P., G Aide, O., Oliviero, M., et al., 2007, The significance of multiple blue-grey dots (granularity) for the dermoscopic diagnosis of melanoma. *Br J Dermatol*, 157, 907–13.

Braun, R.P., Kaya, G., Masouye, I., Krischer, J. & Saurat, J.H., 2003, Histopathologic correlation in dermoscopy: a micropunch technique. *Arch Dermatol*, 139, 349–51.

Braun, R.P., Krischer, J. & Saurat, J.H., 2000, The "wobble sign" in epiluminescence microscopy as a novel clue to the differential diagnosis of pigmented skin lesions. *Arch Dermatol*, 136, 940–2.

Braun, R.P., Rabinovitz, H., Krischer, J., et al., 2002, Dermoscopy of pigmented seborrheic keratosis. *Arch Dermatol*, 138, 1556–60.

Dobrosavljevic, D., Brasanac, D., Apostolovic, M. & Medenica, L., 2009, Changes in common melanocytic naevi after intense sun exposure: digital dermoscopic study with a 1-year follow-up. *Clin Exp Dermatol*, 34, 672–8.

Ferrara, G., Argenziano, G., Soyer, H.P., et al., 2005, The spectrum of Spitz nevi: a clinicopathologic study of 83 cases. *Arch Dermatol*, 141, 1381–7.

Ferrara, G., Argenziano, G., Soyer, H.P., et al., 2002, Dermoscopic-pathologic correlation: an atlas of 15 cases. *Clin Dermatol*, 20, 228–35.

Ferrara, G.A., Argenziano, Z., Cerio, R.G., et al., 2009, Histopathologic diagnosis of melanocytic skin neoplasms. *PLoS One*, 4.

Guillod, J.F., Skaria, A.M., Salomon, D. & Saurat, J.H., 1997, Epiluminescence videomicroscopy: black dots and brown globules revisited by stripping the stratum corneum. *J Am Acad Dermatol*, 36, 371–7.

Hofmann-Wellenhof, R., Soyer, H.P., Wolf, I.H., et al., 1998, Ultraviolet radiation of melanocytic nevi: a dermoscopic study. *Arch Dermatol*, 134, 845–50.

Hofmann-Wellenhof, R., Wolf, P., Smolle, J., et al., 1997, Influence of UVB therapy on dermoscopic features of acquired melanocytic nevi. *J Am Acad Dermatol*, 37, 559–63.

Krischer, J., Skaria, A., Guillod, J., et al., 1997, Epiluminescent light microscopy of melanocytic lesions after dermoepidermal split. *Dermatology*, 195, 108–11.

Marchell, R., Marghoob, A.A., Braun, R.P. & Argenziano, G., 2005, Dermoscopy of pigmented Spitz and Reed nevi: the starburst pattern. *Arch Dermatol*, 141, 1060.

Marghoob, A.A., Cowell, L., Kopf, A.W. & Scope, A., 2009, Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*, 145, 618.

Massi, D., de, G.V. & Soyer, H.P., 2001, Histopathologic correlates of dermoscopic criteria. *Dermatol Clin*, 19, 259–68, vii.

Menzies, S.W., 2002, Dermoscopy of pigmented basal cell carcinoma. *Clin Dermatol*, 20, 268–9.

Menzies, S.W., Crotty, K.A., Ingvar, C. & Mccarthy, W.H., 2003, *An Atlas of Surface Microscopy of Pigmented Skin Lesions*, Sydney: McGraw-Hill Book Company.

Menzies, S.W., Crotty, K.A. & Mccarthy, W.H., 1995, The morphologic criteria of the pseudopod in surface microscopy. *Arch Dermatol*, 131, 436–40.

Menzies, S.W., Ingvar, C., Crotty, K.A. & Mccarthy, W.H., 1996a, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Menzies, S.W., Ingvar, C. & Mccarthy, W.H., 1996b, A sensitivity and specificity analysis of the surface microscopy features of invasive melanoma. *Melanoma Res*, 6, 55–62.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Menzies, S.W., Westerhoff, K., Rabinovitz, H., et al., 2000, Surface microscopy of pigmented basal cell carcinoma. *Arch Dermatol*, 136, 1012–16.

Menzies, S.W.C., Crotty K.A., Ingvar, C., Mccarthy, W.H., 2009, *Dermoscopy an Atlas*, Sydney: McGraw-Hill.

Pehamberger, H., Binder, M., Steiner, A. & Wolff, K., 1993, In vivo epiluminescence microscopy: improvement of early diagnosis of melanoma. *J Invest Dermatol*, 100, 356S–62S.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

Peris, K., Ferrari, A., Argenziano, G., Soyer, H. P. & Chimenti, S., 2002, Dermoscopic classification of Spitz/Reed nevi. *Clin Dermatol*, 20, 259–62.

Puig, S., Romero, D., Zaballos, P. & Malvehy, J., 2005, Dermoscopy of dermatofibroma. *Arch Dermatol*, 141, 122.

Puppin, D., Salomon, D. & Saurat, J.H., 1993, Amplified surface microscopy. *J Am Acad Dermatol*, 28, 5.

Reisfeld, P.L., 2000, Blue in the skin. *J Am Acad Dermatol*, 42, 597–605.

Saida, T., Miyazaki, A., Oguchi, S., et al., 2004, Significance of dermoscopic patterns in detecting malignant melanoma on acral volar skin: results of a multicenter study in Japan. *Arch Dermatol*, 140, 1233–8.

Schiffner, R., Schiffner-Rohe, J., Vogt, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42, 25–32.

Scope, A., Busam, K.J., Malvehy, J., et al., 2007, Ex vivo dermoscopy of melanocytic tumors: time for dermatopathologists to learn dermoscopy. *Arch Dermatol*, 143, 1548–52.

Soyer, H.P., Argenziano, G., Chimenti, S., et al., 2001, *Dermoscopy of Pigmented Skin Lesions*, Milano: EDRA.

Soyer, H.P., Kenet, R.O., Wolf, I.H., Kenet, B.J. & Cerroni, L., 2000, Clinicopathological correlation of pigmented skin lesions using dermoscopy. *Eur J Dermatol*, 10, 22–8.

Soyer, H.P., Massone, C., Ferrara, G. & Argenziano, G., 2005, Limitations of histopathologic analysis in the recognition of melanoma: a plea for a combined diagnostic approach of histopathologic and dermoscopic evaluation. *Arch Dermatol*, 141, 209–11.

Steiner, A., Pehamberger, H. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. II. Diagnosis of small pigmented skin lesions and early detection of malignant melanoma. *J Am Acad Dermatol*, 17, 584–91.

Stolz, W., Braun-Falco, O., Bilek, P., et al., 2002a, Color Atlas of Dermatoscopy, Berlin: Blackwell Wissenschafts-Verlag.

Stolz, W., Schiffner, R. & Burgdorf, W.H., 2002b, Dermatoscopy for facial pigmented skin lesions. *Clin Dermatol*, 20, 276–8.

Tronnier, M., Alexander, M., Neitmann, M., Brinckmann, J. & Wolff, H.H., 2000, Morphological changes in melanocytic nevi induced by exogenous factors. *Hautarzt*, 51, 561–6.

Wolf, I.H., 2002, Dermoscopic diagnosis of vascular lesions. *Clin Dermatol*, 20, 273–5.

Yadav, S., Vossaert, K.A., Kopf, A.W., Silverman, M. & Grin-Jorgensen, C., 1993, Histopathologic correlates of structures seen on dermoscopy (epiluminescence microscopy). *Am J Dermatopathol*, 15, 297–305.

Zaballos, P., Daufi, C., Puig, S., et al., 2007, Dermoscopy of solitary angiokeratomas: a morphological study. *Arch Dermatol*, 143, 318–25.

Zaballos, P., Puig, S., Llambrich, A. & Malvehy, J., 2008, Dermoscopy of dermatofibromas: a prospective morphological study of 412 cases. *Arch Dermatol*, 144, 75–83.

Zalaudek, I., Argenziano, G., Ferrara, G., et al., 2004, Clinically equivocal melanocytic skin lesions with features of regression: a dermoscopic-pathological study. *Br J Dermatol*, 150, 64–71.

4 Two-step algorithm: Differentiating melanocytic from nonmelanocytic lesions

Ashfaq A. Marghoob and Ralph P. Braun

In 2001, the Board of the Consensus Net Meeting agreed on a two-step algorithm for the classification of pigmented lesions of the skin (Argenziano et al., 2003).

In the first level of decision making, the observer is required to decide whether a lesion is of melanocytic or nonmelanocytic origin (Fig. 4.1). Once the lesion is identified to be of melanocytic origin, the second level of decision making needs to be implemented. This second level process helps characterize the melanocytic lesion as benign, suspect, or malignant. For this purpose the six algorithms mentioned in chapter 6 have been most useful, although many others have been published.

THE REVISED TWO-STEP ALGORITHM

The main purpose of the two-step algorithm is to avoid missing the diagnosis of melanoma. Although some exceptions to the two-step algorithm exist, they, by in large, do not affect the sensitivity for melanoma detection. In other words, the two-step process is designed so as to maximize the sensitivity for melanoma detection (Scope et al., 2006; Blum & Jaworski, 2006; Benvenuto-Andrade et al., 2007; Pan et al., 2008; Wang et al., 2008). With that said, the main shortcoming of the classic two-step algorithm was that it did not adequately address the evaluation process for amelanotic and hypomelanotic neoplasms. These lesions often appear to be structureless or featureless on initial inspection (Argenziano et al., 2007; Kittler et al., 2006; Menzies et al., 1996; Skvara et al., 2005; Puig-Butille et al., 2007). However, upon close scrutiny many of these neoplasms will in fact reveal blood vessels and thus, they are not truly structureless (Zalaudek et al., 2006). These new insights prompted us to modify the two-step algorithm by adding two new decision levels to the classic two-step algorithm (levels 5 and 6 in Fig. 4.2), which are intended to assist clinicians in correctly classifying some of these so-called featureless neoplasms as either melanocytic or nonmelanocytic tumors (Zalaudek et al., 2006).

STEP 1 DECISION: MELANOCYTIC VS. NONMELANOCYTIC LESION

The first step of this two-step dermoscopy decision-making algorithm has seven different levels (Fig. 4.2). However, before utilizing this algorithm it is important to be aware that this algorithm is designed to evaluate lesions on glabrous and nonglabrous skin only. It is not intended for the evaluation of nail, mucosal or hair abnormalities. With that being said, each level requires that the observer evaluate the lesion for the presence of specific dermoscopy criteria in the following sequence.

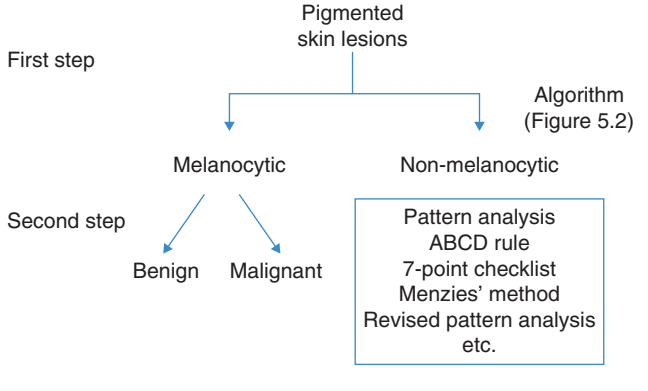


Figure 4.1 Two-step procedure for the differential diagnosis of pigmented lesions.

Level 1: Criteria for Melanocytic Lesions

Search for pigment network (N.B: one major exception; see below) (Fig. 4.3), branched streaks (e.g., atypical network) (Fig. 4.4), streaks (i.e., radial streaming and pseudopods), negative network, aggregated globules (Fig. 4.5), homogenous blue pigmentation (Fig. 4.6), pseudonetwork (face) (Fig. 4.7), or parallel pattern (palms, soles, and mucosa) (Fig. 4.8). If any of these structures or features are present, the lesion is considered of melanocytic origin and hence, one can proceed directly to the second step of the two-step algorithm. In the second step of the algorithm, the presumed melanocytic lesion is evaluated to determine whether it is benign, suspicious, or malignant (Fig. 4.1 and chap. 6).

One major exception to the above is when a lesion manifests a delicate peripheral network with a central scar-like area as seen in a dermatofibroma (Agero et al., 2006). This particular pattern generally trumps the presence of a network, hence preventing the misdiagnosis of a dermatofibroma as a melanocytic lesion. The preceding description, however, is that of a classic dermatofibroma as seen with standard nonpolarized dermoscopy. When dermatofibromas are evaluated using polarized dermoscopy, their appearance can be quite different (see chap. 5e): In particular, with polarized light the central part of the dermatofibroma usually has a pink hue and has white stellate (e.g., chrysalis/crystalline like) structures (Agero et al., 2006). Other exceptions to the two-step algorithm exist are discussed in chapter 10.

A further clarification of homogenous blue pigmentation as seen in blue nevi is also warranted here. The quintessential characteristic that differentiates a blue nevus from other lesions possessing a blue-white veil (Fig. 4.9) is that in a blue nevus the blue pigmentation occupies the entire surface area of the lesion in a homogenous manner (Fig. 4.6). However, it is important to remember that the preceding discussion only pertains to standard nonpolarized contact dermoscopy. With polarized light blue nevi often do not manifest a homogenous blue color, but instead reveal different shades or hues of blue (Benvenuto-Andrade et al., 2007).

If the criteria of Level 1 are not met, then one needs to proceed to Level 2.

Level 2: Criteria for Basal Cell Carcinoma

Search for the presence of specific morphologic criteria for basal cell carcinoma (Menzies et al., 2000), which include arborizing blood vessels (telangiectasias) (Fig. 4.10), leaf-like areas (Figs. 4.10 and 4.11), large blue-gray ovoid nests, multiple blue-gray non-aggregated globules (Fig. 4.12), spoke-wheel-like structures, shiny white areas (Scalvenzi et al., 2008) ,or ulceration (Fig. 4.10). In the absence of a pigment network, these criteria are highly suggestive of basal cell carcinoma. If, on the other hand, these structures are not seen, then proceed to Level 3.

Level 3: Criteria for Seborrheic Keratoses

Look for multiple milia-like cysts (Fig. 4.13), comedo-like openings (Figs. 4.13 and 4.14), crypts, moth-eaten borders (Fig. 4.15), network-like structures, "fissures and ridges" (also known as gyri and sulci) that sometimes give a brain-like or cerebriform appearance to the lesion, fat finger-like structures (Fig. 4.16), or light brown fingerprint-like structures.

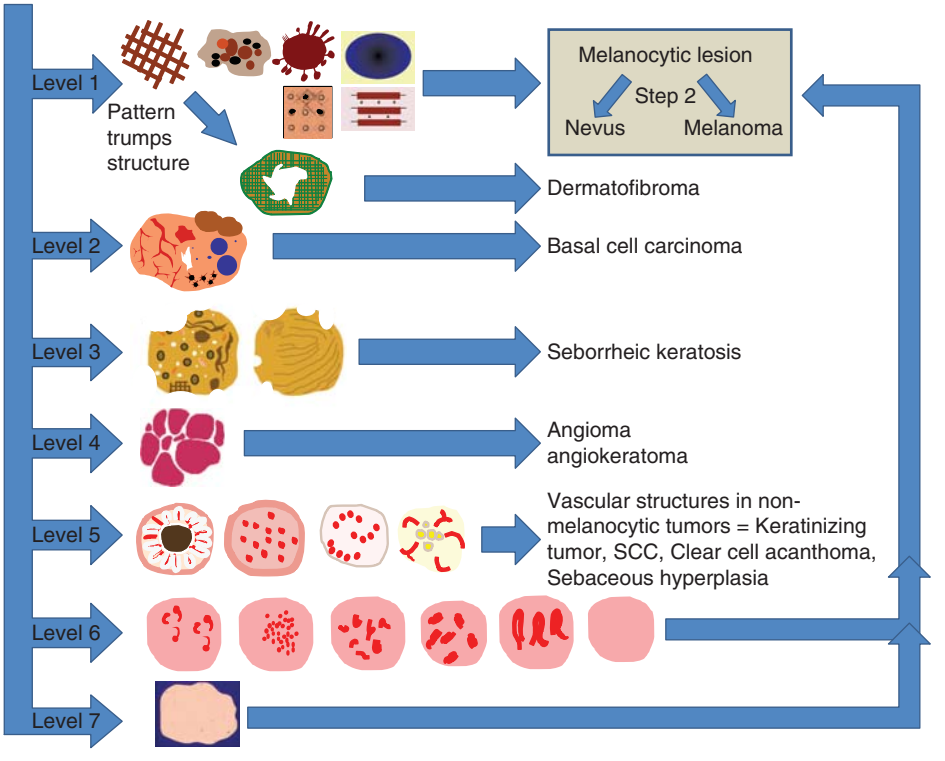
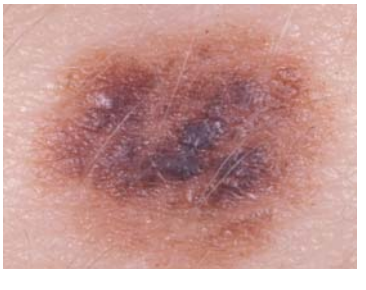


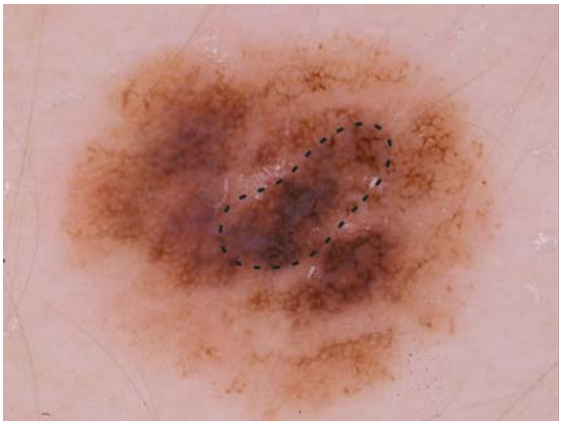
Figure 4.2 Algorithm for the differentiation between melanocytic and nonmelanocytic lesions. *Abbreviation*: SCC, Squamous cell carcinoma.

▲ **Figure 4.3a** Clinical image of a junctional nevus.

◀ **Figure 4.3b** Dermoscopy showing a typical, regular pigment network thinning out toward the periphery.

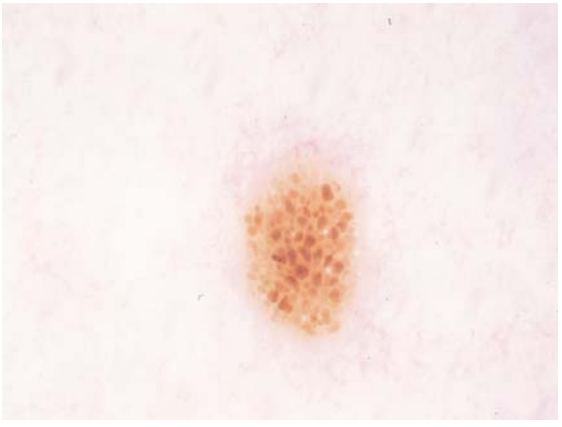


▲ **Figure 4.4a** Clinical image of a dysplastic nevus.



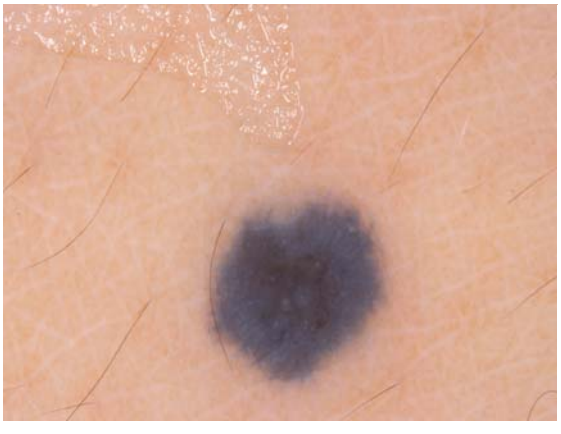
◀ **Figure 4.4b** Dermoscopy showing broken-up/fragmented network, also known as branched streaks, (dotted area) in the center of the lesion.

▲ **Figure 4.5a** Clinical image of a compound nevus.



◀ **Figure 4.5b** Dermoscopy showing a globular architecture with multiple round and ovoid globules.

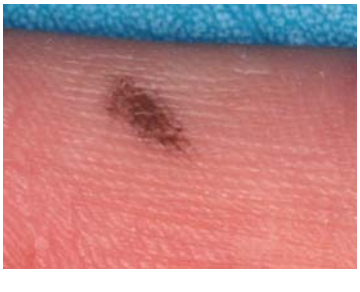
▲ **Figure 4.6a** Clinical image of a blue nevus.



◀ **Figure 4.6b** Dermoscopy showing a homogenous blue pigmentation filling the entire lesion.

▲ **Figure 4.7a** Clinical image of a compound nevus of the face.

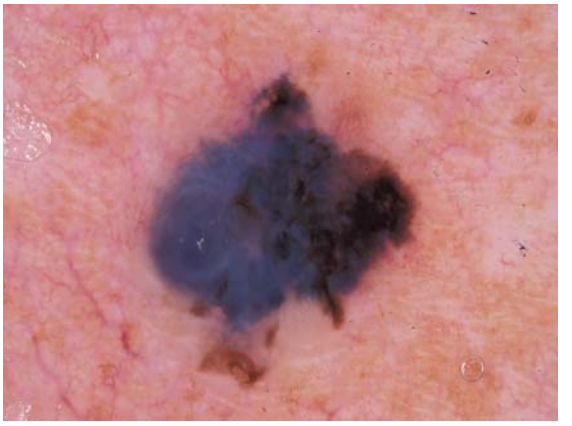
◀ **Figure 4.7b** Dermoscopy showing a typical regular pseudonetwork.



▲ **Figure 4.8a** Clinical image of a junctional nevus on the palm.

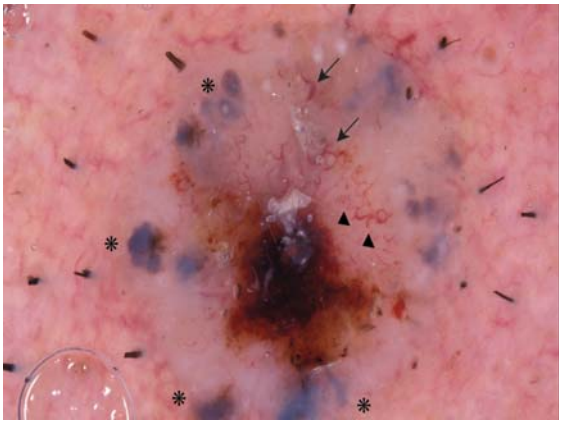
◀ **Figure 4.8b** Dermoscopy showing a lattice-like pattern, which is a variation of the parallel furrow pattern.

▲ **Figure 4.9a** Clinical image of a malignant melanoma (Breslow 1.5 mm Clark IV).



◀ **Figure 4.9b** Dermoscopy showing an irregular confluent bluish-whitish pigmentation, which does not occupy the entire surface area of the lesion. Focal presence of a blue-white veil with multiple hues of blue is considered atypical.

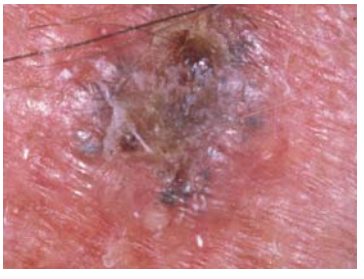
▲ **Figure 4.10a** Clinical image of a pigmented basal cell carcinoma.



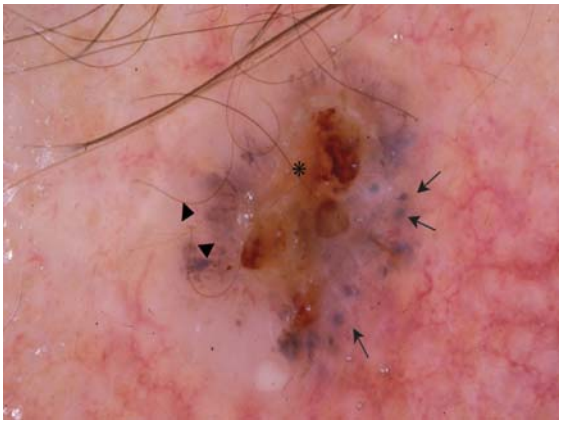
◀ **Figure 4.10b** Dermoscopy showing arborizing telangiectasia (*arrows*), ulceration (*arrowheads*) and multiple leaf-like areas (*asterisks*).

▲ **Figure 4.11a** Clinical image of a nodular pigmented basal cell carcinoma.

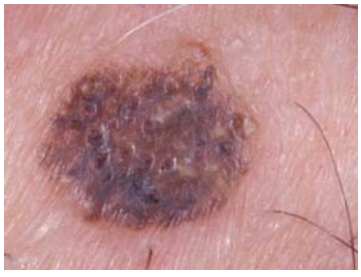
◀ **Figure 4.11b** Dermoscopy showing leaf-like areas, multiple blue-gray ovoid nests (*arrows*), and a telangectasia in the right part of the lesion.



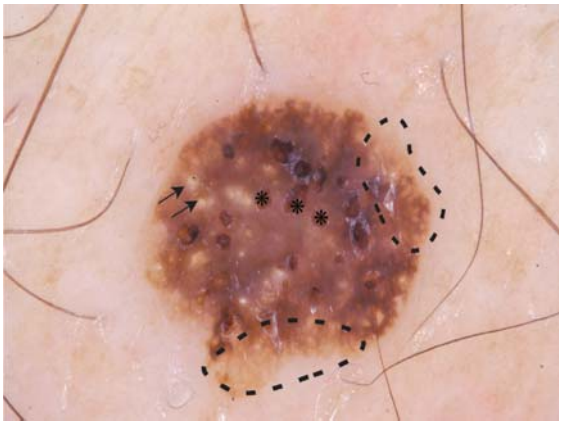
▲ **Figure 4.12a** Clinical image of a pigmented basal cell carcinoma.



◀ **Figure 4.12b** Dermoscopy showing multiple blue-gray non-aggregated globules (*arrows*), blue-gray ovoid nests, ulceration (*asterisks*) and arborized telangiectasia (*arrowheads*).



▲ **Figure 4.13a** Clinical image of a pigmented seborrheic keratosis.

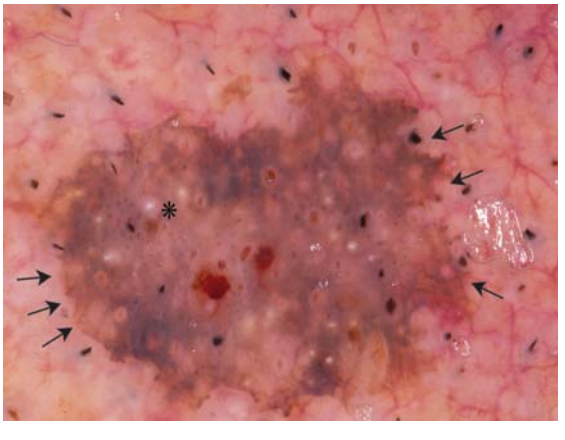


◀ **Figure 4.13b** Dermoscopy showing multiple milia-like cysts (*arrows*), comedo-like openings (asterisks) and network-like structures (*dotted areas*) at the periphery, which are most noticeable in the right part of the lesion. The network like structures is created by ridges (gyri) and sulci. Examining the lesion clinically via side lighting can easily help identify network-like structures in a seborrheic keratosis and differentiate it from a pigment network encountered in a melanocytic lesion. On side lighting the undulating surface created by gyri and sulci in a seborrheic keratosis can be appreciated.

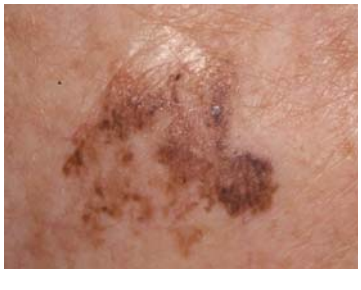
▲ **Figure 4.14a** Clinical image of a pigmented seborrheic keratosis.

◀ **Figure 4.14b** Dermoscopy showing multiple comedo-like openings and a crypt in the right part of the lesion (*arrows*).

▲ **Figure 4.15a** Clinical image of a pigmented seborrheic keratosis of the face.



◀ **Figure 4.15b** Dermoscopy showing a moth-eaten border (*arrows*) and multiple milia-like cysts (*asterisks*).



▲ **Figure 4.16a** Clinical image of a pigmented seborrheic keratosis of the face.

◀ **Figure 4.16b** Dermoscopy showing fat finger-like structures (*arrows*) and multiple milia-like cysts.

▲ **Figure 4.17a** Clinical image of a hemangioma.

◀ **Figure 4.17b** Dermoscopy showing multiple dark red lacunae.

Figure 4.18 Dermoscopy of malignant melanoma without any of the dermoscopy structures mentioned in Figure 4.2. A blue-white veil, which does not occupy the entire lesion, can be seen.

Although milia cysts and comedo openings are very easy to identify by standard nonpolarized dermoscopy, they may not be as apparent when viewed using polarized light dermoscopy (Benvenuto-Andrade et al., 2007). With that being said, if some of these structures are present, then the lesion is probably a seborrheic keratosis. A word of caution is warranted here regarding milia cysts. The presence of these structures does not automatically equate a diagnosis of seborrheic keratosis because milia cysts can occasionally be seen in basal cell carcinoma and in melanocytic nevi, especially of the congenital type (Stricklin et al., 2011). Thus, milia cysts should be considered a diagnostic criterion only after insuring that the lesion is not a melanocytic lesion or a basal cell carcinoma. If none of the seborrheic keratosis criteria are seen then one needs to proceed to Level 4.

Level 4: Criteria for Vascular Lesions

The presence of red, maroon, or red-blue to black lacunae (also known as lagoon-like structures), indicates that the lesion is a hemangioma or angiokeratoma (Fig. 4.17). If the criteria for levels 1–4 have not been satisfied, one needs to proceed to Level 5.

Level 5: Specific Blood Vessels in Nonmelanocytic Lesions

If none of the morphologic criteria described in the previous levels can be identified, then the lesion does not manifest any obvious features of a melanocytic lesion nor does it manifest any of the features seen in the four common nonmelanocytic tumors. These lesions are usually amelanotic or hypomelanotic. Some have referred to these lesions as "featureless lesions." However, even in these so-called featureless lesions, one may be able to find vascular structures that can assist in their diagnosis. Lesions that appear to be featureless should be closely examined for the presence of blood vessels. It is important to appreciate both the morphology and distribution of these vessels. Hairpin vessels surrounded by a whitish halo is a characteristic of keratinizing tumors, such as keratoacanthomas and seborrheic keratosis (Argenziano et al., 2004; Braun et al., 2002).The presence of glomerular vessels, usually aggregated focally at the periphery of the lesion, identifies the lesion as a squamous cell carcinoma (Argenziano et al., 2004). Besides the morphology and distribution of vessels, the arrangement of the blood vessels and the color surrounding the vessels can also assist in the diagnosis. The presence of blood vessels arranged like "pearls on a string" or in a "serpiginous pattern" is a hallmark of clear cell acanthoma (Argenziano et al., 2004). The presence of crown vessels identifies the lesion as a sebaceous hyperplasia or molluscum contagiosum (Zaballos et al., 2005; Morales et al., 2005).

Level 6: Specific Blood Vessels in Melanocytic Lesions

The presence of predominantly comma shaped blood vessels is a hallmark of intradermal nevi (Menzies et al., 2008). The blood vessel morphology encountered in melanoma includes dotted, linear irregular, atypical hairpin (serpentine) vessel in a pink background, and cork screw or tortuous vessels. If more than one type of vessel morphology is seen within the same lesion, the vascular pattern is termed "polymorphous." The polymorphous pattern that is most commonly associated with melanoma consists of centrally placed dotted and linear/serpentine vessels (Braun et al., 2002). In addition to the blood vessel morphology described above, the presence of multiple shades of pink, also known as milky red areas, can also be seen in melanoma. The milky red color probably represents an increased vascular volume and may be a reflection of neoangiogenesis (Menzies et al., 2008).

Lesions that do not display any of the structures mentioned in levels 1–6 are considered "structureless" and for such lesions one needs to proceed to Level 7.

Level 7: "Structureless" Lesions

Lesions that fail characterization in levels 1–6 are tumors that are often completely featureless or structureless. However, it is important to highlight that these lesions are not always necessarily structureless. Level 7 is simply the default category that includes all lesions that fail to reveal any specific diagnostic structures to help classify them as melanocytic or as one of the non-melanocytic lesions mentioned in levels 1 to 6 of the two-step algorithm. For example, the presence of fine dots, peppering, blue-white veil, crystalline structure, and blotches may be present in these lesions. While these aforementioned structures cannot be used to differentiate melanocytic from non-melanocytic lesions, they can be clues that aid in correctly identifying melanomas and some basal cell carcinomas. With that said, for all lesions in level 7 (the so called "structureless" lesions), it is imperative, it is imperative that melanoma be ruled out (Fig. 4.18). This "worst case scenario" avoids missing melanomas that are devoid of any specific discernable structures (Puig-Butille et al., 2007; Argenziano et al., 2007). Thus, these lesions either should be biopsied or should be subjected to short-term mole monitoring in an attempt to ascertain their biologic behavior.

STEP 2 DECISION: BENIGN NEVUS VS. SUSPECT MELANOCYTIC LESION VS. MELANOMA

Lesions that are identified as being of melanocytic origin in step one of the two-step algorithm include those described in levels 1, 6, and 7 above. Melanocytic lesions–manifesting structures and features described in these levels can be subjected to the second step of the two-step algorithm. In the second step, the presumed melanocytic neoplasm is evaluated to determine whether the lesion is benign, suspect, or malignant. To accomplish this, many different approaches have been proposed (Stolz et al., 1994; Argenziano et al., 2003; Menzies et al., 1996; Pehamberger et al., 1987; Argenziano et al., 1998; Kittler, 2007) (chap. 6).

Key Points

- The two-step dermoscopy algorithm serves as the foundation for the dermoscopic evaluation and differentiation of skin lesions.
- The first step of the modified two-step dermoscopy algorithm is designed to assist clinicians in correctly classifying lesions as being of melanocytic or nonmelanocytic origin.
- The first step consists of seven levels, each of which requires the clinician to search for specific structures and criteria. The presence or absence of these criteria will help in correctly diagnosing most lesions.
- The seven decision levels in step one are as follows:
  - Level 1: Criteria for melanocytic lesions (exceptions include dermatofibromas)
  - Level 2: Criteria for basal cell carcinoma
  - Level 3: Criteria for seborrheic keratosis
  - Level 4: Criteria for vascular lesions
  - Level 5: Specific blood vessels for nonmelanocytic neoplasms
  - Level 6: Specific blood vessels for melanocytic lesions
  - Level 7: Structureless (e.g., devoid of structures that allows for accurate classification of the lesion as a melanocytic or nonmelanocytic lesion. All lesions in level 7 are considered melanocytic by default and melanoma needs to be considered in the differential diagnosis).
- The second step in the two-step dermoscopy algorithm is designed to assist clinicians in correctly segregating melanocytic lesions into benign nevi *versus* potential melanomas (chap. 6).

REFERENCES

Agero, A., Taliercio, S., Dusza, S., et al., 2006, Conventional and polarized dermoscopy features of dermatofibroma. *Arch Dermatol*, 142, 1431–7.

Argenziano, G., Delfino, M. & Russo, N., 2004, Mud and baththerapy in the acne cure. *Clin Ter*, 155, 121–5.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Argenziano, G., Zalaudek, I., Ferrara, G., et al., 2007, Dermoscopy features of melanoma incognito: indications for biopsy. *J Am Acad Dermatol*, 56, 508–13.

Benvenuto-Andrade, C., Dusza, S., Agero, A., et al., 2007, Differences between polarized light dermoscopy and immersion contact dermoscopy for the evaluation of skin lesions. *Arch Dermatol*, 143, 329–38.

Blum, A. & Jaworski, S., 2006, Clear differences in hand-held dermoscopes. *J Dtsch Dermatol Ges*, 4, 1054–7.

Braun, R. P., Rabinovitz, H., Oliviero, M., Kopf, A.W. & Saurat, J.H., 2002, Dermoscopic diagnosis of seborrheic keratosis. *Clin Dermatol*, 20, 270–2.

Kittler, H., 2007, Dermatoscopy: introduction of a new algorithmic method based on pattern analysis for diagnosis of pigmented skin lesions. *Dermatopathol Pract Conc*, 13, 1.

Kittler, H., Guitera, P., Riedl, E., et al., 2006, Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. *Arch Dermatol*, 142, 1113–19.

Menzies, S.W., Ingvar, C., Crotty, K. & McCarthy, W., 1996, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Menzies, S.W., Westerhoff, K., Rabinovitz, H.S., et al., 2000, Surface microscopy of pigmented basal cell carcinoma, *Arch Dermatol*, 136, 1012–16.

Morales, A., Puig-Butille, S., Malvehy, J. & Zaballos, P., 2005, Dermoscopy of molluscum contagiosum. *Arch Dermatol*, 141, 1644.

Pan, Y., Gareau, D., Scope, A., et al., 2008, Polarized and nonpolarized dermoscopy: the explanation for the observed differences. *Arch Dermatol*, 144, 828–9.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

Puig-Butille, S., Argenziano, S., et al., 2007, Melanomas that failed dermoscopic detection: a combined clinicodermoscopic approach for not missing melanoma. *Dermatol Surg*, 33, 1262–73.

Scalvenzi, M., Lembo, S., Francia, M. & Balato, A., 2008, Dermoscopic patterns of superficial basal cell carcinoma. *Int J Dermatol*, 47, 1015–18.

Scope, A., Burroni, M., Agero, A., et al., 2006, Predominant dermoscopic patterns observed among nevi. *J Cutan Med Surg*, 10, 170–4.

Skvara, H., Teban, L., Fiebiger, M., Binder, M. & Kittler, H., 2005, Limitations of dermoscopy in the recognition of melanoma. *Arch Dermatol*, 141, 155–60.

Stricklin SM, Stoecker WV, Oliviero MC, Rabinovitz HS. & Mahajan SK., 2011, Cloudy and starry milia-like cysts: how well do they distinguish seborrheic keratoses from malignant melanomas? *J Eur Acad Dermatol Venereol*, 25, 1222–4.

Stolz, W., Riemann, A., Cognetta, A., et al., 1994, ABCD rule of Dermatoscopy: a new practical method for early recognition of malignant melanoma. *Eur J Dermatol*, 4, 521–7.

Wang, S., Dusza, S., Scope, A., et al., 2008, Differences in dermoscopic images from nonpolarized dermoscope and polarized dermoscope influence the diagnostic accuracy and confidence level: a pilot study. *Dermatol Surg*, 34, 1389–95.

Zaballos, P., Guionnet, N., Puig-Butille, S. & Malvehy, J., 2005, Central white network: an additional dermoscopic feature for the diagnosis of dermatofibroma. *Dermatol Surg*, 31, 960–2.

Zalaudek, I., Argenziano, G., Soyer, H., et al., 2006, Three-point checklist of dermoscopy: an open internet study. *Br J Dermatol*, 154, 431–7.

5 Nonmelanocytic lesions

5a Basal cell carcinoma

Steven Q. Wang and Scott W. Menzies

Basal cell carcinoma (BCC) is the most common type of skin cancer in the world. Although mortality related to BCC is negligible, BCCs can be associated with significant morbidity, especially if left untreated and/or if discovered when they have attained relatively large diameters (Miller & Weinstock, 1994). Clinically, this skin cancer can present with a variety of morphologies ranging from erythematous patches to ulcerated nodules. It is not uncommon for BCCs to display pigment within the lesion and, based on the degree of pigmentation, some BCCs can mimic melanomas or other pigmented skin lesions when examined with the naked eye. Furthermore, depending on the subtype of BCC and the degree of pigmentation, the clinical differential diagnosis can be quite broad ranging from benign inflammatory lesions to melanoma. Fortunately, the use of dermoscopy has dramatically improved the diagnostic accuracy and diagnostic confidence of clinicians for both pigmented and nonpigmented BCCs.

PIGMENTED BASAL CELL CARCINOMAS

Dermoscopic features associated with pigmented BCCs have been well characterized (Table 5a.1) (Menzies, 2002; Menzies et al., 2000). Pigmented BCCs should not have a pigment network or streaks (pseudopods) since the presence of these structures are seen primarily in melanocytic tumors (e.g., melanocytic nevi or melanoma). In addition, the presence of one or more of the following structures is required for the diagnosis:

1. *Large blue-gray ovoid nests.* The nests are defined as confluent or nearly confluent, well-circumscribed, pigmented ovoid or elongated areas that are not closely connected to the pigmented tumor body (Menzies et al., 2000). Nests are larger than globules (Fig. 5a.1).
2. *Multiple blue-gray globules.* These are well-defined round or oval structures, larger than dots, but smaller than large ovoid nests. They are not aggregated as would be seen in melanocytic lesions (Menzies et al., 2000). They usually have a blue-gray color; however, depending on the location and degree of melanin within the pigmented basaloid tumor islands, the globules can appear brown or pink (Fig. 5a.2).
3. *Leaf-like structures.* These areas are defined as discrete, bulbous extensions connected at a base area, forming a leaf-like pattern. They are usually brown or gray-blue in color (Fig. 5a.3). This structure is very specific for BCCs. These bulbous extensions can sometimes be mistaken for streaks seen in melanocytic lesions (e.g., melanoma and Spitz nevi). However, streaks in melanocytic lesions tend to be discrete, well-delineated, narrow, relatively in-focus linear extensions that are located at the perimeter of the lesion and are directly connected to the main pigmented tumor mass. Streaks in melanocytic lesions always radiate in a direction pointing away from the main pigmented tumor mass and they radiate toward and into normal skin. In addition, streaks in a melanocytic lesion appear to converge towards the geometric center of the lesion, which is often hyperpigmented and has a blue-white veil. In contrast, extensions seen in leaf-like structures tend to be broader and often appear "fuzzy" (Fig. 5a.4a and b) They do not have to be located at the lesion's perimeter and they do not always have to radiate away from the main tumor mass toward normal skin (Fig. 5a.5a and b). In addition, the extensions seen in BCC tend to converge at a pigmented base. This base together with its "extensions" is present focally and most often located towards the periphery of the tumor and it is this configuration that creates the leaf-like structure. In addition, the geometric center of BCCs manifesting "fuzzy streaks" (leaf-like areas) is often hypopigmented and relatively structureless. (Fig. 5a.4).
4. *Spoke-wheel-like structures.* These are radial projections that are surrounding a central darker point. The projections have a tan, blue, or gray color, and the central point or hub is usually dark brown, blue, or black (Fig. 5a.6). At times the radial projections are not well defined and the spoke-wheel-like structure appears as a brownish round ill marginated globule that has a central darker hub ; this particular pattern is called the concentric structure or concentric globule. (Fig. 5a.7). The spoke-wheel-like structure is highly specific for BCCs (Menzies et al., 2000).
5. *Arborizing telangiectasia.* These consist of multiple branching blood vessels in a tree-like pattern. These vessels are often appreciated in nonpigmented BCCs, and are rarely seen in nevi or other benign pigmented skin lesions (Fig. 5a.8 and Fig. 5a.9).
6. *Ulceration.* These structures consist of shallow erosions that may be covered with congealed blood. They can also appear to have an orange hue if covered with a serous crust. It is important to rule out a previous history of trauma for ulceration to be a valid feature (Fig. 5a.10).

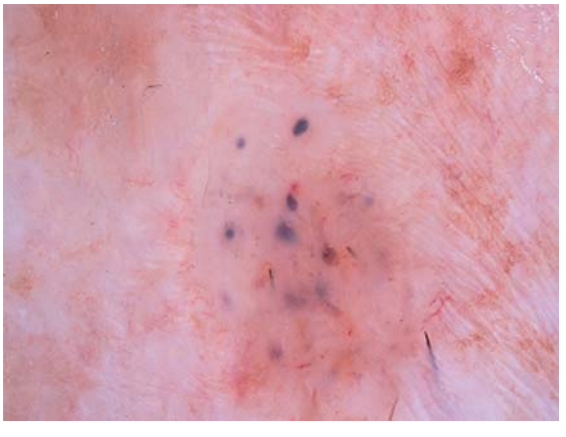
Knowledge of the histologic features of pigmented BCCs assists in correlating the dermoscopic structures to the histopathology structures. Under routine microscopic examination, BCC tumors are seen as clusters or islands of basaloid cells found in the dermis or the dermoepidermal junction. Free melanin, melanin in basal cells and in melanocytes or melanophages can be found within basaloid tumor islands, which in turn is responsible for yielding the pigmentations seen under dermoscopy. The different dermoscopic structures correlate to (*i*) the shape and size of the tumor islands and (*ii*) to the variation in the amount and distribution of the melanin pigment. Pigmentation found in small islands of tumors may be seen as multiple blue-gray globules under dermoscopy. The presence of large amount of pigmentation seen in a large cluster of tumors may correspond to large blue-gray ovoid nests. Although classically the basaloid tumor islands appear with a blue-gray color, depending on their depth, they can also appear with brown colors (Tyndall effect). Depending on the shape and configuration of the pigmented basaloid tumor islands, their appearance can overlap between oval structures, leaf-like, and spoke-wheel-like structures.

The sensitivity and specificity (Table 5a.1) of each of these six structures have been studied by Menzies et al. (2000). The investigators examined 426 pigmented BCCs and reviewed 45 dermoscopic structures with an aim to select out the critical dermoscopic features that distinguish pigmented BCCs from other pigmented skin lesions. Their analysis yielded a practical diagnostic method with 93% sensitivity and 89–92% specificity. Using this method, the diagnosis of a pigmented BCC is made when a lesion lacks a pigment network and has one or more of the specific features listed in Table 5a.1. In 2002, Peris and coworkers independently validated this diagnostic method in their patient population. Lastly, recent dermoscopy studies have elucidated other morphologic features of BCC including features that are seen in dermoscopically non-classic BCCs (Altamura et al., 2010) (Liebman et al., 2011). These features include the following: short fine telangiectasias,

▲ **Figure 5a.1a** Clinical image of basal cell carcinoma.

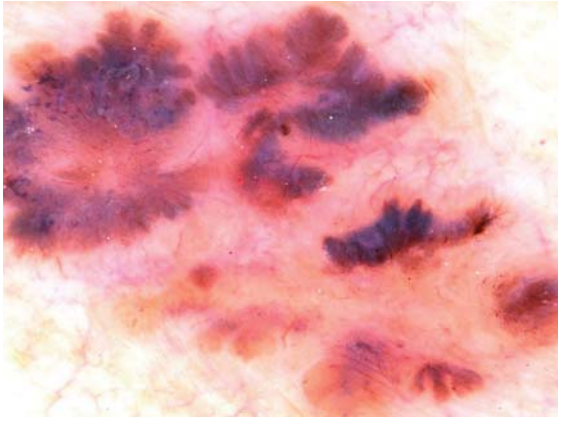
◀ **Figure 5a.1b** No pigment network, and the presence of large blue-gray ovoid nests and multiple blue-gray globules).

▲ **Figure 5a.2a** Clinical image of basal cell carcinoma on the shoulder.



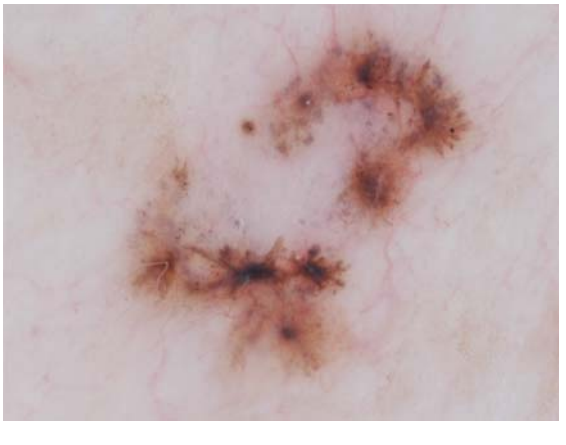
◀ **Figure 5a.2b** Dermoscopy image showing multiple blue-gray non-aggregated globules.

▲ **Figure 5a.3a** Clinical image of basal cell carcinoma.



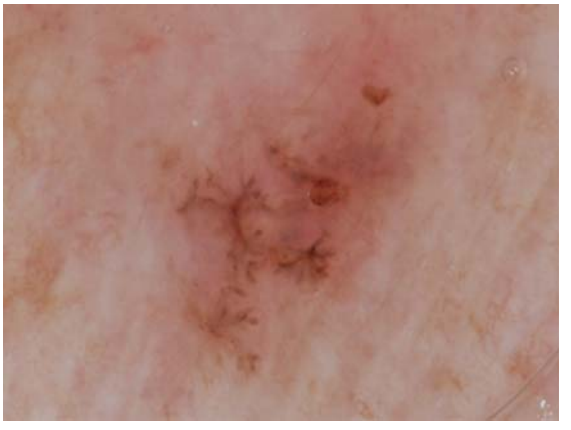
◀ **Figure 5a.3b** A pigmented lesion lacking a pigment network but possessing multiple leaf-like areas.

▲ **Figure 5a.4a** Clinical image of BCC.

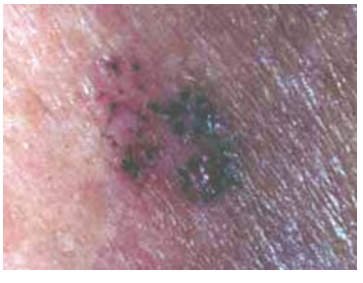


◀ **Figure 5a.4b** This BCC has leaf-like structures. One of the leaf-like structures is shaped like a large spoke-wheel. The extensions seen in BCC tend to be broad and fuzzy. They converge at a pigmented base area. Note that the base area does not appear to be connected to the center of the tumor and is located towards the periphery. The extensions converge at the base area and create a leaf-like structure. *Abbreviation*: BCC, basal cell carcinoma.

▲ **Figure 5a.5a** Clinical image of BCC.



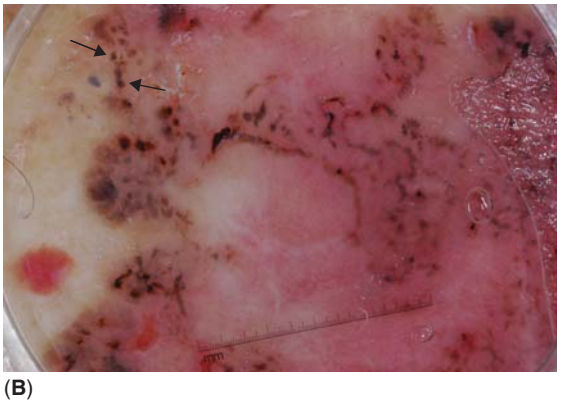
◀ **Figure 5a.5b** This BCC has leaf-like areas, which can be confused for melanocytic streaks. However, unlike melanocytic streaks, the prongs or extensions seen in leaf-like areas can be oriented in a direction pointing toward the main tumor mass—as shown in this case. In addition, as can be seen in this case, the BCC leaf-like extensions do not have to be present at the lesion's perimeter. *Abbreviation*: BCC, basal cell carcinoma.



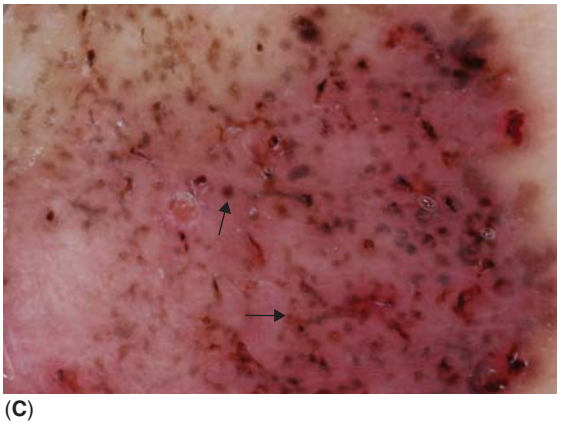
▲ **Figure 5a.6a** Clinical image of basal cell carcinoma.

◀ **Figure 5a.6b** Spoke-wheel-like areas.

(**A**)



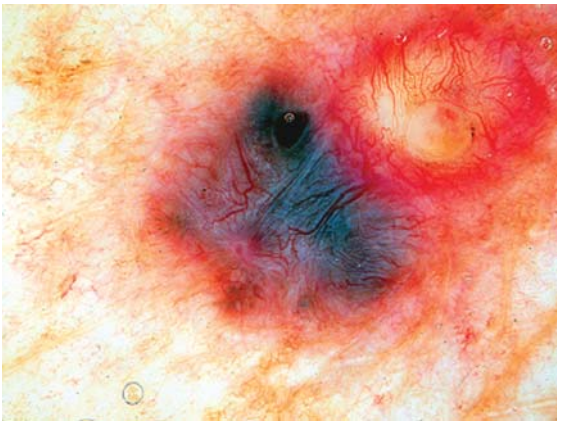
(**B**)



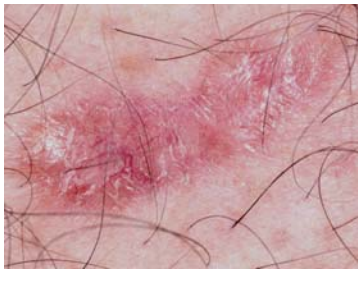
(**C**)

Figure 5a.7 (**A–C**) This pigmented superficial basal cell carcinoma has leaf-like areas, blue-gray globules, as well as brownish concentric globules, and shallow ulcerations with an orange hue. There are also ill-defined spoke-wheel-like structures, which appear as fuzzy globules with a central darker hub.

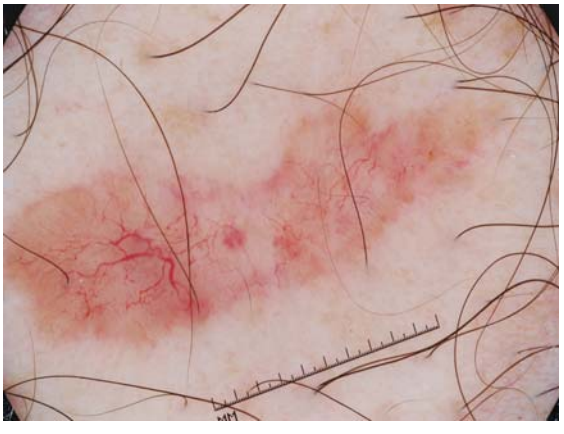
▲ **Figure 5a.8a** Clinical image of basal cell carcinoma.



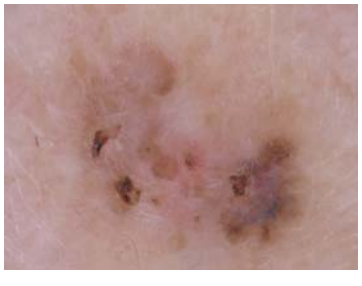
◀ **Figure 5a.8b** Arborizing telangiectasia.



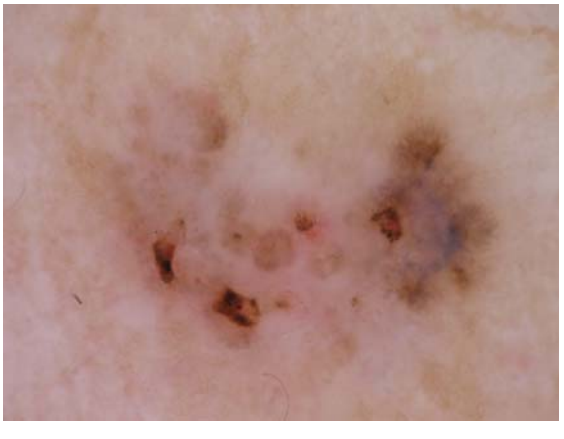
▲ **Figure 5a.9a** Clinical image of nonpigmented basal cell carcinoma.



◀ **Figure 5a.9b** Multiple arborizing blood vessels can be seen.



▲ **Figure 5a.10a** Clinical image of basal cell carcinoma.



◀ **Figure 5a.10b** Dermoscopy image showing multiple shallow serous crusted ulcerations and leaf-like areas. The serous crust manifests itself with an orange hue.

Table 5a.1 Sensitivity and Specificity of Dermoscopic Structures for Pigmented Basal Cell Carcinomas[a] (Menzies et al., 2000)

Features	Sensitivity (%)	Specificity (%)[b]
Large blue-gray ovoid nests	55	97/99
Arborizing telangiectasia	52	77/92
Multiple blue-gray globules	27	87/97
Ulceration	27	87/97
Leaf-like structures	17	100/100
Spoke-wheel-like structures	10	100/100

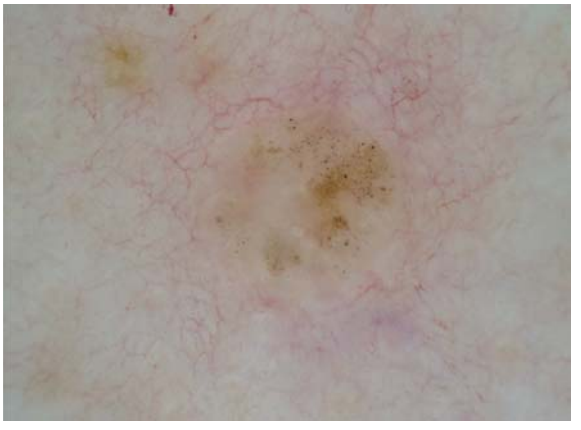
[a]The diagnosis of a pigmented BCC is made when a lesion lacks a pigment network and has one or more of the specific features tabled. This method gives a sensitivity of 93% and specificity of 89–92% for the diagnosis of pigmented BCC.
[b]The specificity represents the percentage of melanomas (left number) or benign pigmented skin lesions (right number) lacking that feature.
Abbreviation: BCC, basal cell carcinoma.

multiple small and shallow erosions with or without crust, concentric structures/globules (variant of spoke-wheel), multiple in-focus brown to blue-gray dots (Fig. 5a.11), and shiny white areas/crystalline structures. All of the aforementioned structures can be seen with both polarized and nonpolarized dermoscopy except for shiny white areas, which can only be appreciated with polarized dermoscopy (Fig. 5a.12).

NONPIGMENTED BASAL CELL CARCINOMAS

Dermoscopic characterization of nonpigmented BCCs has lagged behind that of pigmented BCCs. It was not until the arrival of polarized dermoscopes that dermoscopists began to appreciate the key features associated with nonpigmented BCCs, such as small caliber-sized blood vessels and stromal changes reflected as shiny white areas under polarized dermoscopy. Although these structures can also be seen in pigmented BCCs, their presence in nonpigmented BCCs is crucial for diagnosis. In addition to arborizing blood vessels and ulceration, the other key dermoscopy features

▲ **Figure 5a.11a** Clinical image of a BCC.



◀ **Figure 5a.11b** The predominant dermoscopic structures in this BCC are the presence of multiple brown dots.

(**A**)

(**B**)

(**C**)

Figure 5a.12 (**A**) Non-polarized dermoscopy image of a BCC revealing multiple erosions. (**B**) Polarized dermoscopy image of BCC with a contact glass plate; the crystalline structures/white shiny areas are clearly visible. (**C**) Polarized non-contact dermoscopy image revealing the crystalline structures and the vascular blush commonly seen in malignancies

▲ **Figure 5a.13a** Clinical image of BCC.

◀ **Figure 5a.13b** Dermoscopy image revealing shiny white chrysalis-like structures and a pink blush. The scattered global vascular pattern shows vessels in a loose haphazard distribution in all directions. Small fine telangiectasia are seen, which can include arborizing microvessels. At times this BCC pattern can be difficult to impossible to differentiate from amelanotic melanoma. This dermoscopic image was obtained with polarized light. *Abbreviation*: BCC, basal cell carcinoma.

▲ **Figure 5a.14a** Clinical image of nonpigmented nodular basal cell carcinoma.

◀ **Figure 5a.14b** Dermoscopy image shows large diameter arborizing blood vessels and shiny white areas.

▲ **Figure 5a.15a** Clinical image of superficial nonpigmented basal cell carcinoma.

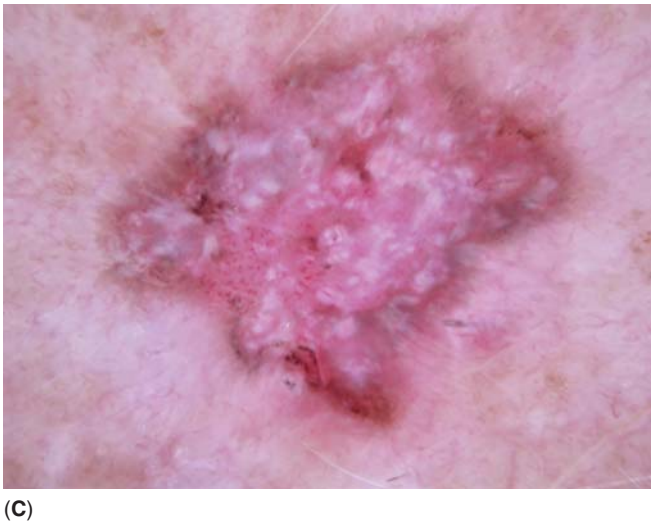
◀ **Figure 5a.15b** Dermoscopy image shows shiny white areas and milky pink areas. Shallow ulcerations and small fine telangiectasias can also be seen. This dermoscopic image was obtained with polarized light.

of nonpigmented BCCs include (Felder et al., 2006; Giacomel & Zalaudek, 2005; Pan et al., 2008):

1. Scattered vascular global pattern, where vessels are seen in a loose haphazard distribution in all directions. This pattern has been reported to occur in 97% of superficial BCCs (Fig. 5a.13).
2. Shiny white to red structureless and milky pink areas, often found in superficial BCC (Fig. 5a.14 and Fig. 5a.15) (Scalvenzi et al., 2008; Felder et al., 2006; Giacomel & Zalaudek, 2005). This feature appears as a dull white structureless area under nonpolarized dermoscopy (Fig. 5a.16) (Marghoob et al., 2009). Under polarized dermoscopy it appears as shiny white or pink areas with or without chrysalis-like structures (Fig. 5a.16c).
3. Small fine telangiectasia (SFT) in superficial BCC (Fig. 5a.15). These are fine, kinked vessels of small caliber with length <1 mm. Unlike the larger arborizing vessels found in more invasive BCC, SFT have few branches, and are distributed irregularly within the whitish area. These vessels have also been termed as "arborizing microvessels" and "small atypical red vessels." The latter are small irregular linear and circular structures that do not take a particular shape or pattern.
4. Corkscrew vessels (Fig. 5a.17). These were found in 52% of superficial BCCs. It is unclear whether these are similar to the corkscrew vessels found in melanoma (particularly in cutaneous metastases).

(**A**)

(**B**)



(**C**)

Figure 5a.16 (**A**) Clinical image of a BCC. (**B**) This partially pigmented basal cell carcinoma reveals a dull white structureless area in the center when viewed with non-polarized dermoscopy. (**C**) Under polarized dermoscopy the dull white area now reveals shiny white and pink areas. In addition, rosette (chap. 5b) (Cuellar et al., 2009) and chrysalis-like structures can also be seen.

▲ **Figure 5a.17a** Clinical image of basal cell carcinoma.

◀ **Figure 5a.17b** Dermoscopy image revealing a few tortuous corkscrew blood vessels. Similar vessels can be seen in cutaneous melanoma metastasis, nodular melanoma, and desmoplastic melanoma.

Key Points

1. BCC do not have network, pseudopods or brown aggregated globules.
2. The key positive features of pigmented BCC include: large blue-gray ovoid nests, multiple blue-gray non-aggregated globules, leaf-like structures, spoke-wheel-like structures, arborizing telangiectasia, and ulceration.
3. Additional features that can assist in diagnosing BCC include the presence of multiple erosions with or without serous crust, multiple in-focus brown dots, short fine telangiectasia, and shine white areas/crystalline structures.
4. The key features of non-pigmented BCC include short fine or arborizing telangiectasia, shallow erosions and shiny white areas.
5. At times it can be very difficult to differentiate a pigmented BCC from melanoma. The leaf-like projections can sometimes mimic streaks seen in melanoma. In addition, the blue-gray globules in BCC can sometimes have a brown color and resemble irregular globules seen in melanoma. However, with experience, most of the time it is possible to differentiate BCC from melanoma (see table below). Although errors in clinically differentiating some BCCs and melanomas from each other exist, it has no impact on clinical management since a biopsy will be preformed regardless of whether the clinical diagnosis is correct or incorrect between BCC and melanoma.

	BCC	Melanoma / CMN / Spitz
Globules	• Blue-gray (sometimes brown) • Not aggregated • Tend not to be present within a brown background • Usually see other BCC features such as arborizing vessels	• Browns & black (sometimes blue) present in a brown background • Usually aggregated • Usually see other melanocytic features such as network
Streaks	• Fuzzy • Some radiate towards tumor mass • Tend to converge in focal area towards the periphery creating leaf-like structures • central part of lesion often white / hypopigmented / structureless	• Sharper in focus • Always radiate away from tumor mass • Tend to converge towards the geometric center of the lesion • the center of the lesion is usually pigmented/ hyperpigmented and has a blue-white veil

REFERENCES

Altamura D., Menzies S.W., Argenziano G., et al., 2010, Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *J Am Acad Dermatol*, 62, 67–75.

Cuellar, F., Vilalta, A., Puig, S., et al., 2009, New dermoscopic pattern in actinic keratosis and related conditions. *Arch Dermatol*, 145, 732.

Felder, S., Rabinovitz, H., Oliviero, M. & Kopf, A., 2006, Dermoscopic differentiation of a superficial basal cell carcinoma and squamous cell carcinoma in situ. *Dermatol Surg*, 32, 423–5.

Giacomel, J. & Zalaudek, I., 2005, Dermoscopy of superficial basal cell carcinoma. *Dermatol Surg*, 31, 1710–13.

Liebman T.N., Lopez N.J., Balagula Y., et al., 2011, Dermoscopic Features of Basal Cell Carcinomas: Differences in Appearance Under Non-Polarized and Polarized Light. *Dermatol Surg*.

Marghoob, A.A., Cowell, L., Kopf, A.W. & Scope, A., 2009, Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*, 145, 618.

Menzies, S.W., 2002, Dermoscopy of pigmented basal cell carcinoma. *Clin Dermatol*, 20, 268–9.

Menzies, S.W., Westerhoff, K., Rabinovitz, H., et al., 2000, Surface microscopy of pigmented basal cell carcinoma. *Arch Dermatol*, 136, 1012–16.

Miller, D.L. & Weinstock, M.A., 1994, Nonmelanoma skin cancer in the United States: incidence. *J Am Acad Dermatol*, 30, 774–8.

Pan, Y., Chamberlain, A.J., Bailey, M., et al., 2008, Dermatoscopy aids in the diagnosis of the solitary red scaly patch or plaque-features distinguishing superficial basal cell carcinoma, intraepidermal carcinoma, and psoriasis. *J Am Acad Dermatol*, 2008; 59: 268–74.

Peris, K., Altobelli, E., Ferrari, A., et al., 2002, Interobserver agreement on dermoscopic features of pigmented basal cell carcinoma. *Dermatol Surg*, 28, 643–5.

Scalvenzi, M., Lembo, S., Francia, M.G. & Balato, A., 2008, Dermoscopic patterns of superficial basal cell carcinoma. *Int J Dermatol*, 47, 1015–18.

5b Actinic keratosis, Bowen's disease, keratoacanthoma, and squamous cell carcinoma

Iris Zalaudek, Alan Cameron, and Cliff Rosendahl

INTRODUCTION

The spectrum of premalignant and malignant keratinizing tumors comprises actinic (solar) keratosis (AK), Bowen's disease (BD), keratoacanthoma (KA), and squamous cell carcinoma (SCC). Although pigmented variants do exist, the great majority of these tumors are nonpigmented, meaning their dermoscopic diagnosis is based mainly on the assessment of vascular patterns. Other associated, but nonspecific features, such as erythema, scale, erosion, or keratin, may provide further clues to the diagnosis (Argenziano et al., 2004; Kreusch & Koch, 1996; Kreusch & Rassner, 1990). In contrast to the well-defined dermoscopic criteria of pigmented tumors, dermoscopic features of nonpigmented keratinizing tumors are less well established (Mogensen & Jemec, 2007). Although the utility of vascular patterns in the diagnosis of nonpigmented tumors has been recognized for some time (Kreusch & Rassner, 1990), their assessment has gained more importance in recent years. This may in part reflect technical improvements in the ability to visualize blood vessels under dermoscopy.

When using contact dermoscopy, pressure applied to the contact plate may compress blood vessels, thereby rendering the vessel invisible. Using a viscous immersion medium, such as ultrasound gel permits examination of lesions without excessive pressure being applied to the contact plate, which, in turn, enhances our ability to visualize vascular structures. However, the development of polarized light dermoscopy instruments that can be used without the need to directly contact the skin has eliminated the effect of pressure-induced compression of blood vessels. This in turn has provided us with an excellent method for analyzing the superficial cutaneous vascular architecture.

Before discussing the dermoscopic features of specific keratinizing tumors, it is important to acknowledge the following points.

- Most of the described dermoscopic patterns of AK, BD, KA, and SCC are based on case series and these patterns have not yet been formally evaluated for their diagnostic specificity and sensitivity.
- These tumors may be viewed as a spectrum of keratinocyte dysplasia. Therefore, the clinical and dermoscopic features of the various keratinizing tumors do show some overlap.
- There are many competing (and sometimes contradictory) terms used to describe vascular structures, which are often introduced in an ad hoc fashion. This may cause confusion, particularly for beginners in dermoscopy. We will use the terms defined in a recent study (Argenziano et al., 2004), and will additionally provide a new geometric classification system, introduced by Kittler and co-workers (Kittler et al., 2008) (chap. 6h). The definitions are summarized in Table 5b.1. For patterns not included in either of these systems, we will use the terms as originally described.
- Diagnosis based on vessel morphology is considerably less specific than diagnosis based on assessment of other dermoscopic structures because the same vessel morphology may be found in different tumor types, and even in inflammatory lesions. However, assessing the arrangement and distribution of vessels within the lesion may provide improved specificity. For example, BD, stasis dermatitis, and psoriasis may all contain glomerular (coiled) vessels. However, in BD the vessels are typically arranged focally in small clusters or groups, whereas in the latter entities the vessels are regularly distributed throughout the lesion. Therefore, the diagnosis of nonpigmented skin lesions is often based on the following: (*i*) clinical assessment (e.g., texture, firmness), (*ii*) assessment of vascular morphology, (*iii*) assessment of architectural arrangement and distribution of vessels, and (*iv*) assessment of additional criteria (e.g., scale, rosette structure (Zalaudek et al., 2006a; Zalaudek et al., 2006b)

NONPIGMENTED ACTINIC KERATOSIS

Nonpigmented AK on the face show four dermoscopic features (the so-called strawberry pattern): (*i*) A background erythema sparing the hair follicles and resembling a pink-to-red "pseudonetwork" (white circles on a red background) (Fig. 5b.1), (*ii*) white-to-yellow surface scale, (*iii*) fine, wavy vessels (straight or coiled) surrounding the hair follicles, and (*iv*) hair follicle openings surrounded by a white halo and filled with a yellowish keratotic plug (white circle surrounding a yellow clod) (Fig. 5b.2) (Zalaudek et al., 2006b; Peris et al., 2007a).

On nonfacial skin, AK usually exhibits (Zalaudek et al., 2012) nonspecific patterns with features, such as surface scale and keratin, and sometimes dotted vessels (Fig. 5b.3).

An additional clue to the diagnosis of AK is the rosette sign, which can only be seen with polarized light (Cuellar et al., 2009).The rosette sign consists of a white four-leaf clover-shaped structure (Fig. 5b.4). It probably represents an optical effect of polarized light interacting with follicular openings that contain orthokeratosis and parakeratosis. Although the rosette sign can be seen in actinic damaged skin and in tumors such as basal cell carcinoma (BCC) (Fig. 5a.14c) and melanoma, they are more commonly encountered in AK and thin SCCs (Cuellar et al., 2009).

PIGMENTED ACTINIC KERATOSIS

Pigmented variants of AK (pAK) are less common than nonpigmented AK, and in our experience occur more often in darker skin phototypes. Both clinically and dermoscopically the structures seen in pAK may overlap with those visualized in lentigo maligna (LM) and include asymmetric pigmented follicular openings, annular–granular pattern, and rhomboidal structures (Schiffner et al., 2000; Stolz et al., 2002). Differentiating some pAK from LM may only be possible via palpation; pAK having a rough texture as compared with a smooth texture in LM. Dermoscopically, a diagnosis of pAK is supported by the presence of a prominent pseudonetwork located between keratin-filled ostial openings; a finding rarely seen in LM (Fig. 5b.5) (Peris et al., 2007b; Pock et al., 2007; Zalaudek et al., 2006b). In addition, dermoscopy of LM may reveal a darker dot located within ostial openings (some call this the isobar sign); a finding rarely seen in pAK (Fig. 5b.6).

Although dermoscopy cannot reliably differentiate pAK from LM, it may help guide the best location to biopsy. Biopsying areas revealing the most suspicious features, such as annular–granular structures, asymmetric follicular openings, dots within the ostial openings, or rhomboidal structures, may provide the pathologist with the most diagnostically relevant tissue to examine (Fig. 5b.7) (Bauer et al., 2006).

NONPIGMENTED BOWEN'S DISEASE

BD represents SCC in situ of the skin, also known as intraepidermal carcinoma. The archetypal dermoscopic pattern of BD is one of surface scale and glomerular (coiled) vessels, arranged in focal clusters

Table 5b.1 Definitions of the Different Morphologic Types of Vessels Associated with Keratinizing Tumors, Including Actinic Keratosis, Bowen's Disease, Keratoacanthoma, and Squamous Cell Carcinoma

Argenziano et al., 2004	Definition	Kittler et al., 2008	Definition
Dotted	Tiny red dots densely aligned next to each other	Dots	Vessels appear as tiny round spots not extending in any direction (no length and no breadth)
Glomerular	Variation on the theme of dotted vessels. They are tortuous capillaries often distributed in clusters mimicking the glomerular apparatus of the kidney	Coiled	Vessels appear as lines compactly convoluted
Hairpin	Vascular loops sometimes twisted and bending, usually surrounded by a whitish halo when seen in keratinizing tumors	Looped	Vessels appear as lines with one major bend, which is sharp (180°) and results in a reversal of direction (U-turn)
Linear–irregular	Linear, irregularly shaped, sized and distributed red structures	Straight	Vessels appear as lines without a bend
		Serpentine	Vessels appear as lines with more than one bend (in a snake-like fashion)
Strawberry	Erythema resembling a marked pink-to-red "pseudonetwork" around the hair follicles intermingled with fine, linear-wavy vessels surrounding the hair follicles. Often hair follicle openings filled with yellowish keratotic plugs surrounded by a white halo are additionally presented	Red and/or white circles surrounding yellow clods	A circle is a curved line equidistant from a central point; clods are well circumscribed, solid objects larger than dots that may take any shape
Polymorphous	Any combination of two or more different types of vascular structures. The most frequent is that one occurring between linear-irregular and dotted vessels	Monomorphous	One vascular pattern dominates by far
		Polymorphous	Two or more vascular patterns are present

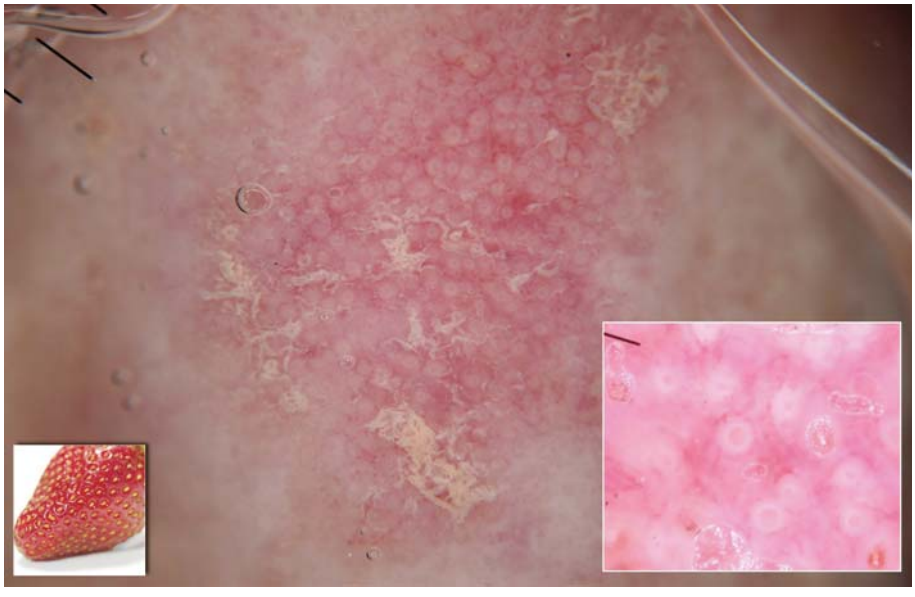


Figure 5b.1 Nonpigmented facial actinic keratosis showing the strawberry pattern, which consists of background erythema that is interrupted by multiple small keratin filled follicular ostia (red and white circles with a central yellow clod). In addition, surface scale is visible. At higher magnification, coiled vessels around the hair follicle ostia can often be seen (inset on right).

(Fig. 5b.8) (Bugatti et al., 2007; Bugatti et al., 2004; Stante et al., 2004; Zalaudek & Argenziano, 2004; Zalaudek et al., 2004; Zalaudek et al., 2006a). The simultaneous finding of surface scale and focal clusters of glomerular vessels has been reported to give a 98% diagnostic probability that the lesion in question is BD (Pan et al., 2008) (Fig. 5b.9).

Although it is easy to see glomerular vessels clearly during the face-to-face examination, it is often difficult to capture their coiled morphology on images. Due to their small size, lack of contrast, and camera resolution these glomerular vessels usually appear in images as irregular to roundish, loosely packed, fuzzy red globular structures or as dots (Fig. 5b.10). Thus, when analyzing images, these glomerular vessels can be confused for dotted vessels as seen in melanocytic skin tumors, such as Spitz nevi. The focal, clustered, asymmetric distribution of the vessels in BD *versus* the symmetric distribution of vessels in spitzoid neoplasms may help differentiate these entities (Fig. 5b.11) (Argenziano et al., 2004; Zalaudek et al., 2006a; Zalaudek et al., 2006b).

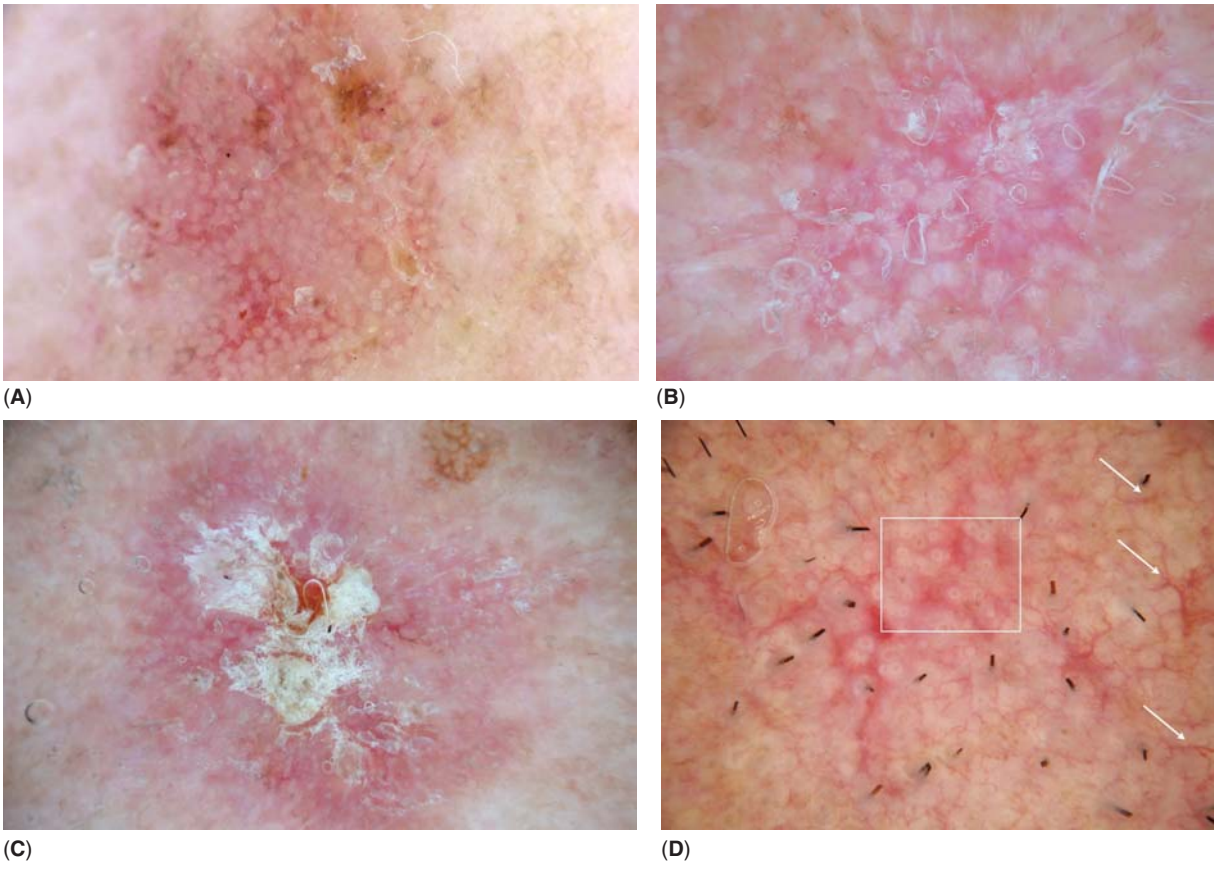


Figure 5b.2 Dermoscopy of nonpigmented facial actinic keratosis typically reveals a red pseudonetwork (red circles) (**A, B**), surface scale (**C**) and keratin-filled hair follicle ostia, which appear as targetoid white-to-yellow roundish structures (**D**, in square) that are surrounded by erythema. The elongated teleangiectasia (**D**, arrows) are the normal vessels of the dermal plexus visible through the thinned, actinically damaged skin.

Figure 5b.3 Dermoscopy of actinic keratosis that are not located on the face often reveal nonspecific features, such as hyperkeratosis.

PIGMENTED BOWEN'S DISEASE

Pigmented Bowen's disease (pBD) is encountered less frequently than its nonpigmented counterpart and it is more common in darker skin phenotypes. In our analysis of more than 50 consecutive cases, (Cameron et al., 2010) the following dermoscopic patterns were found in pBD: (*i*) brown or grey dots (these dots are a strong clue when arranged as linear radial lines at the periphery of the lesion Fig. 5b.12); (*ii*) pink or skin colored eccentric structureless areas (Fig. 5b.13); and (*iii*) glomerular (coiled) vessels, arranged randomly, as clusters, or in radial lines (Figs. 5b.12, 5b.13).

Occasionally, pBD may mimic melanoma (Fig. 5b.13). Features that support a diagnosis of pBD are the presence of an adherently scaly surface, and the presence of dermoscopically brown or grey dots arranged in linear radial lines at the periphery, and focal glomerular (coiled) vessels. In contrast, the brown/gray dots in melanoma do not follow any pattern and the blood vessel morphology usually consists of dotted (red dots) or polymorphous vessels.

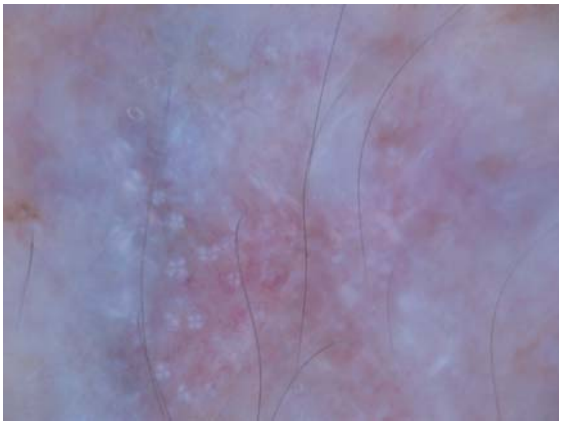
BOWENOID ACTINIC KERATOSIS

The Bowenoid actinic keratosis is one that reveals nearly full thickness dysplasia of keratinocytes histologically. Not surprisingly, its dermoscopic appearance is similar to that of Bowen's disease (Fig. 5b.14). However, in our experience the glomerular vessels in Bowenoid actinic keratosis tend to be regularly distributed and not arranged in focal clusters as seen in classic Bowen's disease.

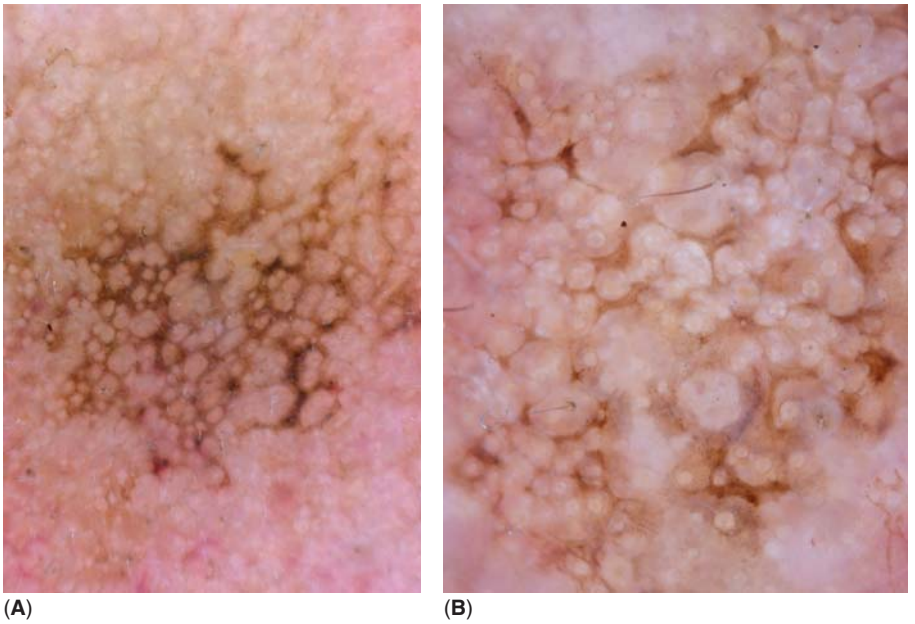
KERATOACANTHOMA

KA is considered to be a well-differentiated variant of SCC. It is distinguished by its clinical course of initial rapid growth followed by spontaneous involution over a period of a few months. Dermoscopically, KA is characterized by a central yellowish to brownish structureless mass of keratin, which is typically surrounded by elongated and sometimes thick telangiectasias. The vessel morphology may be hairpin (looped) or linear–irregular (serpentine or branched serpentine). A white-to-yellow background halo (Figs. 5b.15 and 5b.16) usually surrounds these blood vessels. Glomerular (coiled) vessels may also be seen (Kreusch & Koch, 1996; Kreusch, 2002; Argenziano et al., 2004). These well differentiated squamous neoplasms often reveal pearl like structures surrounded by a white circle (Fig 5b.16).

▲ **Figure 5b.4a** This is a clinical image of an actinic keratosis with focal transition to squamous cell carcinoma in situ

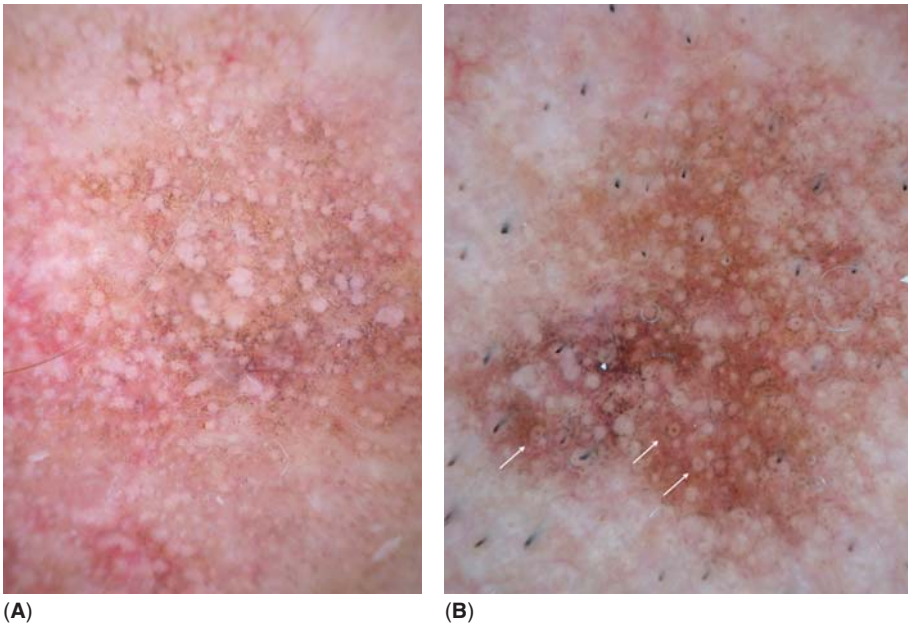


◀ **Figure 5b.4b** Under dermoscopy multiple rosettes consisting of white four-leafed clover-shaped structures can be seen. The rosette sign can only be seen with polarized light dermoscopy.



(**A**) (**B**)

Figure 5b.5 Typical dermoscopic appearance of pigmented facial actinic keratosis showing polygonal lines forming rhomboidal structures (**A**); and superficial pseudonetwork characterized by thickened brown short lines between keratin-filled hair follicles of irregular size (**B**).



(**A**) (**B**)

Figure 5b.6 Side-by-side comparison between (**A**) pigmented actinic keratosis and (**B**) lentigo maligna. Both tumors show multiple small gray dots (annular–granular pattern). Note that the hair follicle openings of the actinic keratosis lack the central black dot (also known as the isobar sign) as seen in the case of lentigo maligna (arrows).

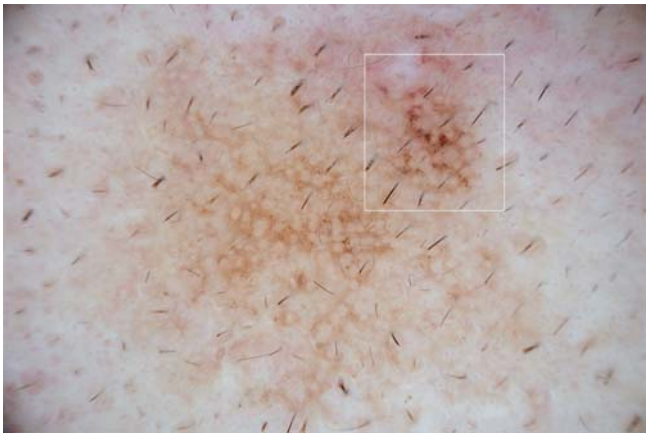


Figure 5b.7 Dermoscopy may help guide biopsy of equivocal cases. The most suspicious area under dermoscopy is the one showing enhanced gray brown annular–granular pattern (square). The biopsy was therefore taken from this area. The histopathologic diagnosis was pigmented actinic keratosis.

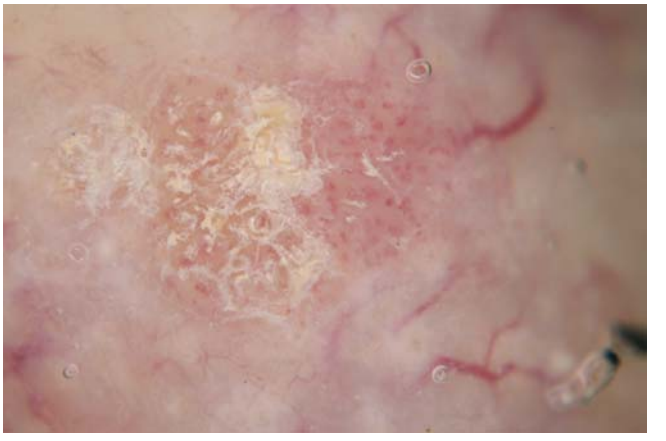


Figure 5b.9 Glomerular (coiled) vessels or a combination of the former with hairpin (looped vessels) and surface scale are frequently seen in squamous cell carcinoma in situ.

▲ **Figure 5b.8a** Clinical image of Bowen's disease. Notice the adherent surface scale.

(**B**)

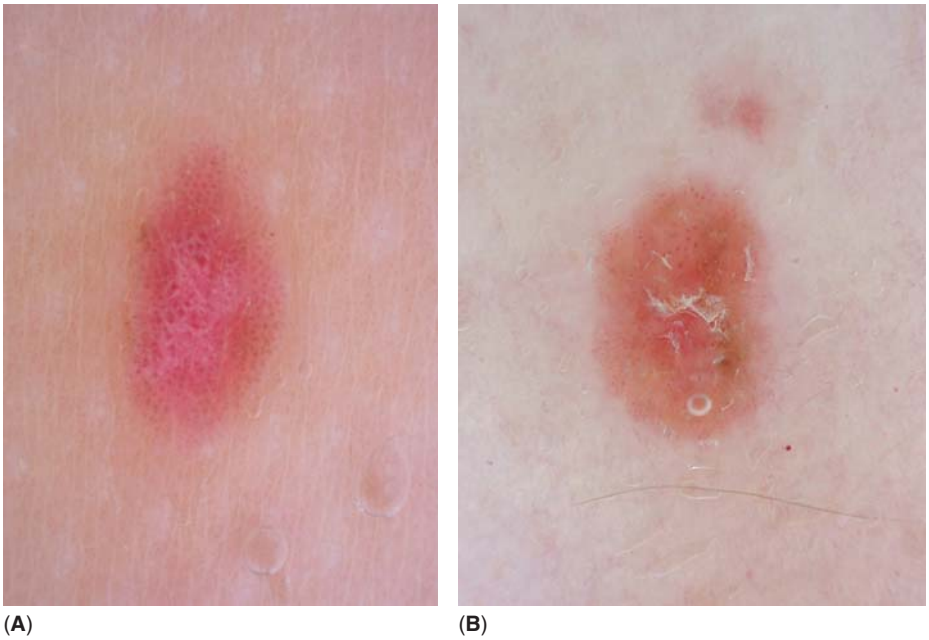
(**C**)

◀ **Figure 5b.8b** Dermoscopy reveals numerous different blood vessel morphologies; however, the archetypal vessel morphology is the glomerular (coiled) type as highlighted in the magnification in **C**.

▲ **Figure 5b.10a** Clinical image of Bowen's disease.

◀ **Figure 5b.10b** Dermoscopy of Bowen's disease shows surface scale and glomerular vessels (coiled vessels) arranged in focal clusters.

◀ **Figure 5b.10c** Higher magnification of glomerular (coiled) vessels surrounded by a white halo.



(**A**) (**B**)

Figure 5b.11 Comparison of (**A**) nonpigmented Spitz nevus and (**B**) Bowen's disease. Although at 10-fold magnification the vessels in both tumors appear as dots, they are homogenously distributed in the Spitz nevus, whereas they appear a little larger and clustered in Bowen's disease. Additional clues to the correct diagnosis include the reticular depigmentation (negative network) and chrysalis lines in the Spitz nevus and the surface scale in Bowen's disease.

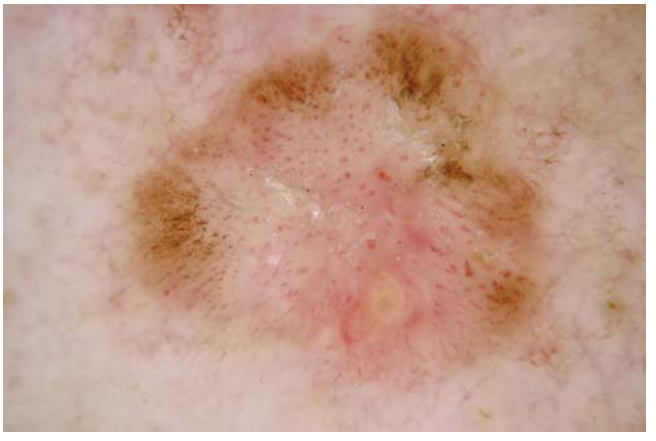


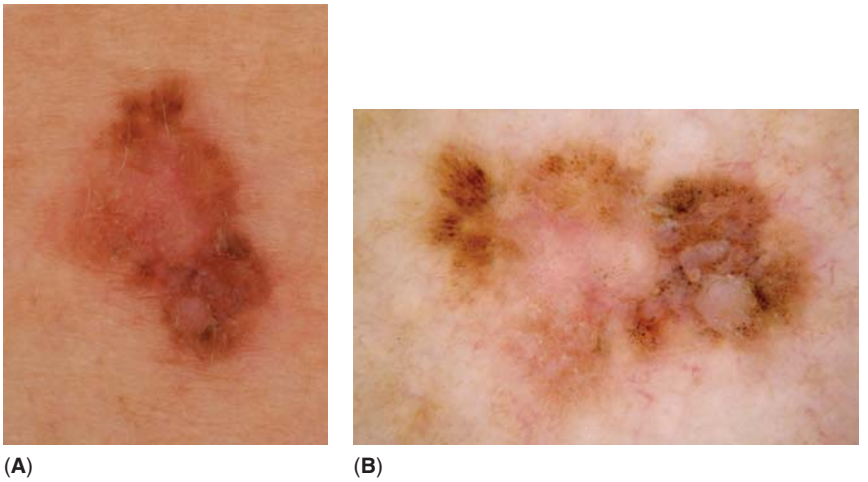
Figure 5b.12 Partially pigmented Bowen's disease showing clustered glomerular (coiled) vessels and small brown globules and dots at the periphery arranged in a radial (linear) configuration within a homogenous light brown background.

INVASIVE SQUAMOUS CELL CARCINOMA

Invasive scc typically reveals a central mass of keratin and ulceration surrounded by hairpin vessels, linear-irregular vessels and targetoid hair follicles (also called white circles) over a white structureless area (Zaladek et al., 2012). In our experience, invasive SCC frequently exhibits vessel patterns similar to KA. Hairpin (looped), dotted, glomerular (coiled) and linear–irregular vessels (serpentine) are seen and they are often surrounded by a whitish background halo (Figs. 5b.17–5b.19). Combinations of these vascular morphologies result in the so-called polymorphous pattern. Ulceration and blood crusts, if present, appear as irregularly distributed reddish-orange to brownish to black blotches on the surface of the tumor (Felder et al., 2006; Pan et al., 2008). Furthermore, invasive SCC often arises in association with AK and therefore, it is not surprising that the strawberry pattern described for AK can be seen adjacent to and contiguous with the SCC (Fig. 5b.20).

PIGMENTED INVASIVE SQUAMOUS CELL CARCINOMA

Pigmented invasive SCC is rare and reveals dermoscopically a diffuse, homogeneous blue pigmentation with distinct, irregularly distributed,



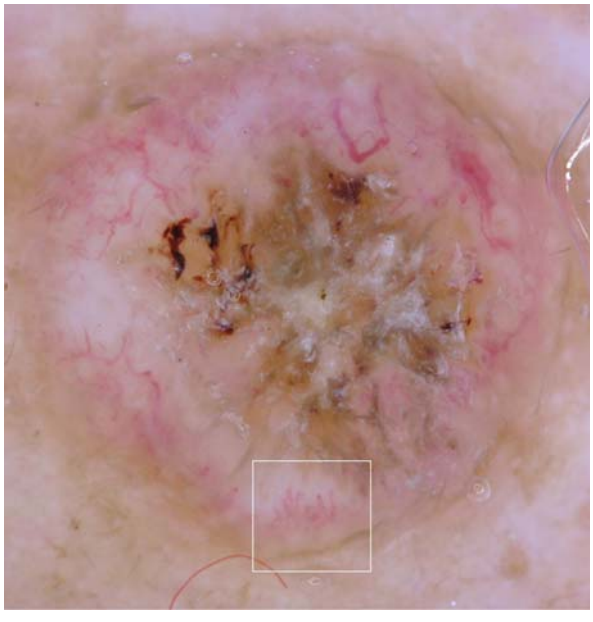
(**A**) (**B**)

Figure 5b.13 (**A**) Pigmented lesion suggestive for melanoma. Note, however, that the lesion has surface scale; (**B**) dermoscopy reveals brown dots arranged in radial lines, an eccentric pink structureless zone and monomorphic glomerular (coiled) vessels. Histopathology confirmed the diagnosis of pigmented Bowen's disease.

▲ **Figure 5b.14a** Clinical image of a Bowenoid actinic keratosis.

◀ **Figure 5b.14b** Dermoscopic features of Bowenoid actinic keratosis showing glomerular (coiled) vessels of irregular size that are uniformly distributed.

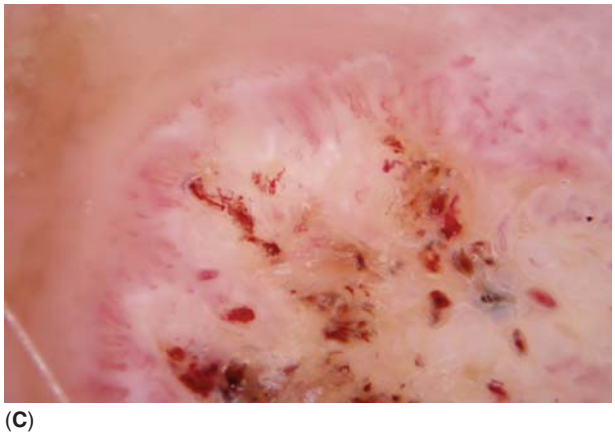
▲ **Figure 5b.15a** Clinical image of a keratoacanthoma.



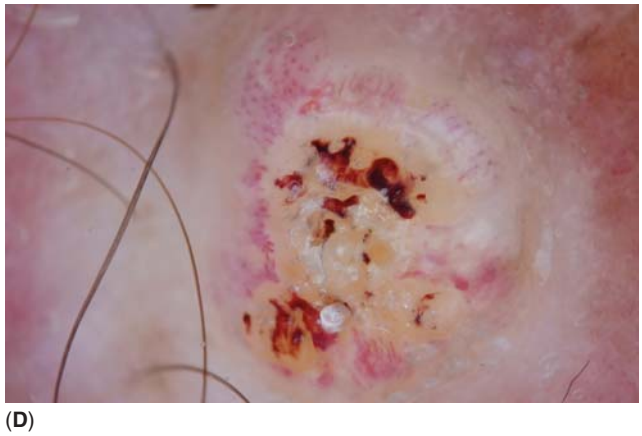
◀ **Figure 5b.15b** Dermoscopic features of keratoacanthoma. While clinically the central crust is easy to identify, only dermoscopy allows the visualization of large linear irregular vessels (also known as serpentine branched) and hairpin (also known as looped) vessels (square) on a white background.

(**A**)

(**B**)



(**C**)



(**D**)

Figure 5b.16 Dermoscopy of keratoacanthoma is quite repetitive and characterized by a central keratin crust surrounded by linear vessels of different caliber. Although looped and serpentine vessels are most common in KA, dotted (red dots) or glomerular (coiled) vessels can also be seen on occasion (**D**). In addition, keratin pearl-like structures and white circles, which often surround these pearl-like structures can often be seen (**B**).

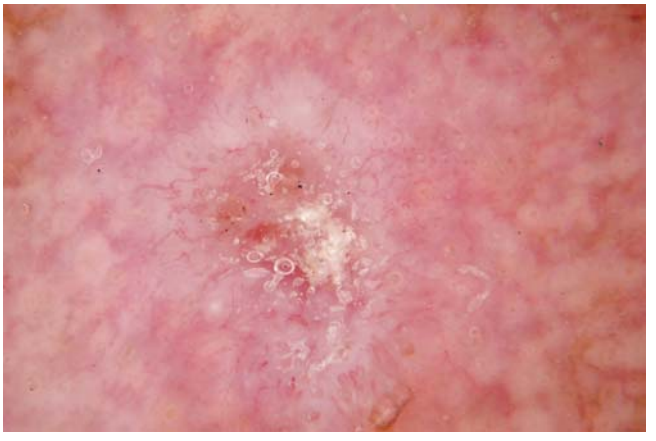


Figure 5b.17 Invasive squamous cell carcinoma showing scale-crust and polymorphous vascular morphologies, including linear–irregular or serpentine, hairpin or looped, and dotted vessels. The individual blood vessels appear on a white background.

Figure 5b.18 Minimal invasive squamous cell carcinoma at a higher magnification, showing polymorphism of vascular structures. In addition, targetoid appearing keratin-filled follicular ostia are apparent.

Figure 5b.19 Poorly differentiated invasive squamous cell carcinoma showing irregularly distributed and irregularly shaped hairpin or looped vessels (arrows) and glomerular or coiled vessels (circle) on a mainly white-to-yellow structureless background.

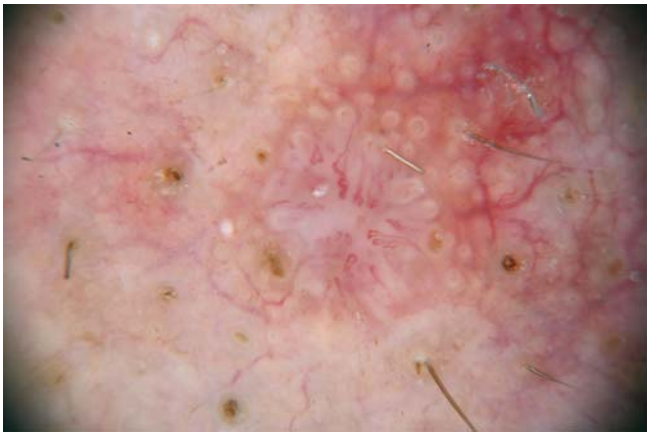


Figure 5b.20 Minimally invasive squamous cell carcinoma arising in association with an actinic keratosis. Elongated hairpin (looped) vessels are seen in the SCC; the adjacent skin to the right shows the typical "strawberry" (white circles) pattern of actinic keratosis.

Key Points

1. Four factors to evaluate when attempting to diagnose nonpigmented tumors:
   (*i*) clinical features, such as the presence of adherent surface scale
   (*ii*) dermoscopic morphology of vascular structures
   (*iii*) architectural arrangement and distribution of vessels seen under dermoscopy
   (*iv*) additional dermoscopic criteria, such as the rosette sign or strawberry pattern
2. Common vascular structures and patterns encountered in keratinizing tumors
   (*i*) hairpin (looped) vessels with a whitish halo
   (*ii*) glomerular (coiled) vessels
   (*iii*) linear–irregular (serpentine)
   (*iv*) dotted
   (*v*) strawberry-red pseudonetwork (white circles on a red background)
   (*vi*) polymorphous
3. Nonpigmented actinic keratosis on the face typically reveals a "strawberry" pattern composed of background erythema that spares the hair follicles (ostial openings). This results in a pink-to-red "pseudonetwork" (white circles on a red background). In addition, white-to-yellow surface scale, blood vessels (straight or coiled) surrounding the hair follicles and hair follicle openings surrounded by a white halo and filled with a yellowish keratotic plug (targetoid appearance) all contribute to the strawberry appearance of these AKs.
4. Nonpigmented Bowen's disease is characterized by glomerular (coiled) vessels, which are typically arranged focally in small clusters.
5. KA shows a central keratin crust surrounded by elongated hairpin (linear looped) or linear irregular (linear straight or serpentine) vessels. These reddish blood vessels typically develop on white background skin, which gives the appearance that the vessels are surrounded by whitish halos.
6. SCC shows similar features to those seen in KA. Common features include keratin crust and polymorphous vessels, including linear–irregular or serpentine, hairpin or looped, glomerular or coiled, and dotted morphologies.
7. Pigmented variants of keratinizing tumors can be difficult to differentiate from melanoma.

blue-gray granular structures. If ulcerated, dark brown to black crusts are visible. Due to the pigmentation, vessels are usually not seen (Zalaudek & Argenziano, 2004; Zalaudek et al., 2004). The differential diagnosis includes pigmented BCC and melanoma.

REFERENCES

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Bauer, J., Leinweber, B., Metzler, G., et al., 2006, Correlation with digital dermoscopic images can help dermatopathologists to diagnose equivocal skin tumours. *Br J Dermatol*, 155, 546–51.

Bugatti, L., Filosa, G. & De Angelis, R., 2004, Dermoscopic observation of Bowen's disease. *J Eur Acad Dermatol Venereol*, 18, 572–4.

Bugatti, L., Filosa, G. & De Angelis, R., 2007, The specific dermoscopical criteria of Bowen's disease. *J Eur Acad Dermatol Venereol*, 21, 700–1.

Cameron A., Rosendahl C., Tschandl P., Riedl E., Kittler H., 2010, Dermatoscopy of pigmented Bowen's disease. *J Am Acad Dermatol*, 62, 597–604.

Cuellar, F., Vilalta, A., Puig, S., et al., 2009, New dermoscopic pattern in actinic keratosis and related conditions. *Arch Dermatol*, 145, 732.

Felder S., Rabinovitz H., Oliviero M., Kopf A., 2006, Dermoscopic differentiation of a superficial basal cell carcinoma and squamous cell carcinoma in situ. *Dermatol Surg*, 32, 423–5.

Kittler, H., Riedl, E., Rosendahl, C. & Cameron, A., 2008, Dermatoscopy of unpigmented lesions of the skin: a new classification of vessel morphology based on pattern analysis. *Dermatopathol Pract Conc*, 14, 4.

Kreusch, J. & Koch, F., 1996, Auflichtmikroskopische Charakterisierung von Gefassmustern in Hauttumoren. *Hautarzt*, 47, 264–72.

Kreusch, J. & Rassner, G., 1990, Structural analysis of melanocytic pigment nevi using epiluminescence microscopy. Review and personal experiences. *Hautarzt*, 41, 27–33.

Kreusch, J.F., 2002, Vascular patterns in skin tumors. *Clin Dermatol*, 20, 248–54.

Mogensen, M. & Jemec, G.B., 2007, Diagnosis of nonmelanoma skin cancer/keratinocyte carcinoma: a review of diagnostic accuracy of nonmelanoma skin cancer diagnostic tests and technologies. *Dermatol Surg*, 33, 1158–74.

Pan Y., Chamberlain AJ., Bailey M., et al., 2008, Dermatoscopy aids in the diagnosis of the solitary red scaly patch or plaque-features distinguishing superficial basal cell carcinoma, intraepidermal carcinoma, and psoriasis. *J Am Acad Dermatol*, 59, 268–274.

Peris, K., Micantonio, T., Piccolo, D. & Concetta, M., 2007a, Dermoscopic features of actinic keratosis. *J Dtsch Dermatol Ges*, 5, 970–6.

Pock, L., Drlik, L. & Hercogova, J., 2007, Dermatoscopy of pigmented actinic keratosis - A striking similarity to lentigo maligna. *Int J Dermatol*, 46, 414–16.

Schiffner, R., Schiffner-Rohe, J., Vogt, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42, 25–32.

Stante, M., De Giorgi, V., Massi, D., Chiarugi, A. & Carli, P., 2004, Pigmented Bowen's disease mimicking cutaneous melanoma: clinical and dermoscopic aspects. *Dermatol Surg*, 30, 541–4.

Stolz, W., Schiffner, R. & Burgdorf, W.H., 2002, Dermatoscopy for facial pigmented skin lesions. *Clin Dermatol*, 20, 276–8.

Zalaudek, I. & Argenziano, G., 2004, Glomerular vessels in Bowen's disease. *Br J Dermatol*, 151, 720.

Zalaudek, I., Argenziano, G., Leinweber, B., et al., 2004, Dermoscopy of Bowen's disease. *Br J Dermatol*, 150, 1112–16.

Zalaudek, I., Di Stefani, A. & Argenziano, G., 2006a, The specific dermoscopic criteria of Bowen's disease. *J Eur Acad Dermatol Venereol*, 20, 361–2.

Zalaudek, I., Giacomel, J., Argenziano, G., et al., 2006b, Dermoscopy of facial nonpigmented actinic keratosis. *Br J Dermatol*, 155, 951–6.

Zalaudek, I., Giacomel, J., Schmid, K., et al., 2012, Dermatoscopy of facial actinic keratosis, intraepidermal carcinoma, and invasive squamous cell carcinoma: a progression model. *J Am Acad Dermatol*, 66, 589–97.

5c Solar lentigines, seborrheic keratoses, and lichen planus-like keratosis

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SOLAR LENTIGO

Solar lentigines are sharply circumscribed, uniformly pigmented macules that are located predominantly on the sun-exposed areas of the skin, such as the dorsal aspects of the hands, the shoulders, and the scalp. These lentigines are a result of hyperplasia of keratinocytes and melanocytes, with increased accumulation of melanin in the keratinocytes. They are induced by ultraviolet light exposure. Unlike freckles, solar lentigines persist indefinitely. Nearly 90% of Caucasians over the age of 60 years have these lesions. Due to the increased prevalence of lentigines in the elderly, these lesions are sometimes referred to as lentigo senilis. However, younger individuals who have a tendency to burn after ultraviolet exposure can also develop lentigines after acute or prolonged ultraviolet light exposure (Reguiaï et al., 2008; Bastiaens et al., 2004).

Clinically, solar lentigines may be oval, round, or irregular in shape and can vary from a few millimeters to a few centimeters in diameter. Most lesions have a uniform light brown color (Fig. 5c.1); however, there are instances when they vary from dark brown to black. One variant of solar lentigo, "ink-spot" lentigo, has a jet-black color (Fig. 5c.2) (Kaddu et al., 1997; Argenziano, 2004). Actinic purpura or other signs of solar damage can frequently be found in the skin surrounding solar lentigines.

A solar lentigo is a benign lesion that can evolve to form a pigmented seborrheic keratosis (Fig. 5c.3) (Zaballos et al., 2007; Chamberlain & Ng, 2009). Histologically, it is characterized by club-shaped rete ridges with small nub-like extensions. In addition, there is an increased number of melanocytes and increased pigmentation in the basal keratinocytes.

Although most solar lentigines are easily recognized on clinical examination, some lesions pose diagnostic challenges because their clinical appearance resembles that of melanoma (Fig. 5c.4). Dermoscopy can be helpful in correctly differentiating a solar lentigo from melanoma.

The key dermoscopic features of solar lentigines are as follows (Fig. 5c.5):

1. *Moth-eaten border:* The presence of a sharply demarcated and irregularly curved border is characteristic of solar lentigines. Often, portions of the border are scalloped, giving a moth-eaten appearance (Figs. 5c.1 and 5c.3) (Menzies et al., 1996a; Schiffner et al., 2000)
2. *Homogenous light brown pigmentation:* Many lesions have no structures or networks, only containing light brown and structureless areas (Fig. 5c.6); the term "jelly sign" had been proposed to describe the pigment quality of these lesions (Fig. 5c.7). The pigment appears as if jelly had been smeared on the skin surface (Menzies, 2009; Menzies et al., 1996b).
3. *Pigment network:* There may be an area of faint, reticulation (Figs. 5c.1 and 5c.3). This correlates with the presence of melanocytes and melanin-filled keratinocytes in the rete ridges (Yadav et al., 1993).
4. *Fingerprint-like areas:* They are areas consisting of fine parallel running lines of light brown to dark brown colors. They resemble the dermatoglyphics of a human fingerprint (Figs. 5c.1 and 5c.8) (Kopf et al., 2006; Schiffner et al., 2000).
5. *Pseudonetwork:* Lentigines located on the scalp and face share features of pigmented melanocytic lesions in this special location (see chap. 9c for further information) revealing a pseudonetwork pattern. This is created when a diffusely pigmented area is interrupted by nonpigmented adnexal openings (Fig. 5c.9). (Schiffner et al., 2000; Cognetta et al., 2001)
6. *Symmetric follicular pigmentation:* In a solar lentigo the pigment around hair follicles is distributed in a symmetric fashion creating small brown circles (Fig. 5c.10). The pigment is usually light brown in color and similar to the color of the rest of the lesion. While the pigment is usually distributed symmetrically around the follicle, some follicles may appear asymmetrically pigmented. These asymmetrically pigmented follicles appear as brown crescent shaped structures. However, these asymmetric follicles will also have a brown color similar to the rest of the lesion. If the color of the pigment around the follicle, whether symmetric or asymmetric, is of a grayish hue or differs from the rest of the lesion then melanoma needs to enter the differential diagnosis.

Ink-spot lentigines have their own distinct dermoscopic pattern (Figs. 5c.2, and 5c.11). These lesions have a very prominent black-pigmented network, which has an almost three-dimensional quality under dermoscopy. The network lines can be either thin or thick in width, and the network ends abruptly at the edge of the lesion (Kaddu et al., 1997; Argenziano, 2004).

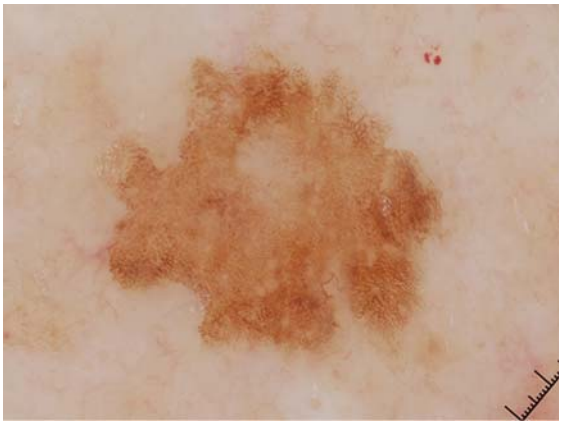
SEBORRHEIC KERATOSES

Seborrheic keratoses are benign epithelial lesions that can appear on any part of the body except for the mucous membranes, palms, and soles. The lesions are quite prevalent in people older than 30 years. The etiology of seborrheic keratoses remains unclear. Ultraviolet light exposure may be responsible for the development of some seborrheic keratoses because they appear to evolve from solar lentigines (Fig. 5c.3); however, many develop in areas of the skin naturally protected from ultraviolet light exposure, such as the inframammary (intertriginous) areas.

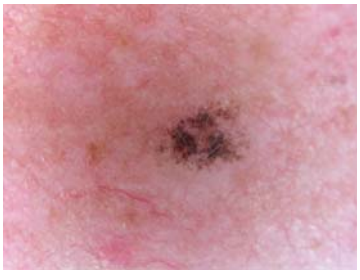
Clinically, early seborrheic keratoses are light- to dark brown oval macules with sharply demarcated borders (solar lentigo). As the lesions progress, they transform into plaques with a waxy or stuck-on appearance. The surfaces of these lesions have a warty and keratotic appearance (Pehamberger et al., 1993; Pehamberger et al., 1987; Steiner et al., 1987). Often, the lesions have follicular plugs scattered over their surfaces. The size of the lesions varies from a few millimeters to a few centimeters. Histologically, there are several distinct forms of seborrheic keratoses. In general (Soyer et al., 2000), the lesions are characterized by papillomatous epidermal hyperplasia of uniform and monotonous keratinocytes and the presence of pseudocysts (Yadav et al., 1993; Braun et al., 2002). The diagnosis of most seborrheic keratoses is straightforward. However, some seborrheic keratoses, especially the deeply pigmented variant, can simulate malignant melanomas. Thin, early lesions have moth-eaten borders and fingerprint-like structures as described above for solar lentigines. Thicker pigmented seborrheic keratoses have the typical dermoscopy features as follows (Fig. 5c.12) (Braun et al., 2002; Soyer et al., 2000):

1. *Milia-like cysts:* They are white-to-yellow, round structures that appear very bright when contrasted with their dark brown or black surroundings (Figs. 5c.13, 5c.14) (Braun et al., 2002). The presence of multiple milia-like cysts in pigmented seborrheic keratoses conjures up an image of "stars in the sky." Milia-like cysts can also be seen in nonpigmented seborrheic keratosis (Fig. 5c.15). Milia-like cysts can also be seen in other lesions such as basal cell carcinoma and in

▲ **Figure 5c.1a** This light brown macule with irregular borders is a solar lentigo.



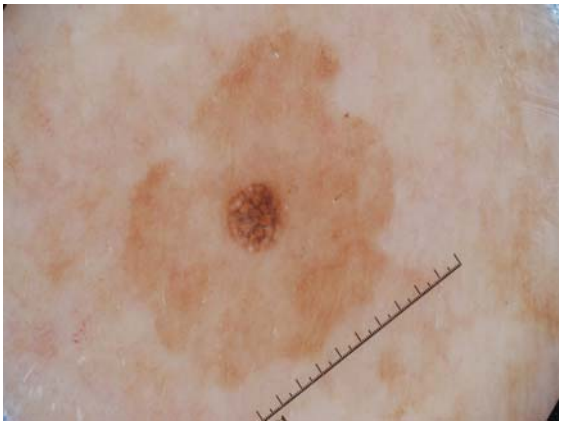
◀ **Figure 5c.1b** Dermoscopy reveals a uniformly light brown lesion with a border that resembles a garment that has been eaten by moths. Fingerprint-like structures are also evident. In addition, in some areas faint network-like structures are visible.



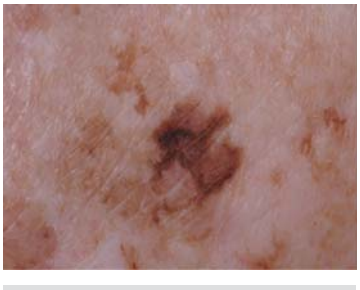
▲ **Figure 5c.2a** Clinical image of an ink-spot lentigo.

◀ **Figure 5c.2b** Dermoscopic image revealing a prominent black network that has an almost three-dimensional quality. Some clinicians use the metaphor of a chicken-wire fence to describe the quality of the network in ink spot lentigines.

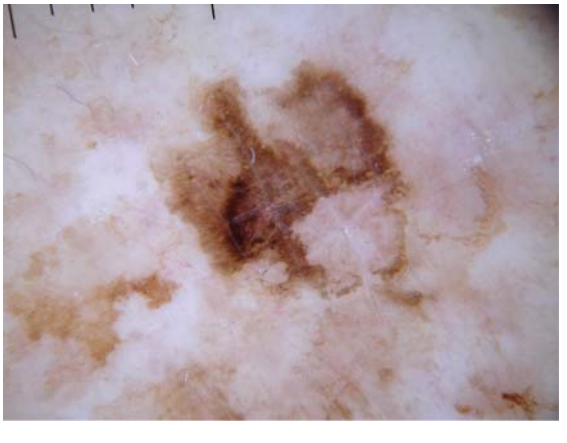
▲ **Figure 5c.3a** Clinical image of solar lentigo transitioning into a seborrheic keratosis.



◀ **Figure 5c.3b** Dermoscopy reveals features of a lentigo consisting of a tan lesion with a moth-eaten border and fingerprint-like structures. In some areas faint network-like structures are visible. In the center of the lesion is a raised papule with ridges and multiple milia-like cysts; both of these structures are commonly seen in seborrheic keratosis.



▲ **Figure 5c.4a** This irregularly pigmented lentigo has clinical features that resemble melanoma.



◀ **Figure 5c.4b** Dermoscopy: although this lesion has a moth-eaten border, its overall pattern is atypical and resembles a melanoma.

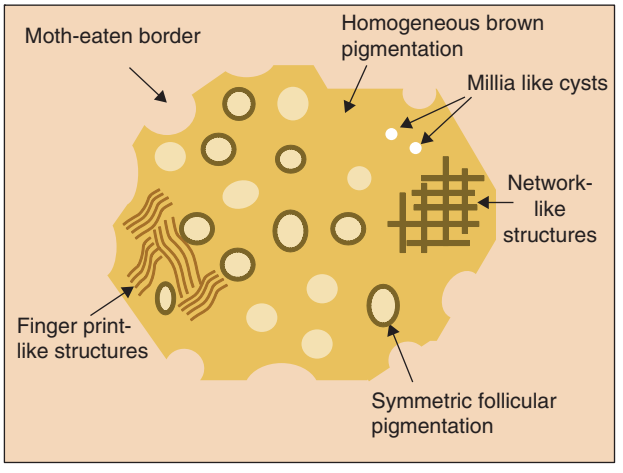
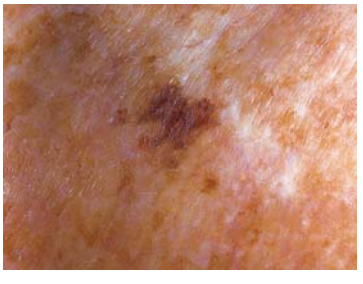


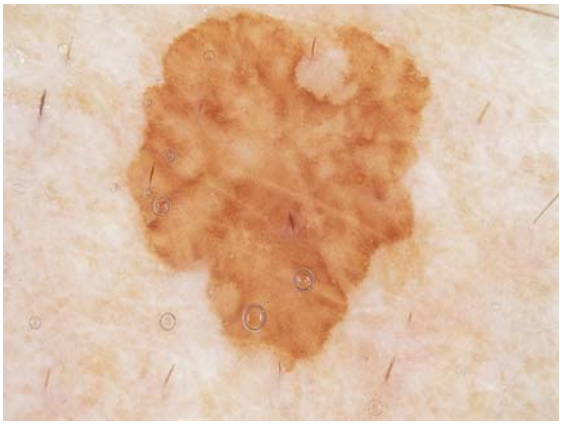
Figure 5c.5 Schematic drawing of the criteria of solar lentigines/early seborrheic keratosis.

melanocytic lesions including congenital nevi and melanoma. However, if the lesion is non-melanocytic and is not a basal cell carcinoma then the presence of milia-like cyst is diagnostic of seborrheic keratoses specially if more then three are seen. It is interesting to note that the quality of milia-like cysts appear somewhat different in seborrheic keratosis and melanocytic lesions. In melanoma and congenital nevi the cysts appear "starry", which is defined as small, bright and sharp. In seborrheic keratosis they appear "cloudy", defined as larger and hazier in appearance (Stricklin et al., 2011). Histologically, the cysts correspond to intraepidermal, keratin-filled cysts (Yadav et al., 1993; Soyer et al., 2000; Braun et al., 2002). It is important to be aware that milia-like cysts are more conspicuous with non-polarized dermoscopy and are often difficult to visualize with polarized dermoscopy (see chapter 2, Figure 2.9).

2. *Comedo-like openings:* They are round to ovoid craters that have black or brown comedo-like plugs. Histologically, they



▲ **Figure 5c.6a** Clinical photograph of a light brown solar lentigo.

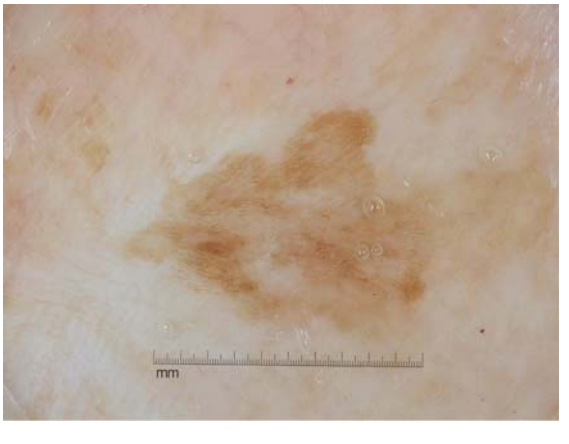


◀ **Figure 5c.6b** Dermoscopic photograph of a lentigo. The lesion is a characteristic light brown to tan color, with a sharply demarcated border. The superior portion of the border has a scalloped and moth-eaten appearance. The pigment appears as if it has been smeared onto the skin. This is known as the jelly sign.

▲ **Figure 5c.7a** Clinical image of a lentigo.

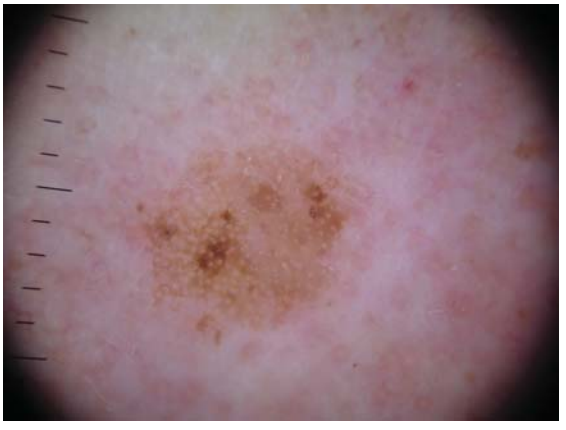
◀ **Figure 5c.7b** Dermoscopy reveals smudging of pigment at approximately 9 o'clock. This smudging is known as the jelly sign.

▲ **Figure 5c.8a** Clinical image of a solar lentigo.



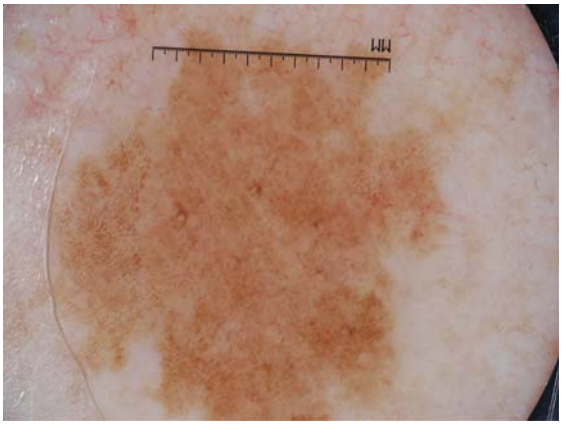
◀ **Figure 5c.8b** Dermoscopic image: this lesion is an excellent illustration of the finger-print pattern. There are many linear and striated network lines arranged parallel to each other. These lines do not interconnect to form a clear reticulated network.

▲ **Figure 5c.9a** Clinical image of a light brown macule. This lesion is a lentigo.



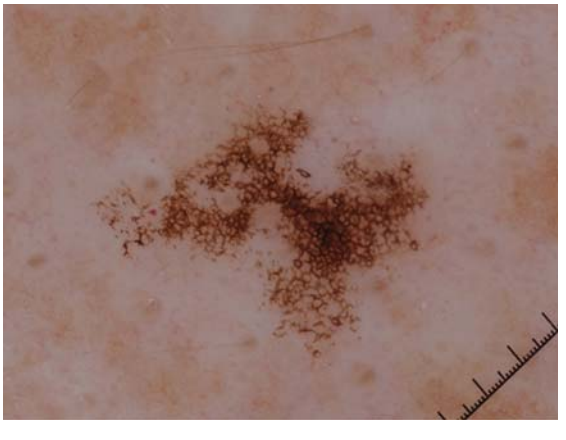
◀ **Figure 5c.9b** Dermoscopy reveals a pseudonetwork pattern.

▲ **Figure 5c.10a** Clinical image of a lentigo, which consists of a homogenous tan macule with irregular borders.



◀ **Figure 5c.10b** Dermoscopy reveals fingerprint-like structures and symmetrically pigmented follicular openings. Note that the follicular pigmentation has the same color as the rest of the lesion. This is characteristic of a lentigo.

▲ **Figure 5c.11a** This darkly pigmented macule has an irregular border.



◀ **Figure 5c.11b** Dermoscopy: prominent dark and thick network of an ink-spot lentigo.

correlate with keratin-filled invaginations of the skin surface (Figs. 5c.17 and 5c.18) (Yadav et al., 1993; Soyer et al., 2000; Braun et al., 2002).

3. *Fissures and ridges:* Fissures (sulci) are comedo-like openings, which are not round but rather linear and appear as dark brown to black linear to curvilinear structures within the lesion (Figs. 5c.19). The presence of numerous fissures and ridges can result in the formation of network-like structures or result in a cerebriform pattern. Histologically, they represent deep invaginations of the epidermis, filled with keratin (Yadav et al., 1993; Soyer et al., 2000; Braun et al., 2002).
4. *Network-like structures:* Interlacing fissures and ridges can create an appearance of network-like structures (Fig. 5c.20). The quality of the grid of network-like structures in a seborrheic keratosis differs from the network grid seen in melanocytic nevi by being significantly larger. However, at times the network-like structure in a seborrheic keratosis can look very similar to that of a nevus (Figs. 5c.21 and 5c.22) (Braun et al., 2002). Examining the lesion clinically via side lighting can make the ridges more evident, thereby making it easier to differentiate network-like ridges in seborrheic keratosis from pigment network seen in melanocytic lesions.
5. *Cerebriform pattern:* Multiple fissures (sulci) and ridges (gyri) may produce a cerebriform pattern (Figs. 5c.23 and 5c.24), where the structures resemble sulci and gyri of the brain (brain-like appearance). These features are generally associated with an acanthotic seborrheic keratosis (Braun et al., 2002).
6. *Fat-fingers:* They are linear and wide dermoscopic structures corresponding to ridges. They often appear as short sausage-shaped structures (Fig. 5c.25) (Kopf et al., 2006). Colors of these structures vary from tan/brown, blue and can be hypopigmented (Fig. 5c.26). The name has been given to these structures because their shapes can resemble a straight finger (linear), bent finger (curvilinear), or finger tip (oval–circular) (Kopf et al., 2006).

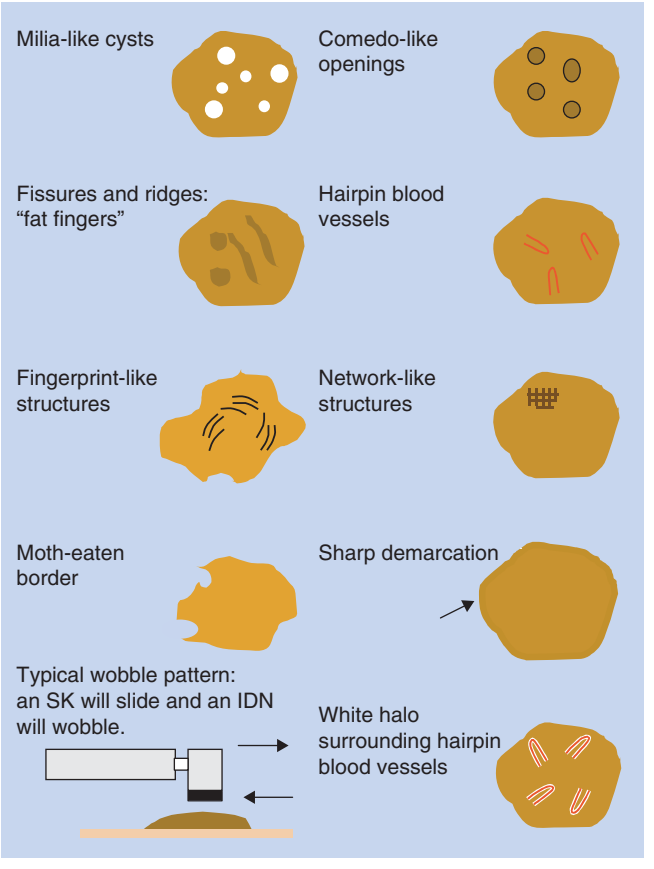
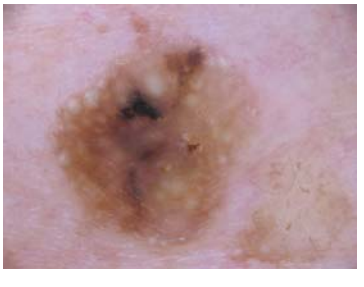


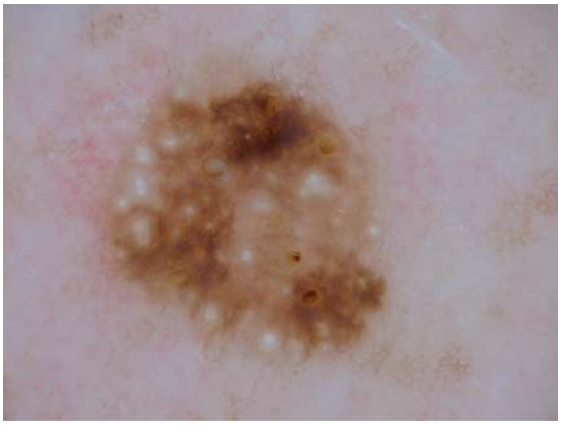
Figure 5c.12 Dermoscopy criteria of pigmented seborrheic keratoses.

7. *Sharply demarcated borders:* As known from clinical examination, seborrheic keratoses often have sharply demarcated borders (Braun et al., 2002).
8. *Typical hairpin blood vessels:* Some seborrheic keratoses are associated with hairpin vessels (Figs. 5c.13, 5c.27, and 5c.28). These hairpin vessels can appear as perfect "U"-shaped vessels of as "U"-shaped vessels that are twisted upon themselves. Typical hairpin blood vessels have a whitish halo around the blood vessel corresponding to the surrounding keratin. It is important to note that some melanomas can have hairpin vessels, but these vessels generally do not have the surrounding white halo but, rather have a pink halo. Similar hairpin vessels on a pink background can be seen in irritated seborrheic keratosis (Braun et al., 2002; Marghoob et al., 2005; Argenziano et al., 2004).
9. *Wobble test:* This is a dynamic test that can only be performed with a contact dermoscopy device. The test is performed as follows: once the contact plate of the dermoscope is firmly pressed down (pressure in vertical direction) against the lesion, it is then moved slightly back and forth in the horizontal plane (parallel to the skin surface). Seborrheic keratosis will appear to stick to the glass plate and move en bloc with the movement of the dermoscopic face plate. In other words, they will slide back and forth. In contrast, nevi will not move en bloc but, rather roll back and forth. In other words, intradermal nevi will wobble (Braun et al., 2000).

Knowledge of the above-described dermoscopic features and patterns seen in seborrheic keratosis will often prove valuable in differentiating seborrheic keratoses from other lesions, including melanoma. However, irritated or traumatized seborrheic keratoses can mimic melanoma or squamous cell carcinoma (Fig. 5c.29). In these cases the history of trauma or the presence of typical criteria for seborrheic keratoses in another part of the lesion might

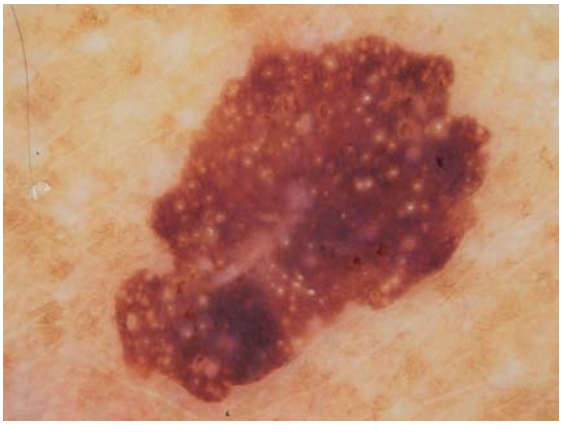


▲ **Figure 5c.13a** Clinical image of a seborrheic keratosis.



◀ **Figure 5c.13b** Dermoscopy reveals multiple milia-like cysts and a few comedo-like openings.

▲ **Figure 5c.14a** Clinical image.



◀ **Figure 5c.14b** A darkly pigmented and raised seborrheic keratosis. Differential diagnoses include atypical nevus and melanoma. Dermascopic examination shows a lack of network within the lesion, suggesting this is not a melanocytic lesion. The sharp border, presence of comedo-like openings, and milia-like cysts confirm this is a seborrheic keratosis.

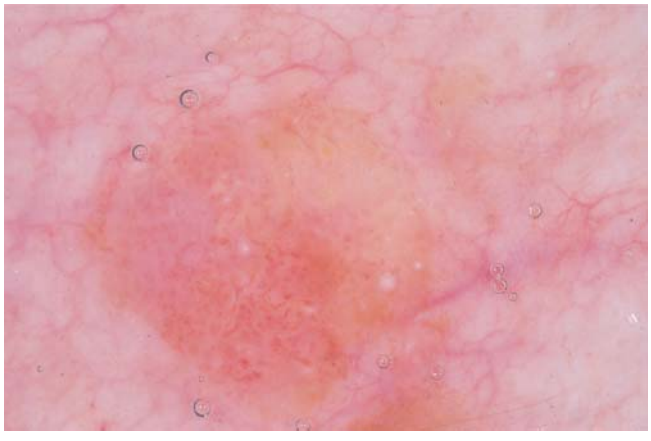
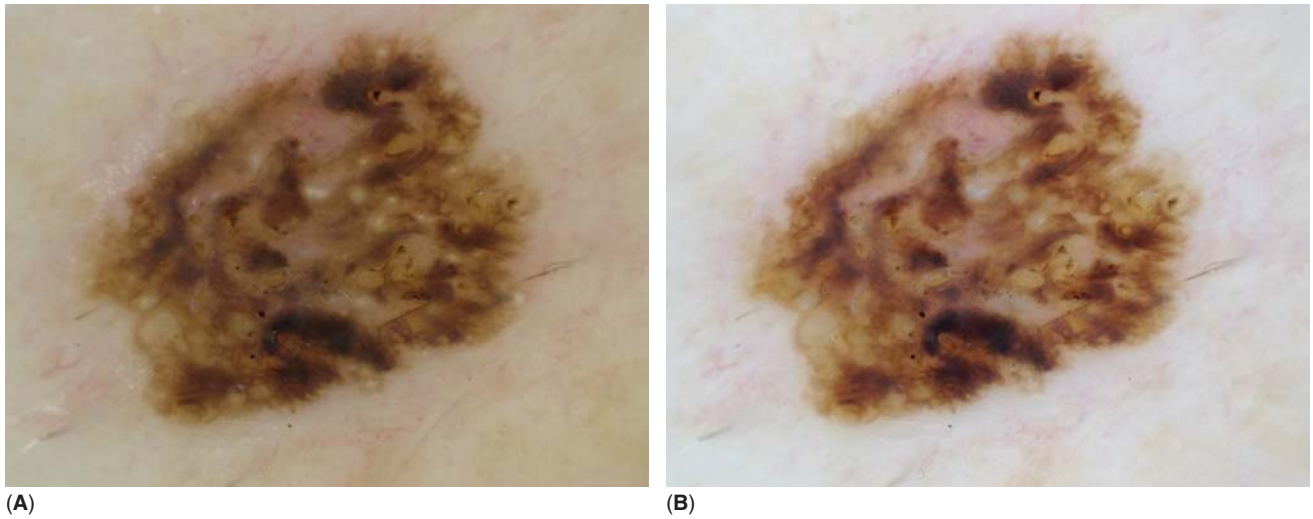


Figure 5c.15 Seborrheic keratosis with many hairpin blood vessels and a few milia-like cysts.

be comforting (Figs. 5c.30 and 5c.31). However, it is important to remember that skin cancer can develop within a seborrheic keratosis, and thus a biopsy is justified for atypical appearing seborrheic keratosis (Fig. 5c.32).

Lichen Planus-like Keratosis

Lichen planus-like keratosis (LPLK) is a relatively common skin lesion found on actinically damaged skin (Vazquez-Lopez et al., 2003; Zaballos et al., 2005). Clinically, LPLK usually occurs as a solitary lesion with sharply demarcated borders. It may be macular or slightly raised, and has brown, tan-brown, violaceous, or red-brown color. There is also a pink variant of LPLK that resembles a basal cell carcinoma. Clinical diagnosis of LPLK lesions is often difficult since they can mimic cutaneous malignancies. Histologically, LPLK shares some of the features seen in lichen planus. Although the etiology of LPLK remains unknown, it is believed to be mediated by an immunologic or inflammatory response to a pre-existing lesion, such as a seborrheic keratosis, solar lentigo, or actinic keratosis.



(**A**) (**B**)

Figure 5c.16 (**A**) This is a seborrheic keratosis viewed with a non-polarized dermoscope. Notice that the lesion reveals multiple milia-like cysts. (**B**) When the lesion is viewed with polarized dermoscopy the milia cysts become less conspicuous.

Figure 5c.17 Dermoscopic photograph of a seborrheic keratosis. The lesion has sharp borders and numerous comedo-like openings.

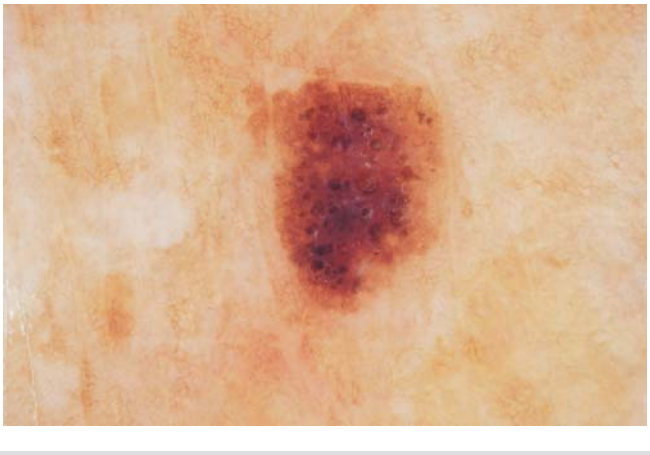
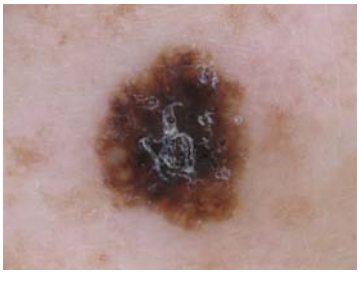


Figure 5c.18 Clinical image of a seborrheic keratosis. Dermoscopy reveals numerous comedo-like openings and a few milia-like cysts.

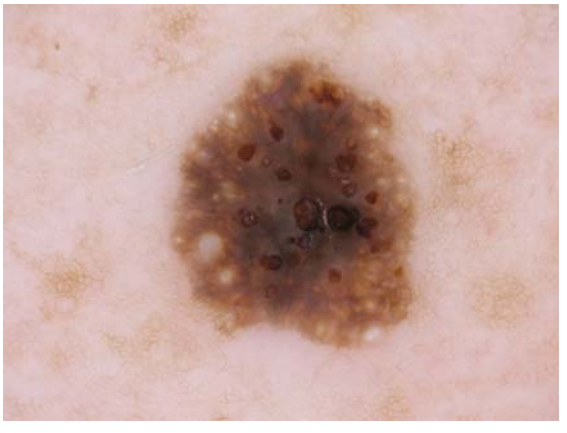
Figure 5c.19 Seborrheic keratosis with a characteristic white-blue pigmentation. Large comedo-like openings and fissures (sulci) are present.

Dermoscopy can frequently help differentiate LPLK from other lesions(Bugatti & Filosa, 2007; Zalaudek & Argenziano, 2006); however, it does not help differentiate most pink or skin colored LPLK lesions from basal cell carcinoma and melanoma because these pink lesions tend to be devoid of any dermoscopic structures (structureless or featureless lesions). To complicate matters, LPLK often reveal crystalline structures, which can also be seen in basal cell carcinoma and melanoma. With that being said, the key dermoscopic features of LPLK are as follows (Zaballos et al., 2005; Zaballos et al., 2004):

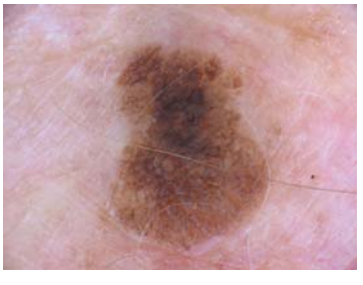
1. *Diffuse granular pattern:* This is characterized by the presence of diffuse granularity (peppering) of brown, grey, bluish-grey, or white grey colors. These granules tend to be coarse are scattered throughout the lesion in a homogenous fashion (Figs. 5c.33 and 5c.34).
2. *Localized granular pattern:* The presence of grayish-brown granularity (peppering) localized to one focal area within the lesion. Since the regression is only occurring in a part of the lesion, the typical dermoscopy features of the original lesion



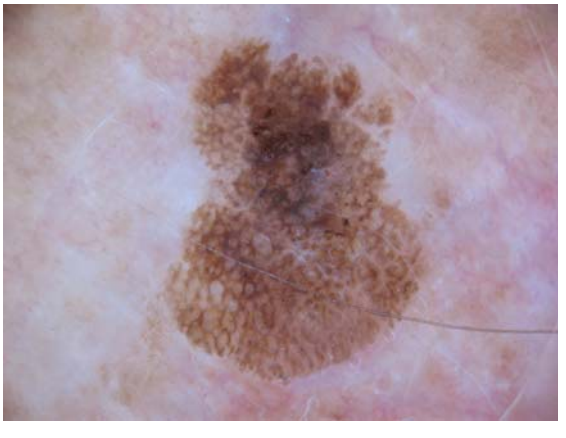
▲ **Figure 5c.20a** Clinical image of a seborrheic keratosis.



◀ **Figure 5c.20b** Dermoscopy reveals interlacing ridges and sulci, resulting in the formation of what appears like a network. Note that the lines of the network-like areas are broader and the holes are larger as compared with the network grid seen in nevi. In network like areas the lines are created by ridges and the holes are due to sulci.

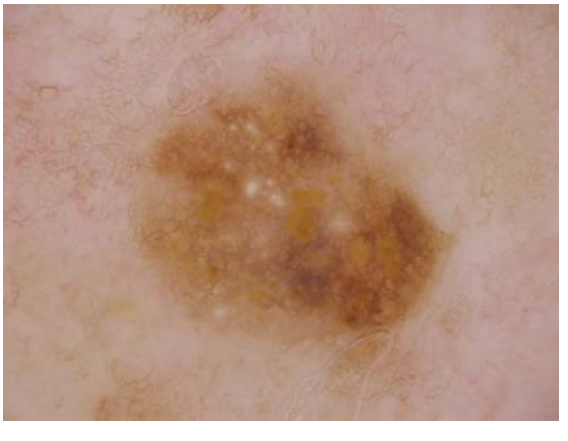


▲ **Figure 5c.21a** Clinical image of seborrheic keratosis.



◀ **Figure 5c.21b** Dermoscopy reveals network-like structures, which are larger than one would expect from a pigment network. This appearance is caused by ridges and multiple comedo-like openings. Examining the lesion clinically via side lighting will help confirm that the network like areas are due to ridges.

▲ **Figure 5c.22a** Clinical image of a seborrheic keratosis.



◀ **Figure 5c.22b** Dermoscopy reveals network-like structures that can at times resemble the network seen in nevi. However, this seborrheic keratosis can be identified due to the presence of multiple milia-like cysts and yellowish comedo-like openings.

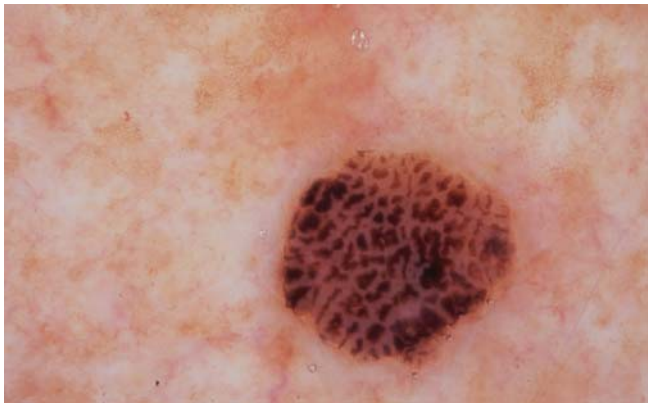


Figure 5c.23 Dermoscopic example of seborrheic keratosis with a cerebriform pattern, which is created by the ridges and sulci.

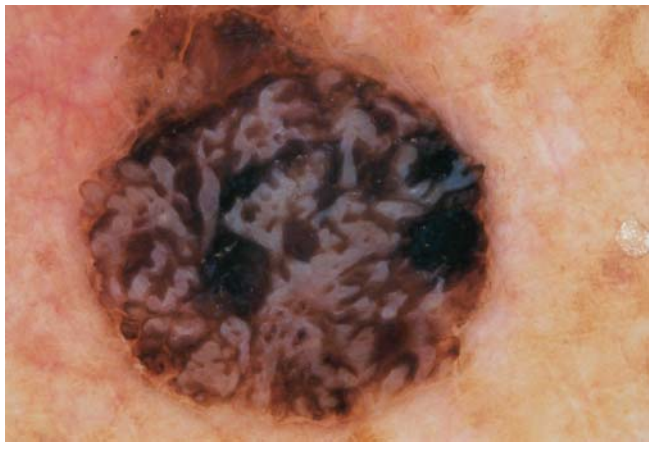
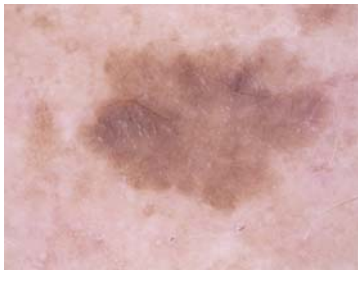
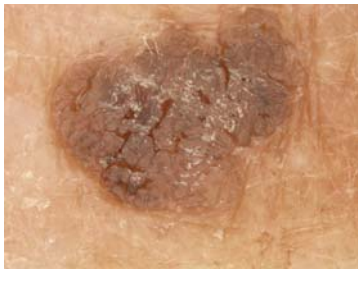


Figure 5c.24 Dermoscopic photograph of a seborrheic keratosis showing the cerebriform pattern.

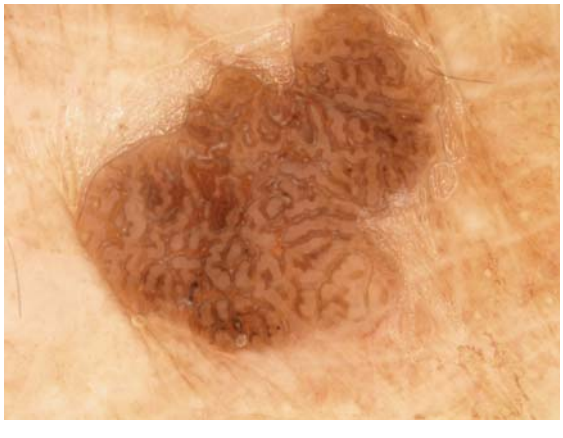


▲ **Figure 5c.25a** Clinical image of a seborrheic keratosis.

◀ **Figure 5c.25b** Dermoscopy reveals numerous curvilinear pigmented ridges, which are also called fat-finger like structures.

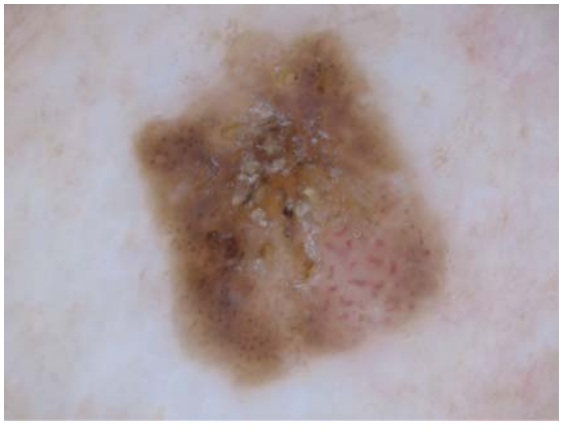


▲ **Figure 5c.26a** Clinical image of a seborrheic keratosis.

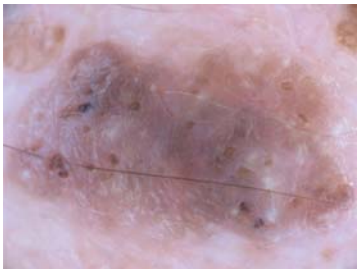


◀ **Figure 5c.26b** Dermoscopy reveals numerous curvilinear hypopigmented ridges, which are called fat-finger-like structures.

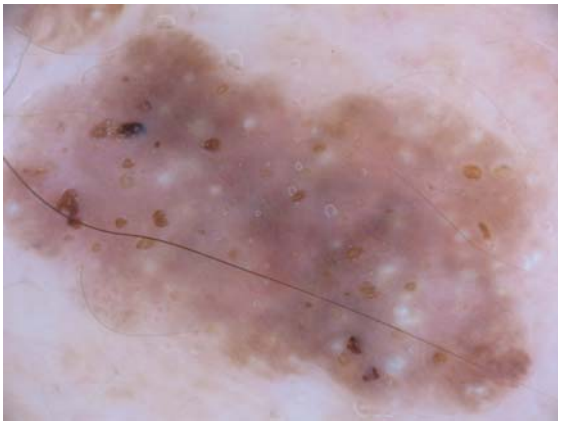
▲ **Figure 5c.27a** This seborrheic keratosis appears as an "ugly duckling" lesion on the back of this patient..



◀ **Figure 5c.27b** Dermoscopy reveals multiple dark thrombosed capillaries. Hairpin vessels with a white halo can be seen in the right lower corner of this seborrheic keratosis.



▲ **Figure 5c.28a** Clinical image of an irritated seborrheic keratosis.

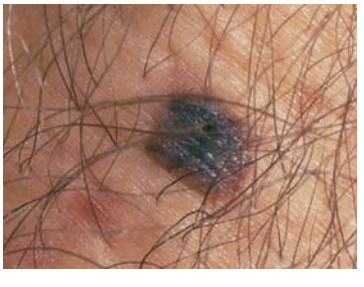


◀ **Figure 5c.28b** Dermoscopy reveals numerous milia-like cysts, comedo-like openings and hairpin vessels with a white halo.

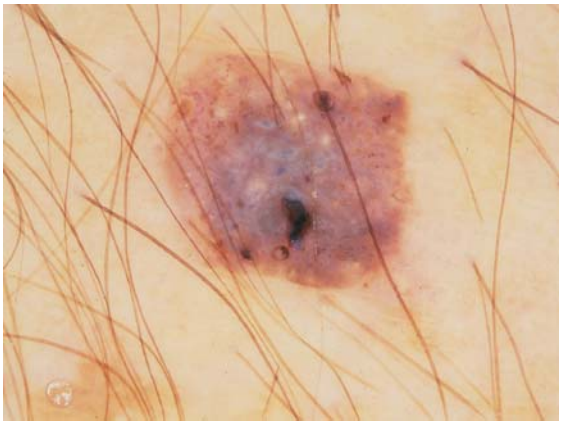
◀ **Figure 5c.28c** Dermoscopy magnified image: note multiple hairpin vessels, some of which are twisted upon themselves.

▲ **Figure 5c.29a** Clinical image of an atypical appearing seborrheic keratosis. This lesion appears as an "ugly duckling" lesion on the shoulder of this patient.

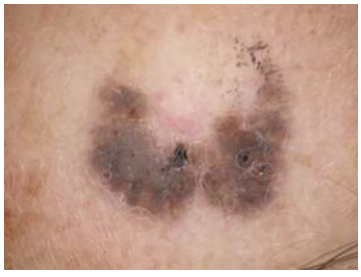
◀ **Figure 5c.29b** Dermoscopy reveals a few comedo-like openings; however, the overall dermoscopic pattern remains difficult to differentiate from melanoma.



▲ **Figure 5c.30a** Clinical image of a seborrheic keratosis.

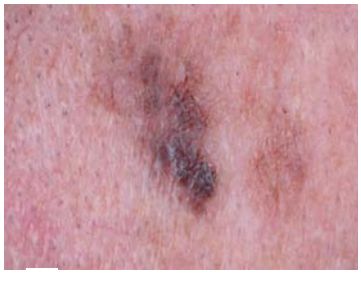


◀ **Figure 5c.30b** A pigmented seborrheic keratosis. Dermoscopic examination shows a lesion with a sharp border and multiple milia-like cysts. Numerous hairpin vessels can also be seen.

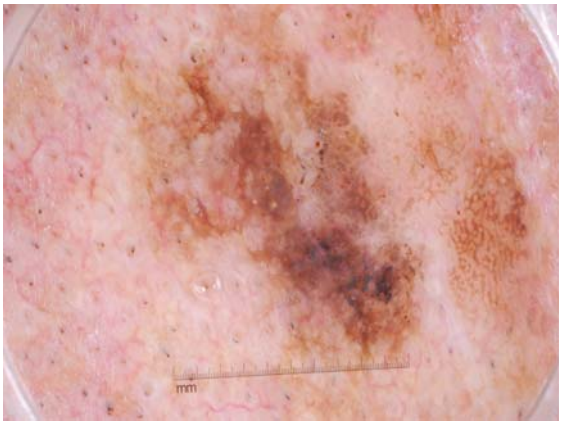


▲ **Figure 5c.31a** Clinical image of a traumatized seborrheic keratosis.

◀ **Figure 5c.31b** Dermoscopy reveals regression structures; however, the presence of multiple milia-like cysts and comedo-like openings is reassuring that the lesion is a seborrheic keratosis. The lesion was biopsied and was consistent with an irritated seborrheic keratosis.

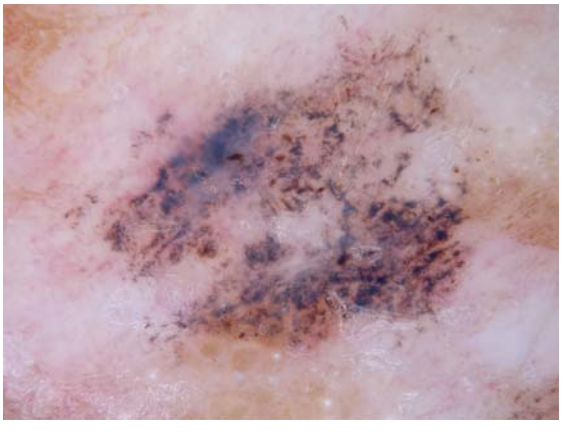


▲ **Figure 5c.32a** Clinical image of an irregular pigmented lesion.

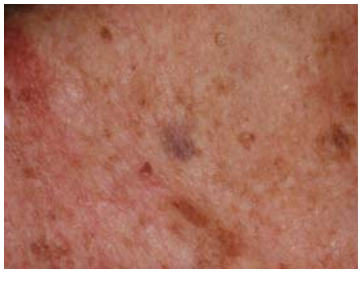


◀ **Figure 5c.32b** Dermoscopy: dermoscopy reveals fingerprint-like areas, fat-finger-like structures, and milia-like cyst. In addition, regression structures consisting of granularity and a blue white veil are also seen focally within the lesion. This lesion was biopsied and disclosed the presence of a 1.5 mm melanoma arising within a seborrheic keratosis.

▲ **Figure 5c.33a** Clinical image of a lichen planus-like keratosis.

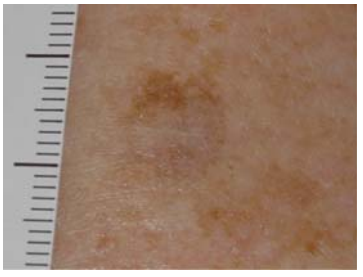


◀ **Figure 5c.33b** Dermoscopic image showing diffuse clumped bluish-grey granules.

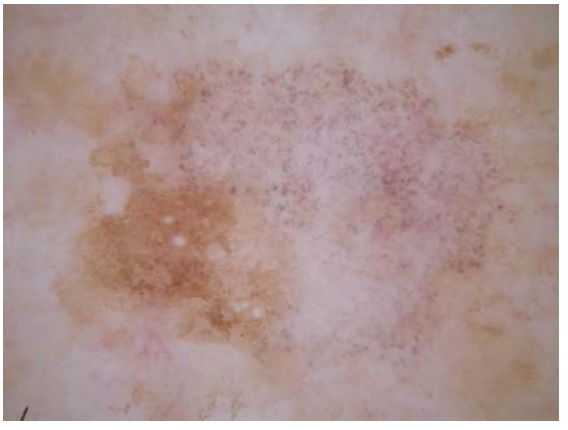


▲ **Figure 5c.34a** Clinical image of a lichen planus-like keratosis.

◀ **Figure 5c.34b** Dermoscopic image showing diffuse fine and course granules.

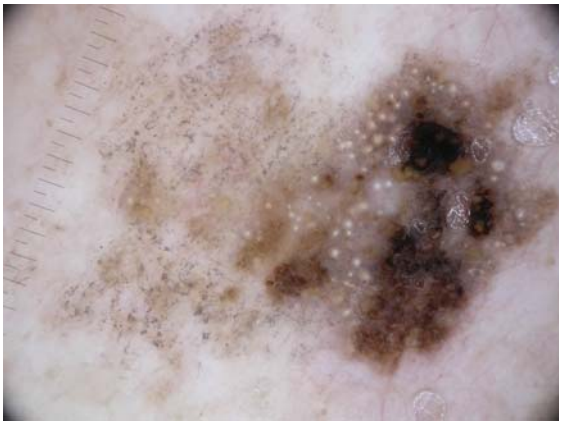


▲ **Figure 5c.35a** Clinical image of a lichen planus-like keratosis.



◀ **Figure 5c.35b** Dermoscopic image: on the right half of the lesion, there are localized fine and coarse granules. On the left half of the lesion, there are two milia-like cysts, fingerprint-like areas, and a moth-eaten border; all features consistent with a diagnosis of a regressing solar lentigo/seborrheic keratosis.

▲ **Figure 5c.36a** Clinical image of a lichen planus-like keratosis.



◀ **Figure 5c.36b** Dermoscopic image: on the left half of the lesion, there is coarse granularity. On the right half of the lesion, there are milia-like cysts and comedo-like openings. The biopsy was consistent with a seborrheic keratosis undergoing regression.

(seborrheic keratosis, solar lentigo, actinic keratosis) can still be found (Laur et al., 1981) (Figs. 5c.35 and 5c.36).

The coarse granules in LPLK can be confused with the multiple blue-grey dots (also known as regression structures) seen in melanomas. One differentiating feature, however, is the size of the granules. In LPLK, the granules tend to be larger, coarser, and often appear clumped. In contrast, in melanoma, the blue-grey dots are much smaller and finer in size.

Key Points

Solar lentigines can sometimes clinically resemble melanoma. However, most can be distinguished from melanoma by the presence of the following key dermoscopic features of solar lentigines:

- *Moth-eaten border*
- *Homogenous light brown pigmentation and the jelly sign*
- *Faint pigment network*
- *Fingerprint-like area*
- *Pseudonetwork*
- *Symmetrically pigmented follicular openings*

Dermoscopic features of seborrheic keratoses include the presence of:

- *Milia-like cysts*
- *Comedo-like openings*
- *Fissures and ridges (Gyri and sulci)*
- *Network-like structures*
- *Cerebriform pattern*
- *Fat-fingers*
- *Sharply demarcated borders*
- *Typical hairpin blood vessels with a white halo*

Dermoscopic features of LPLK:

- *Diffuse granular pattern*
- *Localized granular pattern*
- *Crystalline structures*

REFERENCES

Argenziano, G., 2004, Dermoscopy of melanocytic hyperplasias: subpatterns of lentigines (ink spot). *Arch Dermatol*, 140, 776.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Bastiaens, M., Hoefnagel, J., Westendorp, R., Vermeer, B.-J. & Bouwes Bavinck, J.N., 2004, Solar lentigines are strongly related to sun exposure in contrast to ephelides. *Pigment Cell Res*, 17, 225–9.

Braun, R.P., Krischer, J. & Saurat, J., 2000, The "wobble sign" in epiluminescence microscopy as a novel clue to the differential diagnosis of pigmented skin lesions. *Arch Dermatol*, 136, 940–2.

Braun, R.P., Rabinovitz, H.S., Krischer, J., et al., 2002, Dermoscopy of pigmented seborrheic keratosis: a morphological study. *Arch Dermatol*, 138, 1556–60.

Bugatti, L. & Filosa, G., 2007, Dermoscopy of lichen planus-like keratosis: a model of inflammatory regression. *J Eur Acad Dermatol Venereol*, 21, 1392–7.

Chamberlain, A. & NG, J., 2009, Cutaneous melanoma-atypical variants and presentations. *Aust Fam Physician*, 38, 476–82.

Cognetta, A., Stolz, W., Katz, B., Tullos, J. & Gossain, S., 2001, Dermatoscopy of lentigo maligna. *Dermatol Clin*, 19, 307–18.

Kaddu, S., Soyer, H., Wolf, I., Rieger, E. & Kerl, H., 1997, Reticular lentigo. *Hautarzt*, 48, 181–5.

Kopf, A., Rabinovitz, H.S., Marghoob, M., et al., 2006, "Fat fingers:" a clue in the dermoscopic diagnosis of seborrheic keratoses. *J Am Acad Dermatol*, 55, 1089–91.

Laur, W.E., Posey, R.E. & Waller, J.D., 1981, Lichen planus-like keratosis. A clinicohistopathologic correlation. *J Am Acad Dermatol*, 4, 329–36.

Marghoob, M., Braun, R.P. & Kopf, A., 2005, Re: Differentiating vessels from globules on dermoscopy. *Dermatol Surg*, 31, 120; author reply 120.

Menzies, Scott W., 2009, Dermoscopy: An Atlas. Sydney: McGraw-Hill.

Menzies, S.W., Ingvar, C., Crotty, K. & Mccarthy, W., 1996a, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Menzies, S.W., Ingvar, C. & McCarthy, W., 1996b, A sensitivity and specificity analysis of the surface microscopy features of invasive melanoma. *Melanoma Res*, 6, 55–62.

Pehamberger, H., Binder, M., Steiner, A. & Wolff, K., 1993, In vivo epiluminescence microscopy: improvement of early diagnosis of melanoma. *J Invest Dermatol*, 100, 356S–62S.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

Reguiaï, Z., Jovenin, N., Bernard, P. & Derancourt, C., 2008, Melanoma, past severe sunburns and multiple solar lentigines of the upper back and shoulders. *Dermatology*, 216, 330–6.

Schiffner, R., Schiffner-Rohe, J., Vogt, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42, 25–32.

Soyer, H., Kenet, R., Wolf, I., Kenet, B. & Cerroni, L., 2000, Clinicopathological correlation of pigmented skin lesions using dermoscopy. *Eur J Dermatol*, 10, 22–8.

Steiner, A., Pehamberger, H. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. II. Diagnosis of small pigmented skin lesions and early detection of malignant melanoma. *J Am Acad Dermatol*, 17, 584–91.

Stricklin S.M., Stoecker W.V., Oliviero M.C., Rabinovitz H.S., Mahajan S.K., 2011, Cloudy and starry milia-like cysts: how well do they distinguish seborrheic keratoses from malignant melanomas? *J Eur Acad Dermatol Venereol*, 25, 1222–4.

Vazquez-Lopez, F., Maldonado-Seral, C., Lopez-Escobar, M. & Perez-Oliva, N., 2003, Dermoscopy of pigmented lichen planus lesions. *Clin Exp Dermatol*, 28, 554–5.

Yadav, S., Vossaert, K., Kopf, A., Silverman, M. & Grin-Jorgensen, C., 1993, Histopathologic correlates of structures seen on dermoscopy (epiluminescence microscopy). *Am J Dermatopathol*, 15, 297–305.

Zaballos, P., Ara, M., Puig-Butille, S. & Malvehy, J., 2005, Clinical and dermoscopic image of an intermediate stage of regressing seborrheic keratosis in a lichenoid keratosis. *Dermatol Surg*, 31, 102–3.

Zaballos, P., Blazquez, S., Puig-Butille, S., et al., 2007, Dermoscopic pattern of intermediate stage in seborrhoeic keratosis regressing to lichenoid keratosis: report of 24 cases. *Br J Dermatol*, 157, 266–72.

Zaballos, P., Puig-Butille, S. & Malvehy, J., 2004, Dermoscopy of pigmented purpuric dermatoses (lichen aureus): a useful tool for clinical diagnosis. *Arch Dermatol*, 140, 1290–1.

Zalaudek, I. & Argenziano, G., 2006, Dermoscopy subpatterns of inflammatory skin disorders. *Arch Dermatol*, 142, 808.

5d Vascular lesions

Pedro Zaballos, Josep Malvehy, and Susana Puig

INTRODUCTION

Vascular lesions of the skin include true neoplasms, reactive proliferations, and developmental anomalies. They are classified as either hemangiomas (e.g., strawberry hemangioma) or as malformations (e.g., port-wine stain). The clinical differential diagnosis for these lesions can at times be quite broad and can even include melanoma (Warshaw et al., 2009). Fortunately, dermoscopy can help correctly identify many of these vascular lesions. In this chapter, we describe the dermoscopic features of the vascular lesions most frequently encountered in clinical practice (Fig. 5d.1).

HEMANGIOMA

Hemangiomas are defined as benign proliferations of blood vessels. The most common vascular lesions in childhood are the hemangiomas of infancy and, in adulthood, the cherry hemangiomas or Campbell de Morgan spots. The dermoscopic hallmark of hemangiomas is the presence of lacunae (also known as lagoons), which are characterized by well-demarcated, round to oval to angulated, red, reddish-brown (maroon) or reddish-blue (Figs. 5d.2 and 5d.3) areas that correspond histopathologically to dilated, blood-filled vessels in the papillary dermis. Occasionally, the individual dilated blood vessels in a hemangioma are visible under dermoscopy (Figs. 5d.4–5d.6) (Braun et al., 2005). Lacunae commonly vary in size and color within a given lesion and may be either tightly clustered (Figs. 5d.2, 5d.3) or loosely scattered throughout (Fig. 5d.7). They are often located on a background of red (Fig. 5d.4), red-blue (Fig. 5d.3), or red-white (Fig. 5d.2) homogeneous color (Wolf, 2002). The presence of red lacunae together with the absence of the criteria of melanocytic lesions is virtually diagnostic of a benign vascular lesion, such as hemangioma of infancy (Fig. 5d.8a, b) or cherry hemangioma (Figs. 5d.2–5d.5). Hemangiomas that develop a partial thrombosis can acquire a focal blue-black color, and thereby may clinically resemble melanoma (Fig. 5d.9a, b). If the entire lesion develops a thrombosis then it will manifest a jet-black color (Fig. 5d.10).

ANGIOKERATOMA

Angiokeratomas are acquired lesions that result from the ectatic dilatation of pre-existing vessels in the papillary dermis in conjunction with overlying hyperkeratotic epidermis. Four clinical subtypes of angiokeratomas have been described: solitary angiokeratoma (Fig. 5d.11a, b), angiokeratoma of Mibelli, angiokeratoma of Fordyce, and angiokeratoma corporis diffusum. Solitary angiokeratoma is the most common type, representing 70–83% of all angiokeratomas (Zaballos et al., 2007). Although they can develop on any anatomic site and at any age, they most commonly arise on lower extremities of young to middle-aged adults. Clinically, early angiokeratomas present as shiny, soft, nonkeratotic, dark red to violaceous, 2–10 mm papules. Over time, these lesions tend to become slightly larger and firmer, develop a blue-violaceous to black color, and may develop surface scale. Angiokeratomas can undergo sudden enlargement, darkening, or spontaneous bleeding. Thus, it is not surprising that these lesions often raise the clinician's concern for a malignancy. The differential diagnosis may include Spitz or Reed nevus, melanoma, pigmented basal cell carcinoma (BCC), seborrheic keratosis, and other vascular lesions, such as hemangioma or pyogenic granuloma.

A recent study confirmed that dermoscopy is a helpful tool; increasing the clinician's diagnostic accuracy for solitary angiokeratoma (Zaballos et al., 2007). The pattern composed of dark lacunae and a whitish veil was determined to be the most common pattern observed in solitary angiokeratomas, with a sensitivity of 84.4% and a specificity of 99.1%. The presence of "dark lacunae" was the most frequent dermoscopic finding in these lesions (93.8%) and it represents the most important isolated criterion for correctly diagnosing angiokeratomas (Figs. 5d.11 and 5d.12a, b). Dark lacunae are defined as sharply demarcated, ovoid structures, manifesting a dark violaceous to dark blue to black color. These structures correspond histopathologically to wide and dilated vascular spaces in the dermis that are partially or completely thrombosed. The whitish veil refers to an ill-defined structureless area that gives the appearance as if a whitish "ground-glass" film is overlying the area. This feature corresponds to hyperkeratosis and acanthosis, both of which are characteristic histopathologic findings in this tumor (Fig. 5d.12). The presence of a whitish veil has an excellent sensitivity (90.6%) for angiokeratoma; however, the specificity (63.4%) is low because it can frequently be observed in melanomas, BCCs, and occasionally in seborrheic keratoses. Other dermoscopic structures observed in at least 50% of solitary angiokeratomas include red lacunae, erythema, and hemorrhagic crust (Figs. 5d.13a, b and 5d.14a, b).

PYOGENIC GRANULOMA

Pyogenic granuloma is a benign, acquired, vascular lesion of the skin and mucous membranes. The typical lesion presents as a rapidly growing, reddish papule or polyp with a glistening surface, which bleeds easily after minor trauma. Pyogenic granuloma preferentially affects the fingers, hands, face, lips, and oral mucous membranes. Although the exact etiology and pathogenesis of this condition remains unknown, it appears to be

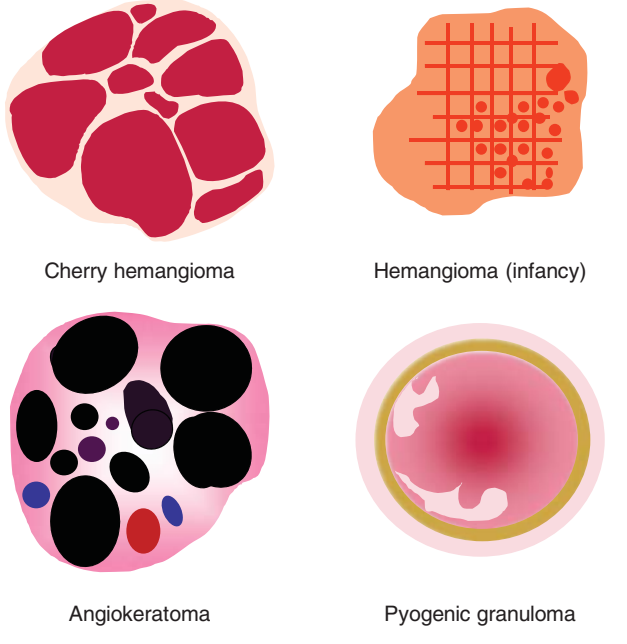
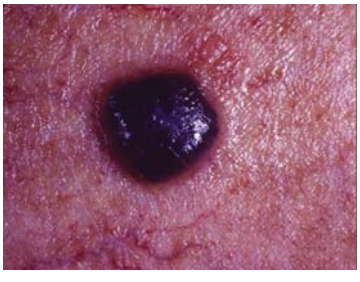


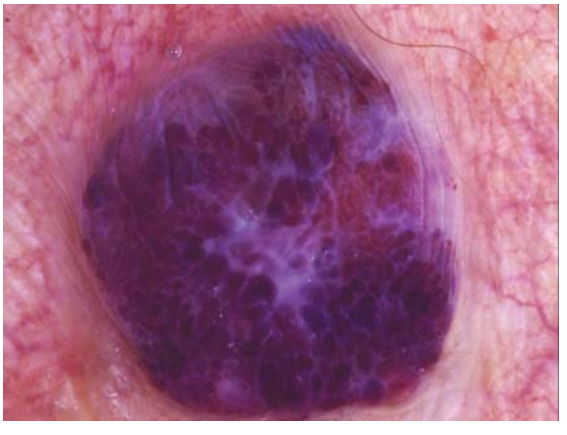
Figure 5d.1 Schematic representation of the dermoscopic patterns for the four most common vascular lesions encountered in clinical practice. Hemangioma with red lacunae (*top left*). Angiokeratoma with black to red-bluish lacunae and a whitish veil (*bottom left*). Hemangioma of the infancy consisting of multiple, small, well-demarcated, red lacunae scattered throughout the lesion on a background of red-whitish homogenous color. Occasionally a red network of vessels is visible (*top right*). Pyogenic granuloma consists of a central red-whitish homogenous area and scattered white rail lines surrounded by a collarette of scale (*bottom right*).

▲ **Figure 5d.2a** Clinical image of a cherry hemangioma.

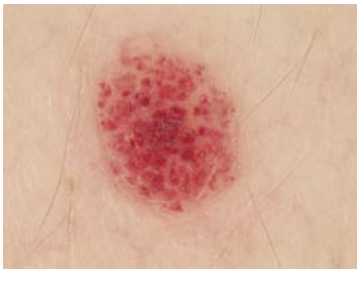
◀ **Figure 5d.2b** Dermoscopy of a cherry hemangioma with multiple, well-demarcated, red lacunae that are tightly clustered.



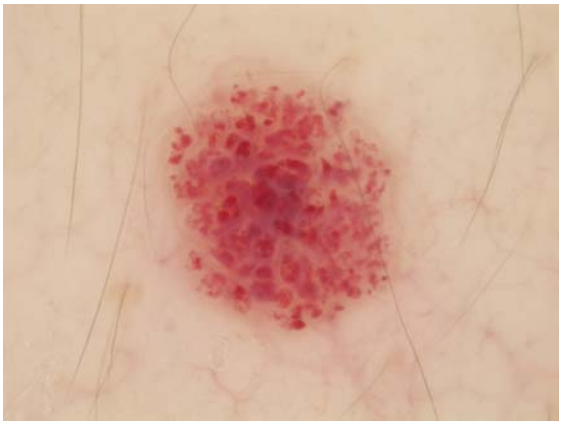
▲ **Figure 5d.3a** Clinical image of a cherry hemangioma.



◀ **Figure 5d.3b** Dermoscopy of a cherry hemangioma demonstrates multiple, well-demarcated red to blue-red lacunae that are tightly clustered.



▲ **Figure 5d.4a** Clinical image of a cherry hemangioma.

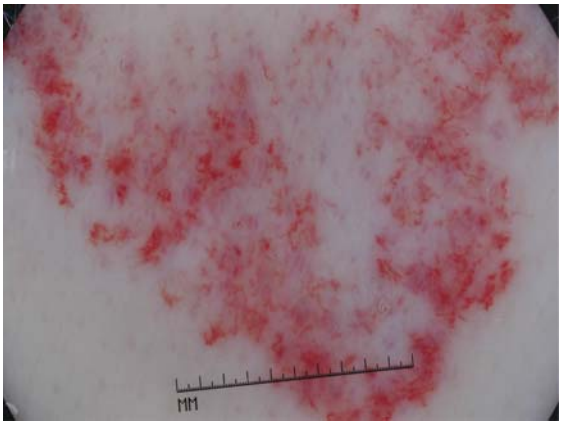


◀ **Figure 5d.4b** Dermoscopy image of a cherry hemangioma with lacunae in the center and dilated vessels at the periphery.

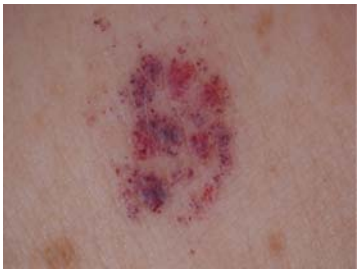
▲ **Figure 5d.5a** Clinical image of cherry hemangioma.

◀ **Figure 5d.5b** Dermoscopy image of cherry hemangioma with multiple dilated serpentine blood vessels.

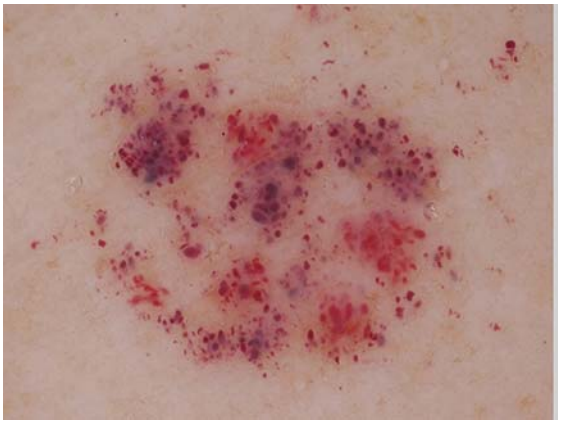
▲ **Figure 5d.6a** Clinical image of a hemangioma of infancy.



◀ **Figure 5d.6b** Dermoscopy reveals numerous torturous and serpentine blood vessels. A few lacunae are also visible.

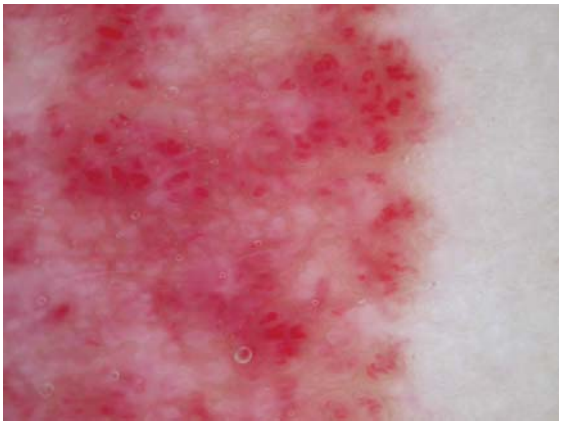


▲ **Figure 5d.7a** Clinical image of a hemangioma.



◀ **Figure 5d.7b** Dermoscopy of this hemangioma reveals multiple loosely packed lacunae.

▲ **Figure 5d.8a** Clinical image of a hemangioma of infancy.

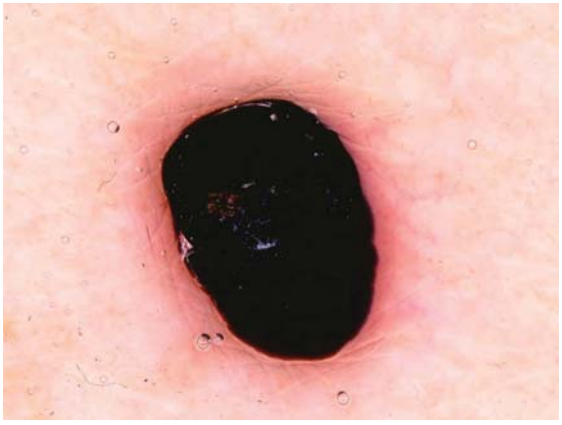


◀ **Figure 5d.8b** Dermoscopy revels multiple, small, well-demarcated, red lacunae that are loosely scattered throughout the lesion on a background of red-whitish homogeneous color. Also, notice the red network of vessels in this hemangioma.

▲ **Figure 5d.9a** Clinical image of a thrombosed hemangioma.

◀ **Figure 5d.9b** Dermoscopy of this partially thrombosed hemangioma shows violaceous lacunae with whitish veil on the right and one dark lacuna on the left. Hemangiomas that develop a partial or total thrombosis can acquire a focal or total blue-black color and resemble melanomas.

▲ **Figure 5d.10a** Clinical image of a thrombosed hemangioma.



◀ **Figure 5d.10b** Dermoscopy shows the lesion as entirely thrombosed and consisting of homogeneous, confluent, dark bluish-black pigment that is sharply demarcated at the periphery. There is also a prominent reddish halo reflecting evidence of physically induced trauma.

▲ **Figure 5d.11a** Clinical image of a solitary angiokeratoma. The clinical diagnosis without dermoscopy was melanoma.

◀ **Figure 5d.11b** On dermoscopy, the lesion reveals multiple dark lacunae and a whitish veil, both of which are commonly seen in solitary angiokeratomas. In addition, maroon lacunae, a haemorrhagic crust, and surface scale can also be seen in this angiokeratoma.

▲ **Figure 5d.12a** Clinical image of a solitary angiokeratoma.

◀ **Figure 5d.12b** Dermoscopy shows multiple dark lacunae with whitish veil and surface scale.

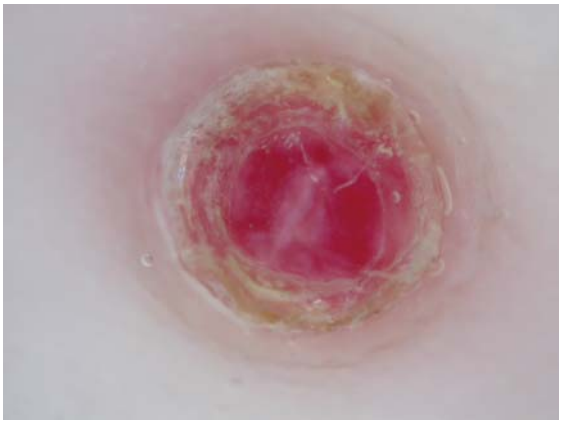
▲ **Figure 5d.13a** Clinical image of a solitary angiokeratoma.

◀ **Figure 5d.13b** Dermoscopy reveals a large central hemorrhagic crust, which is surrounded by a whitish veil. A few dark lacunae and multiple polymorphous blood vessels are visible. This atypical angiokeratoma should be biopsied to rule out the diagnosis of melanoma.

▲ **Figure 5d.14a** Clinical image of a partially thrombosed angiokeratoma.

◀ **Figure 5d.14b** Dermoscopic image. Established lesion consisting partially of poorly defined, blue-red lacunae with an overlying whitish yellow hue. To the left of the lesion is a large focally crusted area of dark, homogenous, confluent blue-black pigmentation. The lesion also contains a subtle surrounding red halo of erythema.

▲ **Figure 5d.15a** Clinical image of a pyogenic granuloma.



◀ **Figure 5d.15b** Dermoscopy shows a central red-whitish homogenous area surrounded by a white collarette. In addition, white lines (or rails) intersecting the red-whitish homogenous areas can be seen.

a reactive hyperproliferative vascular response to a variety of stimuli, such as infective organisms, penetrating injury, hormonal factors, retinoid therapy, or other systemic medications (i.e., docetaxel).

The most frequent dermoscopic pattern of pyogenic granuloma consists of red or red-whitish homogenous areas surrounded by a white collarette; seen in 84% of cases (Figs. 5d.15a, b and 5d.16a, b). The most probable histopathologic correlate of the red or red-whitish homogenous areas is the presence of numerous small capillaries or proliferating blood vessels within a myxoid stroma (Fig. 5d.17a, b). The white collarette of scale correlates with the hyperplastic adnexal epithelium often found at the periphery of many pyogenic granulomas. Another dermoscopic criterion for pyogenic granuloma is the presence of white lines resembling rails within the lesion (Fig. 5d.18a, b). These white lines correspond histologically to the fibrous septa surrounding the capillary tufts or lobules in pyogenic granuloma.

Although the pattern composed of red or red-whitish homogenous areas separated by white lines (rails) and surrounded by a white collarette is characteristic of pyogenic granuloma, amelanotic melanoma should remain in the differential diagnosis and the final diagnosis should rest on the histopathologic evaluation of the lesion.

OTHER VASCULAR LESIONS

Microvenular hemangioma: This lesion is an acquired, slowly growing, asymptomatic, benign vascular tumor that usually presents on the upper limbs, forearms, or trunk of young to middle-aged adults. Clinically, microvenular hemangiomas appear as sharply circumscribed, bright red, solitary lesions varying in size from 0.5 to 2 cm. Scalvenzi et al. (2007) observed, on dermoscopy, a diffuse erythema with multiple well-demarcated small red globules of differing sizes, and a peripheral fine pigment network.

Angioma serpiginosum: Angioma serpiginosum is a benign vascular disorder, characterized clinically by multiple minute, red-to-purple, grouped macules distributed in a serpiginous or gyrate pattern. Histopathology of this lesion reveals ectatic dilated capillaries. As can be predicted, based on the histopathology, dermoscopy reveals numerous small, relatively well-demarcated, round-to-oval red lacunae (Fig. 5d.19a, b). According to Ohnishi et al. (1999) these findings are useful in distinguishing angioma serpiginosum from purpuric dermatosis (e.g., lichen aureus, Schamberg's purpura, Henoch Schonlein purpura, senile purpura) because the latter only reveals irregularly shaped, red to yellow-brown patches with clusters of petechial hemorrhages and/or ill-defined globular structures with blurred borders (not lacunae) (Figs. 5d.20, 5d.21).

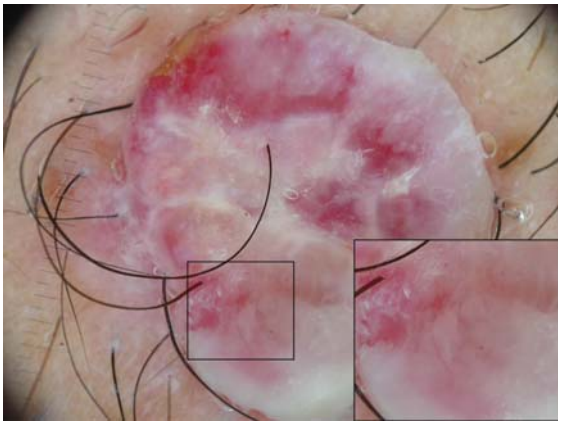
Blue rubber vleb nevus syndrome: This is a rare genodermatosis comprising multiple venous malformations of the skin, gastrointestinal tract and, frequently other sites as well. The dermoscopic findings observed by Mejia-Rodriguez et al., (2008) included a diversity of vascular patterns within each lesion. They observed lesions with reddish or bluish homogenous pigmentation, white linear structures, lacunae, and blood vessels with various morphologies.

Port-wine stain: This is a capillary malformation that is present at birth and persists throughout life. It may be localized or cover extensive areas of the skin surface. Port-wine stains have a predilection to develop on the head/neck, trunk, or limbs. There are two main dermoscopic patterns associated with port-wine stain: (*i*) superficial, composed predominantly of red dotted and globular vessels, and (*ii*) deep, characterized by dilated linear and tortuous vessels. Port-wine stains can also present with a mixed dermoscopy pattern as shown in Fig. 5d.22. Unlike superficial port-wine stains, deep port-wine stains respond poorly to laser ablation. Besides dilated linear and tortuous vessels, other features of deep port-wine stains include the presence of a gray-whitish veil and pale circular

▲ **Figure 5d.16a** Clinical image of a pyogenic granuloma.

◀ **Figure 5d.16b** Dermoscopy reveals another typical pyogenic granuloma pattern with central red-white homogenous areas, large hemorrhagic crust, surface scale, and a surrounding white collarette. Notice the kaleidoscope of colors resembling a rainbow within this lesion. This rainbow pattern is only visible when viewed with polarized light dermoscopy and can be seen in pyogenic granulomas, Kaposi's sarcoma, and scars, just to mention a few entities.

▲ **Figure 5d.17a** Clinical image of an atypical pyogenic granuloma.



◀ **Figure 5d.17b** Dermoscopy reveals a reddish homogeneous area with a white veil. In the lower part of the lesion (square), we can observe polymorphous blood vessels. In this case, the diagnosis of amelanotic melanoma cannot be ruled out and a biopsy is warranted.

▲ **Figure 5d.18a** Clinical image of a pyogenic granuloma.

◀ **Figure 5d.18b** Dermoscopy reveals a few classic features, including reddish homogenous areas, whitish veil, and rail lines. In addition, this lesion manifests the rainbow sign, thus indicating that the image of this lesion was acquired via a polarized light dermoscope. *Source*: Image courtesy of Harold Rabinovitz, MD.

▲ **Figure 5d.19a** Clinical image of angioma serpiginosum consisting of multiple minute, red-to-purple, grouped macules distributed in a serpiginous or gyrate pattern.

◀ **Figure 5d.19b** Dermoscopy reveals numerous small, relatively well-demarcated, round-to-oval red lacunae.

▲ **Figure 5d.20a** Clinical image of an ecchymotic area.

◀ **Figure 5d.20b** Dermoscopy reveals homogenous, blurry reddish-blue areas. The borders tend to be blurry as well.

▲ **Figure 5d.21a** Clinical image of lichen aureus.

◀ **Figure 5d.21b** Dermoscopy of benign pigmented purpura reveals yellowish-brown background color. Within the lesion there are blurry reddish-brown dots and globules.

▲ **Figure 5d.22a** Clinical image of a port-wine stain.

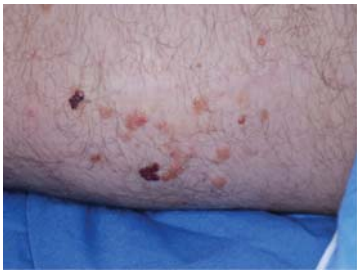
◀ **Figure 5d.22b** Dermoscopy has a mixed pattern with red dotted and globular vessels (superficial pattern) and dilated and tortuous vessels (deep pattern).

areas surrounding a central brownish dot—all features portending a poor response to laser ablation.

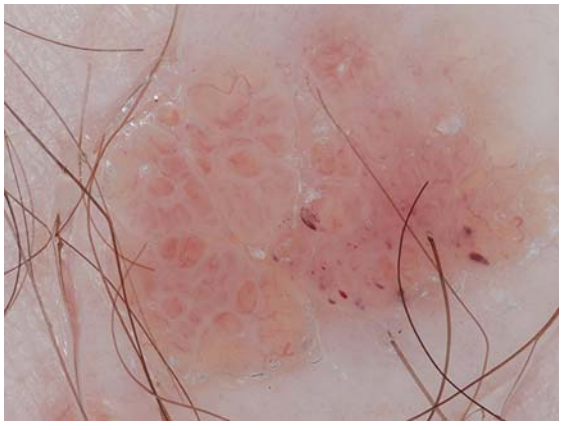
Lymphangioma circumscriptum: This lesion refers to a vascular malformation involving primarily the lymphatic vessels in the dermis. They present clinically as numerous small-vesicle-like lesions grouped in a plaque. On dermoscopy, these lesions show a lacunar pattern composed of clear to tan lacunae surrounded by pale septa. However, depending on the blood vessel component involved, some lacunae can have a pinkish, yellowish, reddish, or violaceous color (Fig. 5d.23a, b).

Targetoid hemosiderotic hemangioma: The so-called hobnail hemangioma is a distinctive, benign vascular proliferation characterized by wedge-shaped dermal proliferation of irregular vascular channels that are lined by endothelial cells with a hobnail morphology. Clinically these lesions appear as small, solitary, red-purple papules or macules that typically, although not always, are encircled by a thin pale area and a peripheral ecchymotic ring, resulting in a targetoid appearance. Patients usually describe cyclic changes in their lesions. Dermoscopy shows a pattern composed of a central area with reddish dark lacunae surrounded by red-brown to violaceous homogenous pigmentation (Fig. 5d.24a, b). In some cases a peripheral delicate pigment network, similar to that seen in dermatofibromas, is present.

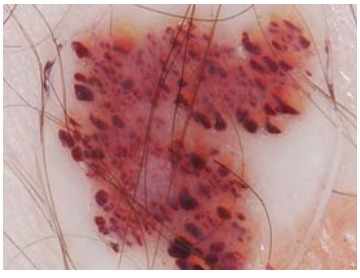
Kaposi's sarcoma: It consists of a multifocal endothelial proliferation predominantly involving the skin, caused by human herpesvirus-8 (HHV-8). HHV-8 induces the formation of vascular channels and the proliferation of spindle-shaped cells. Although Kaposi's sarcoma is considered a low-grade malignant vascular tumor, some consider it a reactive rather than neoplastic process. There are four recognized clinical subsets of Kaposi's sarcoma: classic, endemic, iatrogenic, and HIV related. Clinically the cutaneous lesions begin as reddish-blue macules or flat plaques that gradually enlarge and become nodular. Dermoscopically, some authors have



▲ **Figure 5d.23a** Clinical image of a lymphangioma circumscriptum. This lymphangioma recurred after a wide excision. Dermoscopy reveals multiple different lacunar morphologies.



◀ **Figure 5d.23b** Clustered clear to yellowish lacunae.



▲ **Figure 5d.23c** Clustered maroon and yellowish lacunae.

◀ **Figure 5d.23d** Thrombosed lacunae as seen in angiokeratomas.

▲ **Figure 5d.24a** Clinical image of a targetoid hemosiderotic hemangioma.

◀ **Figure 5d.24b** Dermoscopy reveals a central area composed of dark lacunae, red lacunae, and a whitish veil. A peripheral delicate pigment network surrounds the lesion.

▲ **Figure 5d.25a** Clinical image of classic Kaposi's sarcoma.

◀ **Figure 5d.25b** Different lesions in the same patient often manifest different dermoscopic patterns. This patient had multiple patterns including a pyogenic granuloma-like pattern (*top left*), a blue-yellowish homogenous pattern (*top right*), a reddish homogenous pattern with white structureless areas, scale, and rainbow effect (*bottom left*), and (4) white-reddish homogenous pattern with atypical vessels (*bottom right*).

observed a homogenous pattern with differing colors (i.e., whitish, pinkish, reddish, bluish, or violaceous) in different lesions in the same patient (Fig. 5d.25a, b). In addition, an isolated lesion can occasionally manifest a spectrum of different colors, creating a rainbow-like appearance (Hu et al., 2009) (Fig. 5d.25b). It is however, important to point out that this rainbow pattern is only seen with polarized light dermoscopy. Although the rainbow pattern is commonly encountered in Kaposi's sarcoma, it can also be seen in other entities, including scars, lichen planus, melanoma, stasis dermatitis, and pyogenic granuloma (Figs. 5d.16 and 5d.18) (Cheng et al., 2009). Other dermoscopic features seen in Kaposi's sarcoma include whitish structureless areas, vascular structures, scale, and a white collarette.

Key Points

1. Red/maroon lacunae and black lacunae are the most important single criterion for the diagnosis of hemangioma and angiokeratoma, respectively.
2. Angiokeratoma often exhibits a blue veil, erythema and/or ulceration.
3. Pyogenic granuloma often reveals homogenous red areas, white rail lines, and a collarette of scale.
4. Lymphangiomas reveal numerous clear to yellowish-tan lacunae.

REFERENCES

Braun, R.P., Rabinovitz, H.S., Oliviero, M., Kopf, A.W. & Saurat, J.H., 2005, Dermoscopy of pigmented skin lesions. *J Am Acad Dermatol*, 52, 109–21.

Cheng, S.T., Ke, C.L., Lee, C.H., et al., 2009, Rainbow pattern in Kaposi's sarcoma under polarized dermoscopy: a dermoscopic pathological study. *Br J Dermatol*, 160, 801–9.

Hu, S.C., Ke, C.L., Lee, C.H., et al., 2009, Dermoscopy of Kaposi's sarcoma: areas exhibiting the multicoloured 'rainbow pattern.' *J Eur Acad Dermatol Venereol*, 23, 1128–32.

Mejia-Rodriguez, S., Valencia-Herrera, A., Escobar-Sanchez, A. & Mena-Cedillos, C., 2008, Dermoscopic features in Bean (blue rubber bleb nevus) syndrome. *Pediatr Dermatol*, 25, 270–2.

Ohnishi, T., Nagayama, T., Morita, T., et al., 1999, Angioma serpiginosum: a report of 2 cases identified using epiluminescence microscopy. *Arch Dermatol*, 135, 1366–8.

Scalvenzi, M., De Natale, F., Francia, MG., Balato, A., 2007, Dermoscopy of microvenular hemangioma: report of a case. *Dermatology*, 215, 69–71.

Warshaw, E.M., Lederle, F.A., Grill, J.P., et al., 2009, Accuracy of teledermatology for nonpigmented neoplasms. *J Am Acad Dermatol*, 60, 579–88.

Wolf, I.H., 2002, Dermoscopic diagnosis of vascular lesions. *Clin Dermatol*, 20, 273–5.

Zaballos, P., Daufi, C., Puig, S., et al., 2007, Dermoscopy of solitary angiokeratomas: a morphological study. *Arch Dermatol*, 143, 318–25.

5e Dermatofibromas

Pedro Zaballos, Susana Puig, and Josep Malvehy

INTRODUCTION

Dermatofibroma is a fibrosing cutaneous lesion that is characterized by an increased number of fibrocytes in the dermis and occasionally in the subcutis. It contains a variable admixture of inflammatory cells, coarse collagen bundles, and blood vessels. In addition, the epidermis overlying the tumor is usually acanthotic, papillomatous, and hyperpigmented (Leboit, 2006).

Dermatofibromas are prevalent cutaneous lesions that most frequently affect young to middle-aged adults, with a slight predominance in females. Clinically, dermatofibromas appear as firm, single or multiple firm papules, or nodules that have a relatively smooth surface. Their color varies from light-brown to dark-brown, to purple, red, or yellow. They can develop anywhere on the body surface, with a predilection for the lower extremities and their size can range from a few millimetres to 2 cm. Characteristically, upon lateral compression of the skin surrounding dermatofibromas, the tumors tend to pucker inward producing a dimple-like depression in the overlying skin; a feature known as the dimple or Fitzpatrick's sign. Although the clinical diagnosis of most dermatofibromas is rather straightforward, some may prove challenging to differentiate from melanoma.

DERMOSCOPY

Before embarking on describing the different dermoscopic features and patterns seen in dermatofibromas, it is important to realize that dermatofibromas can appear quite different depending on the type of dermoscope used. In other words, the features seen with nonpolarized light dermoscopy may differ from those seen with polarized light dermoscopy (Agero et al., 2006). These differences can easily be explained based on an understanding of physics of polarized and nonpolarized light (see chap. 2 for more information) and the histopathology of dermatofibromas. The collagenous stroma in a dermatofibroma will appear as a white scar-like area under nonpolarized dermoscopy (Figs. 5e.1–5e.4), whereas it will appear as bright white areas with or without bright white linear lines (i.e., chrysalis-like structures) under contact polarized light dermoscopy (Figs. 5e.1–5e.4). The presence of collagen around broad rete ridges will manifest itself as a white network (Fig. 5e.3). It should come as no surprise that bright white areas, chrysalis-like structures, and white network overlap each other because they all represent dermal collagen (Marghoob et al., 2009). Within the collagenous stroma of a dermatofibroma one can see many vascular channels on histopathology; thus, explaining the common dermoscopic observation of blood vessels within the white areas of a dermatofibroma (Figs. 5e.2 and 5e.5) (Arpaia et al., 2005). These blood vessels tend to be more conspicuous when viewed with polarized noncontact dermoscopy devices (Fig. 5e.2) (Zaballos et al., 2008). The fact that there are many vessels intermingled in the collagenous stroma also explains the reason why the white areas of a dermatofibroma manifests a pink hue when viewed with noncontact polarized light dermoscopy, indicating an increased vascular volume (Figs. 5e.2–5e.4). Histopathology of dermatofibroma also shows increased melanin in keratinocytes, which corresponds dermoscopically with the delicate pigment network seen at the periphery of these tumors (Figs. 5e.1–5e.5) (Zaballos et al., 2008). Lastly, the so-called ring-like or donut-shaped globules seen in some dermatofibromas correspond to widened rete ridges with increased melanin in the keratinocytes (Scope et al., 2008) (Figs. 5e.1 and 5e.3).

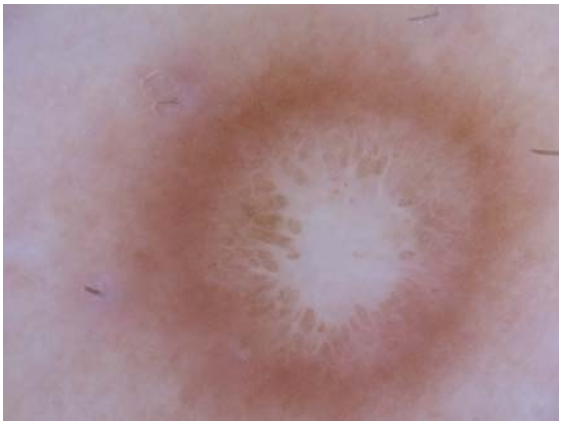
A variety of dermoscopic patterns have been described for dermatofibromas (Fig. 5e.6) (Zaballos et al., 2008). However, the archetypical dermoscopy pattern associated with dermatofibromas consists of a peripheral delicate pigment network with a central scar-like white patch (Figs. 5e.7–5e.9) (Agero et al., 2006; Arpaia et al., 2005; Ferrari et al., 2000b; Kilinc Karaarslan et al., 2007; Zaballos et al., 2008). The pigment network associated with dermatofibromas is usually light-to-medium brown in color, with a fine and delicate quality, which gradually fades into the surrounding skin. The pigment network located toward the center of the lesion often ceases to look like a reticulated mesh but rather begins to resemble "ring-like" globular structures (Scope et al., 2008) (Fig. 5e.3). In approximately 3% of dermatofibromas the pigment network can appear prominent or atypical (Agero et al., 2006; Arpaia et al., 2005; Ferrari et al., 2000a; Scope et al., 2006; Zaballos et al., 2008). The scar-like white patch in dermatofibromas consists of a more or less irregularly outlined and sharply demarcated white area whose histopathologic correlate is increased collagen within the papillary dermis. Ferrari et al. (2000a) found this pattern in 79% of dermatofibromas in their study and Agero et al. (2006) found it in 62% of their cases. Agero et al. (2006) reported a new diagnostic feature consisting of a central white patch with shiny white linear streaks, which are also know as chrysalis-like structures (Figs. 5e.10 and 5e.11) (Marghoob et al., 2009). This feature can only be seen with polarized light dermoscopy (Figs. 5e.2 and 5e.4).

In 2008, Zaballos et al. published the results of a prospective study where they evaluated the dermoscopic features and patterns of 412 dermatofibromas (Zaballos et al., 2008). The authors identified 10 global patterns associated with dermatofibromas (Table 5e.1 and Fig. 5e.6). Some patterns seen in dermtofibromas consist of a single dermoscopic structure (i.e., delicate pigment network, white scar-like patch, homogenous brown pigmentation, or white network). However, most dermatofibromas manifest a pattern created by a combination of the aforementioned structures. Finally, an atypical dermoscopic pattern consisting of atypical dermoscopic structures that are distributed in an irregular manner can also be seen (Figs. 5e.10 and 5e.11). Zaballos et al. (2008) found that the most common dermatofibroma pattern observed in their study was the classic pattern (35%) (Figs. 5e.7–5e.9). The second most frequent pattern observed in dermatofibromas consisted of a delicate pigment network located throughout the lesion (15%) (Figs. 5e.12 and 5e.13). Kilinc Karaarslan et al. (2007) found this pattern in approximately 23% of their cases of dermatofibroma.

In the study by Zaballos et al. (2005), three out of the 10 global dermatofibroma patterns revealed a structure that the authors called the "white network" (Figs. 5e.10, 5e.14, 5e.15). This structure consists of white lines surrounding small islands of brown pigment or surrounding globule-like (i.e., "ring-like") structures. It was found in approximately 18% of dermatofibromas, many of which were large lesions (>1 cm). This white network appears to be a variation of the classic white scar-like patch, bright white linear streaks, or chrysalis-like structures described above (Figs. 5e.14 and 5e.15). The presence of this particular feature together with the presence of a delicate network or blood vessels in a dermatofibroma may warrant a biopsy since similar structures can also be seen in Spitz nevi and melanomas (Figs. 5e.10 and 5e.11).

Another structure found in approximately 25% of dermatofibromas was homogenous areas with brown color with or without a blue-whitish veil (Fig. 5e.16). In addition, some dermatofibromas manifest yellowish pigment, which represents hemosiderin deposits or lipophages (Figs. 5e.14 and 5e.17). The presence of a bluish or red-bluish homogenous area was present in approximately 3% of dermatofibromas and all of these cases were diagnosed histopathologically as hemosiderotic or aneurysmal

▲ **Figure 5e.1a** Clinical image of a dermatofibroma.



◀ **Figure 5e.1b** The image of this dermatofibroma was acquired using a nonpolarized dermoscope. The lesion has a central white scar-like area surrounded by a delicate pigment network. The network located toward the center of the lesion appears as "ring-like" globular structures.

◀ **Figure 5e.1c** This image of the same dermatofibroma was acquired using a polarized dermoscope. The central white area appears much brighter, has a pink hue, and reveals bright white structures (chrysalis and white network). The presence of bright white areas surrounding "ring-like" globules is termed "white network" and this can sometimes be mistaken for a negative network associated with melanoma.

▲ **Figure 5e.2a** Clinical image of a dermatofibroma.

(**B**)

(**C**)

(**D**)

Figure 5e.2 (**B**) Image acquired with nonpolarized dermoscopy reveals central scar-like area surrounded by a delicate network. Within the scar-like area a small cluster of blood vessels can be seen. (**C**) Image acquired with contact polarized dermoscopy reveals bright white areas or chrysalis-like structures, which were not evident with nonpolarized dermoscopy. (**D**) Image acquired with noncontact polarized dermoscopy. This technique eliminates pressure-induced blanching of blood vessels. Notice the presence of chrysalis-like structures and multiple blood vessels within the scar-like area. The entire scar-like area has a pink hue, reflecting an increased vascular volume in this lesion. The diagnosis of dermatofibroma can easily be made in image **B**. The diagnosis of dermatofibroma may prove more challenging in image **D**, with melanoma now entering the differential diagnosis. Viewing lesions with both polarized and nonpolarized dermoscopy provides complementary information, which is likely to help correctly diagnose most dermatofibromas.

▲ **Figure 5e.3a** Clinical image of a dermatofibroma.

(**B**)

(**C**)

(**D**)

Figure 5e.3 (**B**) The image of this dermatofibroma was acquired using a nonpolarized dermoscope. The lesion has a central stellate white scar-like area surrounded by a pigment network. Ring-like globules can be seen in the center of the lesion. (**C**) This image of the same dermatofibroma was acquired via a polarized contact dermoscopy. The central white area now appears brighter. (**D**) This image was acquired through a noncontact polarized dermoscope. The central white areas now appear with a pink hue indicating that there is an increased vascular volume in this lesion. There are also focal white network-like (crystalline structures) areas in the lesion.

▲ **Figure 5e.4a** Clinical image of a dermatofibroma.

(**B**)

(**C**)

(**D**)

Figure 5e.4 (**B**) The image of this dermatofibroma was acquired through a nonpolarized dermoscope. The lesion has a central white scar-like area surrounded by a pigment network. (**C**) This image was acquired through a polarized contact dermoscopy. The central white area now appears brighter and reveals chrysalis-like structures. (**D**) This image was acquired through a noncontact polarized dermoscope. The central area now manifests a pink hue with numerous chrysalis-like structures.

▲ **Figure 5e.5a** Clinical image.

◀ **Figure 5e.5b** Dermoscopy reveals a dermatofibroma with a peripheral network and central scar-like area. Numerous blood vessels can be seen within the white scar-like area.

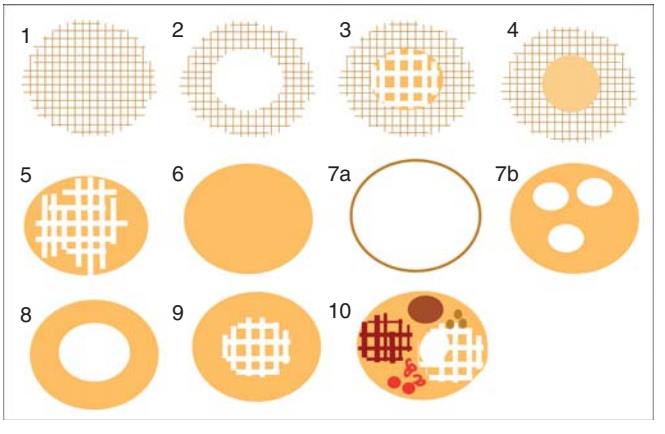


Figure 5e.6 Schematics of the different dermoscopic patterns in dermatofibromas. Dermatofibromas with peripheral delicate pigment network. 1: Delicate pigment network throughout the lesion. 2: Peripheral delicate pigment network and central white scar-like patch. 3: Peripheral delicate pigment network and central white network. 4: Peripheral delicate pigment network and central homogenous area. Dermatofibromas without peripheral delicate pigment network. 5: White network throughout the lesion. 6: Homogenous pigment throughout. 7a: Homogenous white scar-like patch throughout. 7b: Multiple focal white scar-like patch. 8: Peripheral homogenous pigment with central white scar-like patch. 9: Peripheral homogenous pigment with central white network. 10: Atypical pattern. *Source*: Adapted from Zaballos et al. (2008).

Table 5e.1 Dermoscopic Patterns Associated with Dermatofibromas

Patterns	Structures	%
1	Delicate pigment network throughout	14.56
2	Peripheral delicate pigment network and central white scar-like patch	34.7
3	Peripheral delicate pigment network and central white network	9.0
4	Peripheral delicate pigment network and central homogenous pigmentation	4.8
5	White network throughout	2.18
6	Homogenous pigmentation throughout	4.8
7a	White scar-like patch throughout	5.58
7b	Multiple focal white scar-like patches	5.8
8	Peripheral homogenous pigmentation and central white scar-like patch	7.3
9	Peripheral homogenous pigmentation and central white network	5.1
10	Atypical	6.1

Source: Adapted from Zaballos et al. (2008).

▲ **Figure 5e.7a** Clinical image.

◀ **Figure 5e.7b** Dermoscopy of a classic dermatofibroma with peripheral network and central scar-like area.

▲ **Figure 5e.8a** Clinical image of dermatofibroma.

◀ **Figure 5e.8b** Dermoscopy image: typical lesion demonstrating a peripheral delicate pigment network and a central white scar-like patch. There are "ring-like" globular structures at the perimeter of the white scar-like patch.

▲ **Figure 5e.9a** Clinical image of dermatofibroma.

◀ **Figure 5e.9b** Dermoscopy reveals one typical lesion demonstrating a peripheral delicate pigment network and a small central white scar-like patch with linear white streaks (i.e., chrysalis).

▲ **Figure 5e.10a** Clinical image of aneurysmal dermatofibroma.

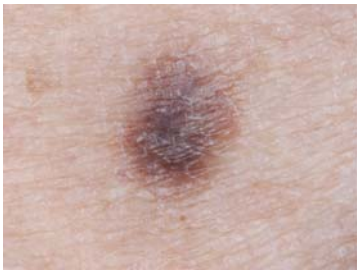
◀ **Figure 5e.10b** With dermoscopy the lesion shows an atypical pattern composed of brownish homogenous area (*right*), a white scar-like patch in the center, red-bluish homogenous area (typical of aneurysmal dermatofibroma) with bright white linear chrysalis-like structures and vascular structures (*left*). In addition, a white network is apparent in the upper and lower part of the lesion. This white network is created when "ring-like" globules or small islands of pigmented rete ridges are surrounded by collagen (i.e., white scar-like area, chrysalis-like, bright white linear streaks). The white network can sometimes be difficult to differentiate from a negative network encountered in melanoma and Spitz nevi. This lesion is unusual enough that a biopsy should be contemplated.

▲ **Figure 5e.11a** Clinical image of aneurysmal dermatofibroma.

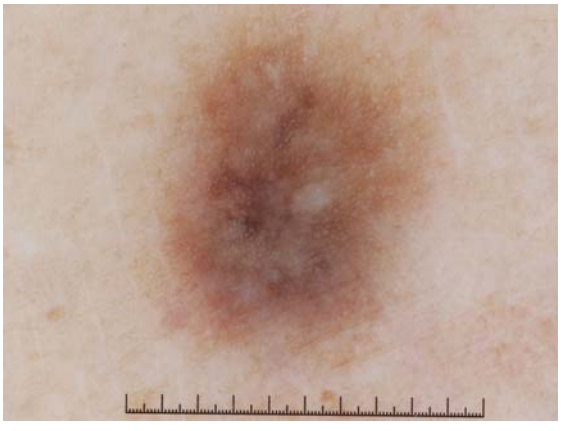
◀ **Figure 5e.11b** Dermoscopy reveals an atypical pattern composed of a peripheral atypical pigment network, a central red-bluish homogenous area with white structures, including chrysalis. Vascular structures, and erythema can also be seen.

▲ **Figure 5e.12a** Clinical image of dermatofibroma.

◀**Figure 5e.12b** Dermoscopy of this dermatofibroma displays a delicate pigment network throughout the lesion.



▲ **Figure 5e.13a** Clinical image of dermatofibroma.



◀**Figure 5e.13b** Dermoscopy of this dermatofibroma displays a pigment network throughout the lesion.

▲ **Figure 5e.14a** Clinical image of a lipidized dermatofibroma.

◀**Figure 5e.14b** Dermoscopy shows a peripheral delicate pigment network, white network, and chrysalis-like structures. We can also observe a yellow coloration in the right part of the lesion, which corresponds histopathologically to areas of lipidization with lipophages and Touton giant cells.

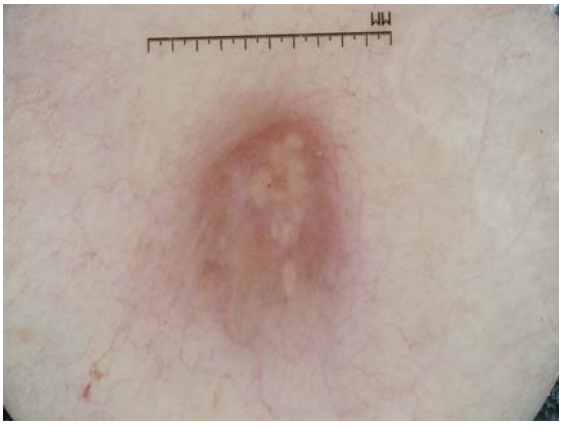
▲ **Figure 5e.15a** Clinical image of dermatofibroma.

◀**Figure 5e.15b** The lesion is dermoscopically composed of a peripheral delicate pigment network and a central white network. The lesion also has vascular structures, including many dotted blood vessels and erythema.

▲ **Figure 5e.16a** Clinical image of an aneurysmal dermatofibroma.

◀ **Figure 5e.16b** Under dermoscopy this variant of dermatofibroma, with a peripheral delicate pigment network and central blue-violaceous homogenous pigmentation, can be mistaken for a melanoma.

▲ **Figure 5e.17a** Clinical image of a biopsy-proven dermatofibroma.



◀ **Figure 5e.17b** Dermoscopy reveals foci of yellow coloration that correspond histopathologically to areas of lipidization with lipophages.

▲ **Figure 5e.18a** Clinical image.

◀ **Figure 5e.18b** Dermoscopy shows a focal area with thickened network and multiple blood vessels. The features in this dermatofibroma can also be seen in melanoma.

dermatofibromas (Figs. 5e.10 and 5e.11) (Blum et al., 2004; Scalvenzi et al., 2007; Zaballos et al., 2006). The most probable histopathologic correlate of this structure is prominent blood-filled spaces and intra- and extracellular hemosiderin deposits. Most hemosiderotic or aneurysmal dermatofibromas manifest a multicomponent or atypical dermoscopy pattern with central bluish or reddish homogenous areas in combination with white structures, peripheral delicate pigment network, and vascular structures; therefore, in such lesions the diagnosis of melanoma must be entertained.

Vascular structures located within the white scar-like areas of a dermatofibroma are quite common (Figs. 5e.5 and 5e.18). Zaballos et al. (2008) found vascular structures in approximately 50% of dermatofibromas, Ferrari et al. (2000a) found them in 29% of cases, and Agero et al found them in 44% of cases (Agero et al., 2006). The most common vascular structures seen in dermatofibromas include erythema (32%), dotted vessels (Fig. 5e.19) (31%), comma vessels (17%), and hairpin vessels (15%) (Fig. 5e.20). Less frequently, glomerular vessels, linear–irregular vessels, and polymorphous/atypical vessels are visible (Fig. 5e.20).

As mentioned previously, "ring-like globules" corresponding to flattened, broad, and hyperpigmented rete ridges is a frequent structure seen in dermatofibromas (Figs. 5e.1 and 5e.21) (Scope et al., 2008). Less frequent dermoscopic structures observed in dermatofibromas include scale, ulceration (presumably induced by external injury) (Fig. 5e.22), fissures (sulci), ridges, and a mamillatted surface resulting from epidermal hyperplasia (Figs. 5e.23–5e.25).

In conclusion, knowing the dermoscopic structures and patterns common to dermatofibromas facilitates in the clinical recognition of these tumors. However, despite this knowledge, some dermatofibromas prove difficult to differentiate from melanocytic neoplasms (Figs. 5e.26 and 5e.27).

▲ **Figure 5e.19a** Clinical image of dermatofibroma.

◀ **Figure 5e.19b** Dermoscopy image shows a nonpigmented dermatofibroma with erythema and numerous dotted vessels (circled area).

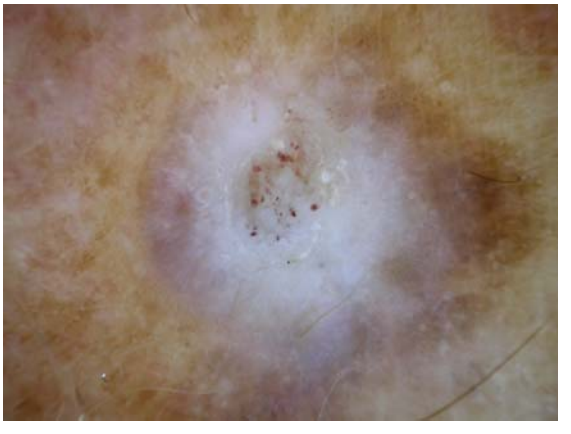
▲ **Figure 5e.20a** Clinical image of dermatofibroma.

◀ **Figure 5e.20b** This dermatofibroma shows many different vascular structures, including hairpin vessels and erythema. Focal areas with a white network can also be seen.

▲ **Figure 5e.21a** Clinical image of a dermatofibroma.

◀ **Figure 5e.21b** Dermoscopy reveals a classic dermatofibroma with numerous ring-like globules.

▲ **Figure 5e.22a** Clinical image of dermatofibroma.

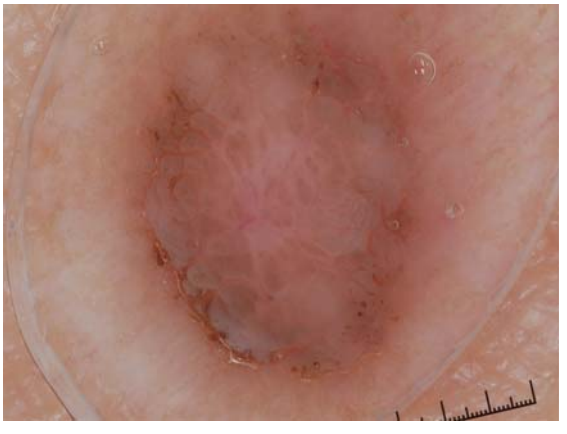


◀ **Figure 5e.22b** This lesion shows an atypical pattern composed of a white scar-like patch with a central area of ulceration and vascular structures. In addition, focal brown pigment (*right*) and globule-like structures (upper right part) are seen, making it impossible to differentiate it from melanoma.

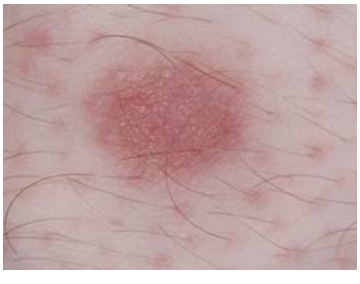
▲ **Figure 5e.23a** Clinical image of a dermatofibroma with a mamillated surface.

◀ **Figure 5e.23b** Dermoscopy shows ring-like globules.

▲ **Figure 5e.24a** Clinical image of a mamillated dermatofibroma.



◀ **Figure 5e.24b** Dermoscopy reveals fissures (sulci) and ridges, which are more commonly associated with seborrheic keratoses.



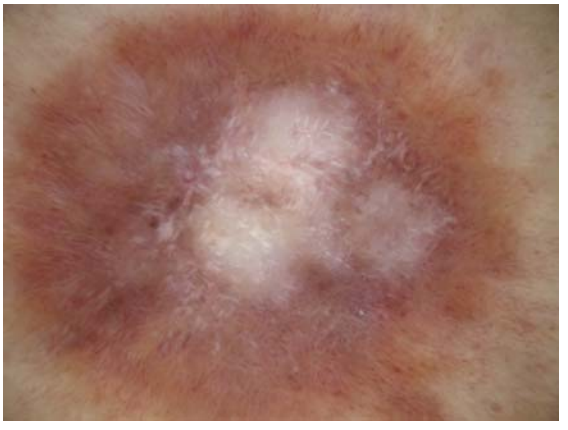
▲ **Figure 5e.25a** Clinical image of a mamillated dermatofibroma.

◀ **Figure 5e.25b** Dermoscopy reveals a homogeneous lesions with numerous dotted vessels.

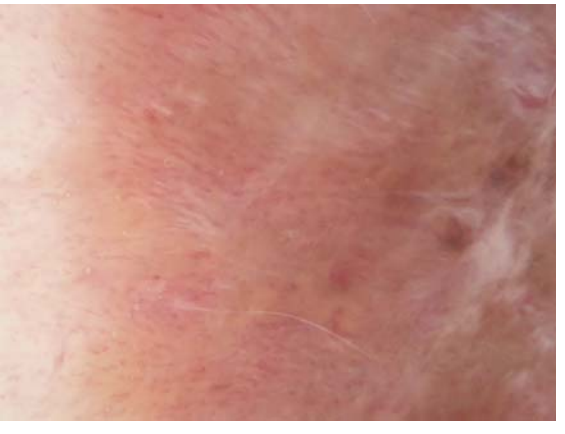
▲ **Figure 5e.26a** Clinical image of a dermatofibroma.

◀ **Figure 5e.26b** Dermoscopy reveals a prominent network, milky red areas, and chrysalis-like structures. The differential diagnosis of this dermatofibroma should include melanoma.

▲ **Figure 5e.27a** Clinical image of a 2 cm dermatofibroma.



◀ **Figure 5e.27b** Dermoscopy reveals peripheral brown homogenous pigment, central bright white areas, chrysalis-like structures, pink hue, and numerous irregular blood vessels.



◀ **Figure 5e.27c** The dermoscopy features described in figure 5e.27b are highlighted in this magnified image of the same lesion.

Key Points

1. The most frequent dermoscopic pattern in dermatofibromas is the combination of white central scar-like patch surrounded by a delicate pigment network.
2. Dermatofibormas can exhibit a wide range of clinical and dermoscopic patterns, some of which can simulate melanoma.
3. Dermatofibromas can manifest different structures and patterns depending on the type of dermoscope used (nonpolarized vs polarized dermoscope). The two different light sources provide complimentary information.

REFERENCES

Agero, A., Taliercio, S., Dusza, S., et al., 2006, Conventional and polarized dermoscopy features of dermatofibroma. *Arch Dermatol*, 142, 1431–7.

Arpaia, N., Cassano, N. & Vena, G., 2005 Dermoscopic patterns of dermatofibroma. *Dermatol Surg*, 31, 1336–9.

Blum, A., Jaworski, S., Metzler, G. & Bauer, J., 2004, Lessons on dermoscopy: Dermoscopic pattern of hemosiderotic dermatofibroma. *Dermatol Surg*, 30, 1354–5.

Ferrari, A., Soyer, H., Peris, K., et al., 2000a, Central white scarlike patch: a dermatoscopic clue for the diagnosis of dermatofibroma. *J Am Acad Dermatol*, 43, 1123–5.

Ferrari, A., Soyer, H., Peris, K., et al., 2000b, Central white scarlike patch: a dermatoscopic clue for the diagnosis of dermatofibroma. *J Am Acad Dermatol*, 43, 1123–5.

Kilinc Karaarslan, I., Gencoglan, G., Akalin, T. & Ozdemir, F., 2007, Different dermoscopic faces of dermatofibromas. *J Am Acad Dermatol*, 57, 401–6.

Leboit, P.E., Burg, G., Weedon, D. & Sarasin, A., 2006, *Pathology and Genetics of Skin Tumours*. Oxford: OUP/IARC/WHO, 355.

Marghoob, M., Cowell, L., Kopf, A. & Scope, A., 2009, Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*, 145, 618.

Scalvenzi, M., Balato, A., de Natale, F., et al., 2007, Hemosiderotic dermatofibroma: report of one case. *Dermatology*, 214, 82–4.

Scope, A., Ardigo, M. & Marghoob, M., 2008, Correlation of dermoscopic globule-like structures of dermatofibroma using reflectance confocal microscopy. *Dermatology*, 216, 81–2.

Scope, A., Benvenuto-Andrade, C., Agero, A. & Marghoob, M., 2006, Nonmelanocytic lesions defying the two-step dermoscopy algorithm. *Dermatol Surg*, 32, 1398–406.

Zaballos, P., Guionnet, N., Puig-Butille, S. & Malvehy, J., 2005, Central white network: an additional dermoscopic feature for the diagnosis of dermatofibroma. *Dermatol Surg*, 31, 960–2.

Zaballos, P., Llambrich, A., Ara, M., et al., 2006, Dermoscopic findings of haemosiderotic and aneurysmal dermatofibroma: report of six patients. *Br J Dermatol*, 154, 244–50.

Zaballos, P., Puig-Butille, S., Llambrich, A. & Malvehy, J., 2008, Dermoscopy of dermatofibromas: a prospective morphological study of 412 cases. *Arch Dermatol*, 144, 75–83.

6 Step 2: Methods to differentiate between melanoma and benign melanocytic nevi

6a Analytic features of melanoma *vs* benign nevi on nonglabrous skin: Colors and structures

Josep Malvehy and Susana Puig

The algorithms used to differentiate melanoma from benign nevi are presented in chapters 6b–6h. This chapter highlights the criteria that are commonly associated with melanoma and will contrast these to the criteria seen in benign nevi. This chapter focuses on features seen in melanocytic lesions located on all areas of the skin except for the palms, soles, nails, scalp, mucosa, and face.

COLORS

Benign lesions usually reveal only one or two colors, whereas melanoma frequently reveals three or more colors. Thus, the number of colors present in a lesion can help differentiate many benign nevi from melanoma. Lesions with 5–6 colors have a sensitivity for melanoma of 53%, specificity of 95%, and an odds ratio of 3. In other words, a melanocytic lesion with five or more colors should always raise the index of suspicion that the lesion under investigation is a melanoma. With that being said, it is also important to appreciate that not all colors have the same impact on the diagnosis of melanoma. The presence of red, white, and/or blue-gray colors in a lesion implies the possible diagnosis of melanoma more so than a lesion manifesting only different shades of brown (Figs. 6a.1 and 6a.2).

Red Color

Red color in the skin represents hemoglobin. Blood vessels will appear as red dots, lines, or globules. The presence of comma vessels is most commonly associated with benign nevi (intradermal nevi) (Fig. 6a.3). In contrast, the presence of dotted and serpentine vessels (i.e., polymorphous) within the same lesion is highly suggestive of melanoma (Fig. 6a.4A, B) (Menzies et al., 2008). An increased blood volume within the lesion will manifest itself as milky red areas. These milky red areas are an important clue to melanoma. In fact, one recent study found that the presence of more than one shade of pink within a melanocytic lesion is a positive predictor of melanoma (Menzies et al., 2008).

Gray Color

Gray color (multiple blue gray granules or granularity) corresponds to melanin in the papillary dermis (Braun et al., 2007). This melanin can be present as free melanin particles in the dermis or as melanin within melanophages located in the papillary dermis. Gray colored granularity encompassing less than 10% of the surface area of the lesion can be seen in nevi and in melanoma (Fig. 6a.5A, B). However, granularity involving more than 50% of the surface area of a melanocytic neoplasm is highly suggestive of melanoma (Fig. 6a.6A, B) (Braun et al., 2007; Zalaudek et al., 2004).

White Color

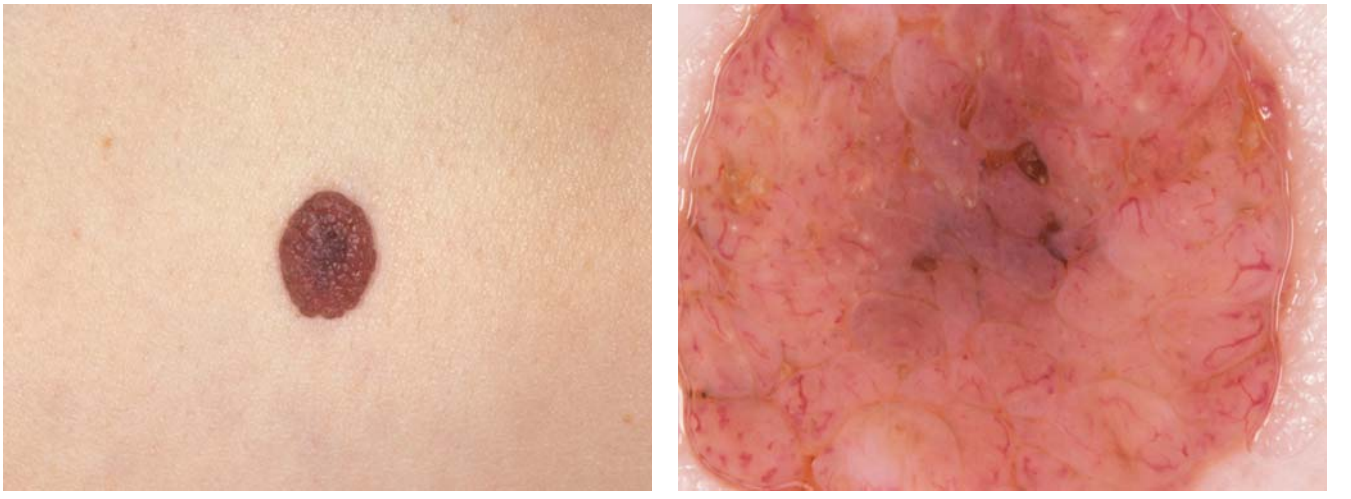
White-colored areas or clods within melanocytic lesions are usually associated with fibrosis or hyperkeratosis (Braun et al., 2007). These white areas often correspond to regression under histopathology. In addition, structures known as chrysalis appear as bright white linear lines that are often oriented orthogonal to each other (Marghoob et al., 2009). The chrysalis structure can only be seen with polarized light. It is hypothesized that these white lines correspond to stromal remodeling. They are most frequently encountered in Spitz nevi and melanoma (Figs. 6a.6A, B and 6a.7).

Black Color

Black color is due to the presence of melanin in the *stratum corneum*, within the upper parts of the epidermis, or throughout all layers of the

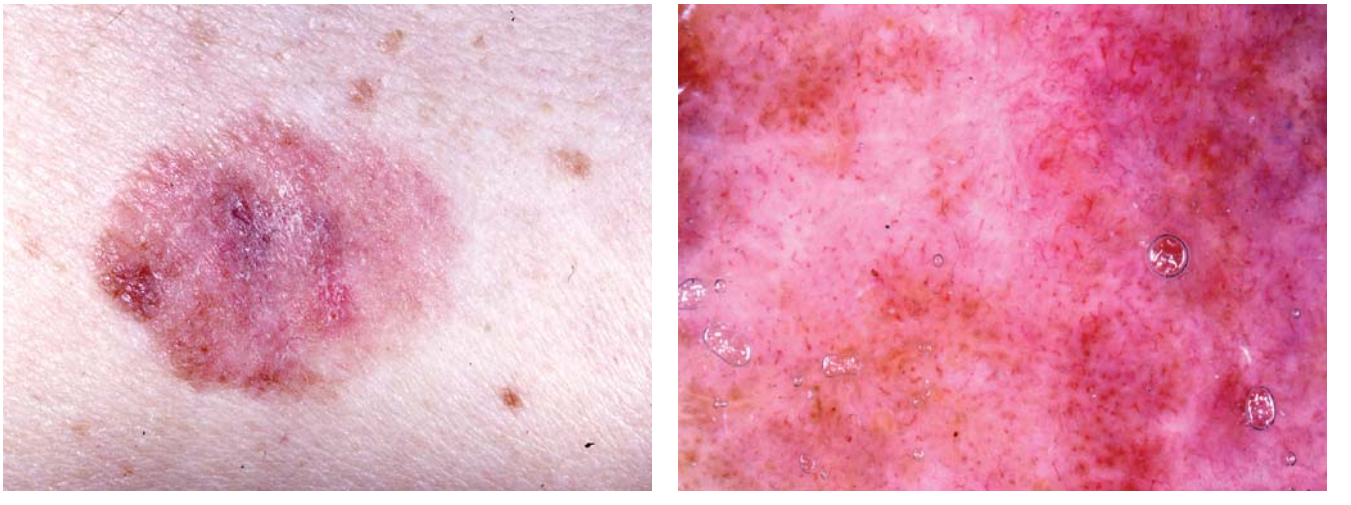
Figure 6a.1 Dermoscopy of a melanoma with multiple colors (black, red, blue, gray, dark brown, light brown, and white). The lesion also presents atypical pigment network, dots, and globules irregularly distributed, irregular blotch, regression structures, atypical vessels, and milky red areas. Dermoscopy image obtained with contact and polarized light.

Figure 6a.2 Benign nevus with only one color (light brown). The lesion presents a pigment network and few typical globules. Dermoscopy image obtained with contact and polarized light.



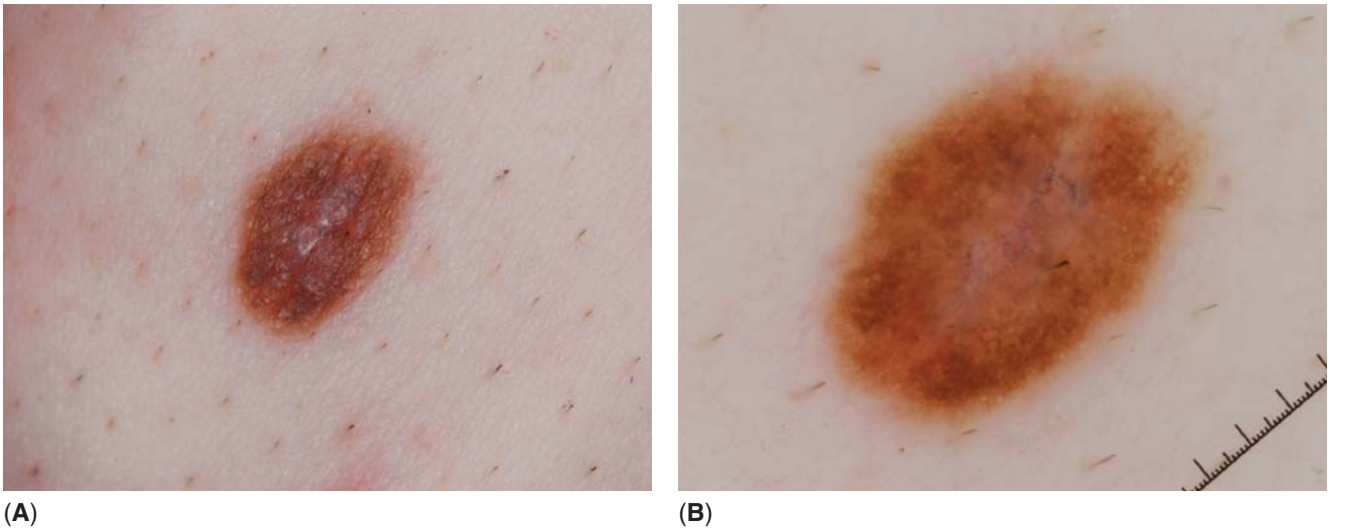
(**A**) (**B**)

Figure 6a.3 (**A, B**) This intradermal benign nevus has many comma-shaped vessels.



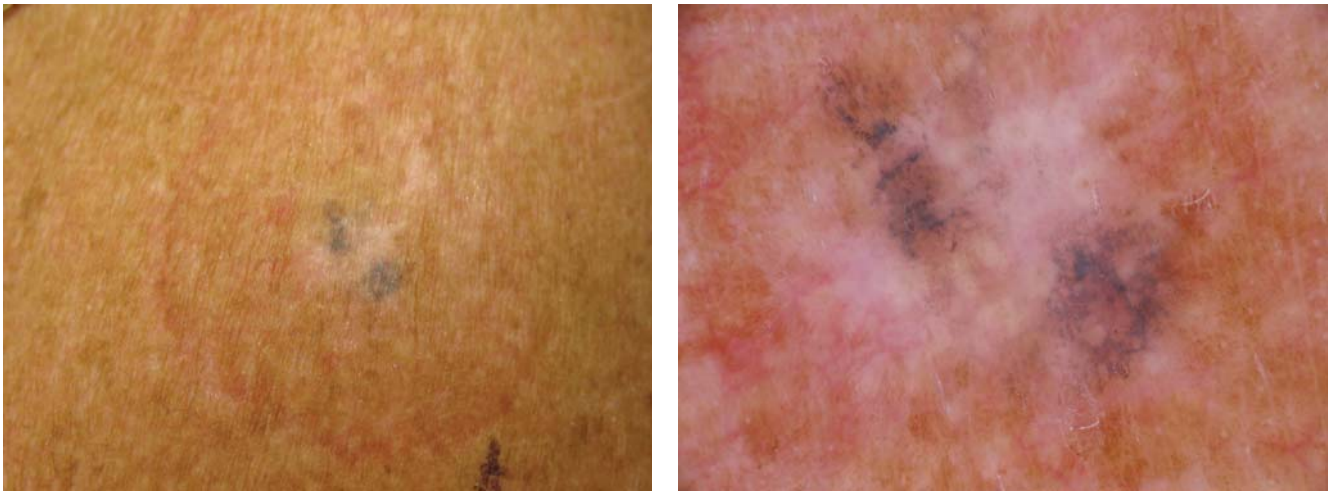
(**A**) (**B**)

Figure 6a.4 (**A, B**) This hypomelanotic melanoma has polymorphous vessels and milky red areas.



(**A**) (**B**)

Figure 6a.5 (**A, B**) This nevus has a focal area of granularity.



(**A**) (**B**)

Figure 6a.6 (**A, B**) This melanoma has extensive regression with granularity/peppering and scar-like depigmentation.

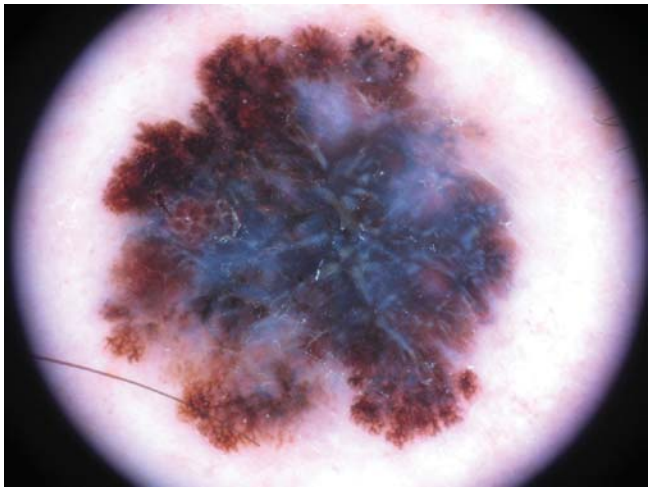


Figure 6a.7 This is a melanoma with multiple colors (black, blue, gray, white, dark brown, and light brown). Pigment network is atypical, with thick lines, small holes, and abrupt cutoff at the periphery. The lesion also shows streaks at the periphery irregularly distributed, dots and globules irregularly distributed, regression structures and chrysalis. Dermoscopy image obtained with contact and polarized light.

epidermis. This melanin may be present within keratinocytes and melanocytes (Braun et al., 2005; Yadav et al., 1993). A high concentration of melanin within keratinocytes located in the stratum corneum appears as a "black lamella" (or blotch), which may be removed using a simple tape stripping method. In contrast, melanin pigment located below the stratum corneum cannot be tape stripped off. In nevi, black color can be seen as a black lamella, centrally located black dots, black dots overlying the network lines, or as a centrally located blotch. In melanoma, black color is often seen as irregular blotches (i.e., off center blotch or presence of multiple blotches) or as atypical dots (i.e., dots not within the center of the lesion and not overlying the network lines). The blotches in melanoma usually correspond to melanin in all layers of the epidermis and also within the dermis. The irregular black dots in melanoma correspond to pagetoid spread (Fig. 6a.8).

Light Brown Color

Light brown color is characteristic of benign melanocytic lesions. However, light brown color in association with atypical blood vessels can be seen in hypopigmented melanoma (Fig. 6a.4). In addition, the presence of light brown structureless areas at the periphery of the lesion is also a warning sign for melanoma. It has been shown that melanomas in fair-skinned individuals may show few colors and structures, being mostly light brown. Thus, the presence of a light brown color is not a guarantee that the lesion will be benign.

Dark Brown Color

Dark brown color may be present in benign and malignant lesions. In melanoma, small brown dots, irregularly distributed and not overlying network lines, correspond to small clusters of atypical melanoma cells in the epidermis (Fig. 6a.8).

MELANOMA-SPECIFIC STRUCTURES (TABLE 6A.1)

Atypical Pigment Network

The pigment network characteristic of melanoma is usually prominent with thick lines and holes of differing sizes (Annessi et al., 2007). The color of the network in melanoma can appear with colors varying from brown to gray to black. The network in nevi tends to be relatively uniform in thickness and color with thinning at the periphery, in melanoma the network appears heterogenous, differing in quality and color from one part of the lesion to another. The network in melanoma will usually manifest color variegation, differing line widths, differing hole sizes, broken-up network creating branched streaks, and abrupt cutoff at the periphery (Figs. 6a.9A, B and 6a.10A, B).

Negative Network

The negative network consists of serpiginous interconnecting hypopigmented lines that surround irregularly shaped pigmented structures, which resemble elongated and curvilinear globules. This structure can be seen with both polarized and nonpolarized dermoscopy. The negative network can sometimes be seen in congenital or acquired nevi, especially Spitz nevi. In benign nevi the negative network will be distributed in a symmetric fashion and often involve the entire lesion. In melanoma the negative network is usually distributed asymmetrically and is found focally within the lesion. (Figs. 6a.11A, B and 6a.12A, B)

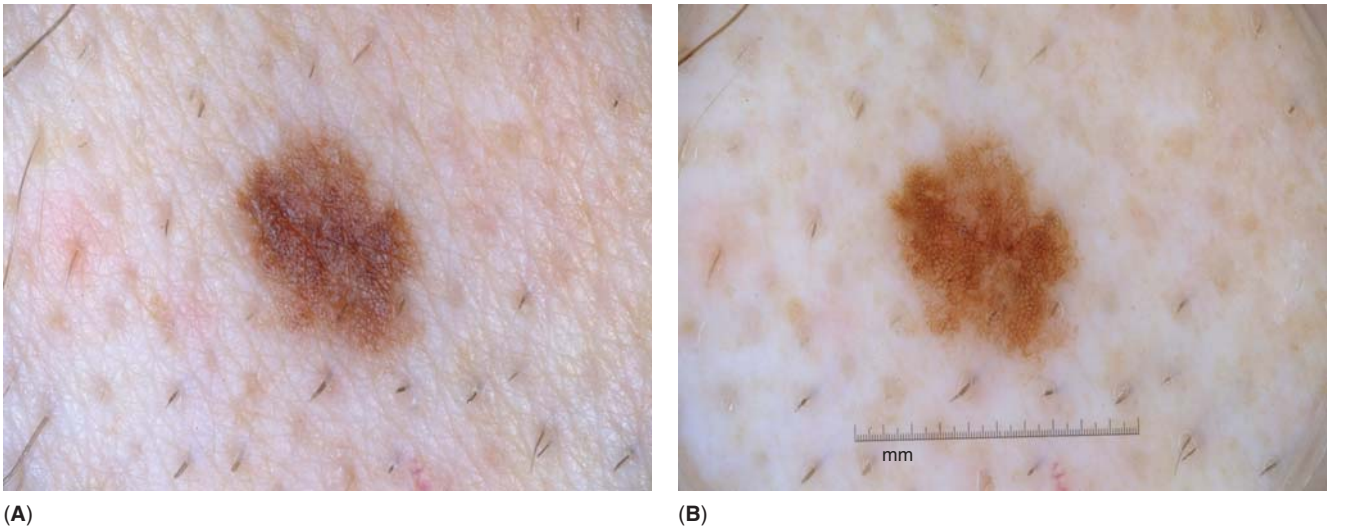
Irregular Streaks (Radial Streaming and Pseudopods)

Streaks consist of pseudopods and/or radial streaming (Argenziano et al., 1998). Streaks present around the entire perimeter of a lesion (i.e., regular streaks), creating a starburst appearance, are characteristic of pigmented Spitz or Reed nevi. The presence of streaks irregularly distributed at the periphery (i.e., irregular streaks) of the lesion is highly suggestive of

Table 6a.1 Melanoma-specific Structures

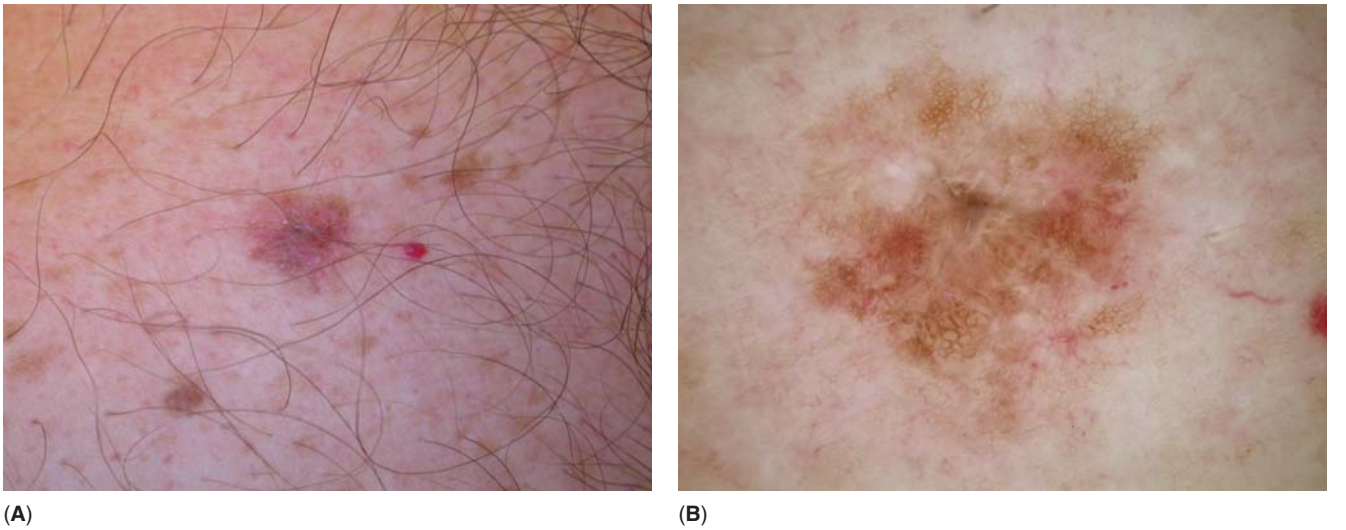
Structure/ feature	Sensitivity (Highest reported) (%)	Specificity (Highest reported) (%)	Odds ratio (Highest reported)
Atypical network	77	89	9.0
Streaks	23	99	5.8
Negative network	22	95	2.0
Chrysalis/crystalline structures	5	99	3.9
Atypical dots & globules	88	97	4.8
Atypical blotch	38	88	4.1
BWV	51	99	13
Regression structures	46	94	8.0
Atypical vessels	63	96	12.5
Peripheral brown structureless areas	63	96	28
5–6 colors	53	95	3.2

Figure 6a.8 The lesion is a melanoma with multiple colors (black, dark brown, light brown, gray, and white). The most important feature in this melanoma is the presence of atypical dots and globules and irregular blotches. In the left part of the lesion, black dots, and globules are clearly visible, in this case corresponding to pagetoid cells and nests in the epidermis. Pigment network is also present at the periphery. Dermoscopy image obtained with contact and polarized light.



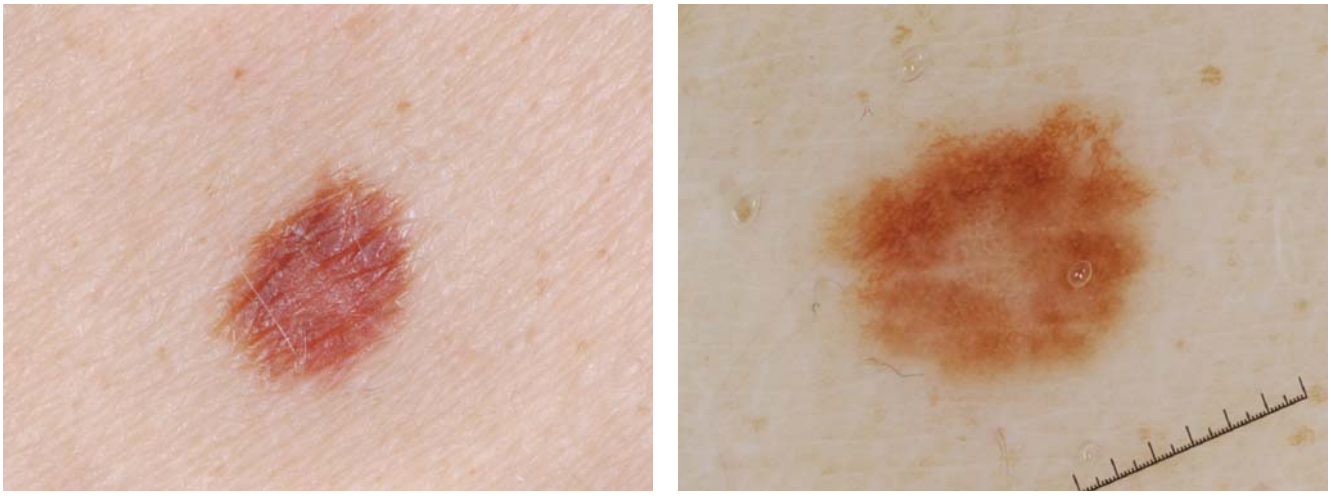
(**A**) (**B**)

Figure 6a.9 (**A, B**) This nevus manifests a typical pigment network.



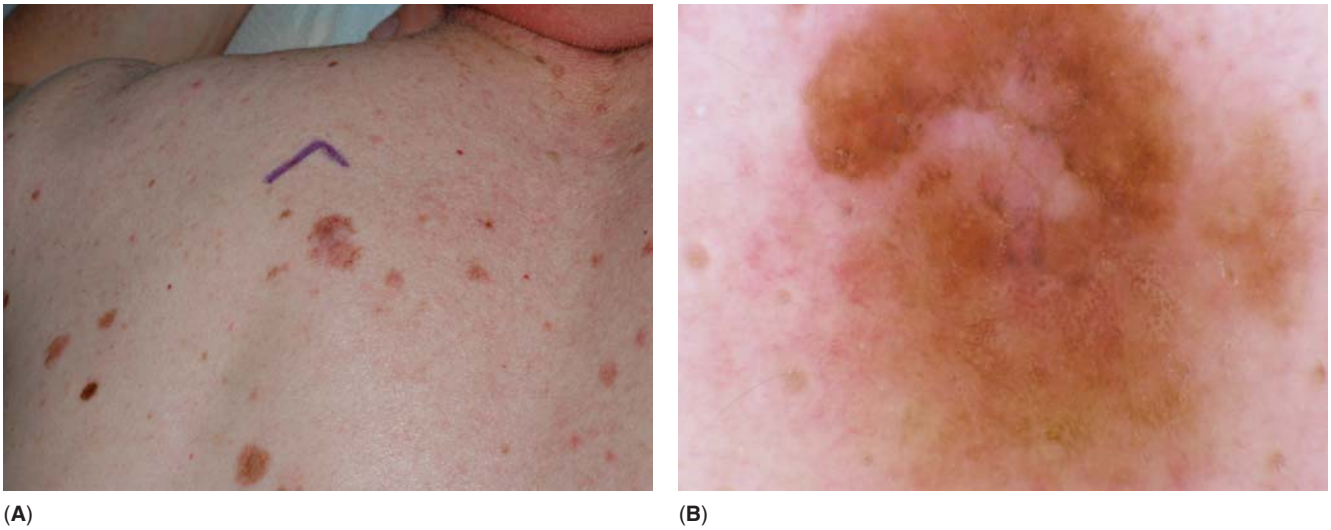
(**A**) (**B**)

Figure 6a.10 (**A, B**) This melanoma manifests an atypical pigment network.



(**A**) (**B**)

Figure 6a.11 (**A, B**) This biopsy-proven benign nevus has a focal negative network present symmetrically within the center of the lesion.



(**A**) (**B**)

Figure 6a.12 (**A**, **B**) This melanoma shows negative pigment network in the lower part of the lesion.

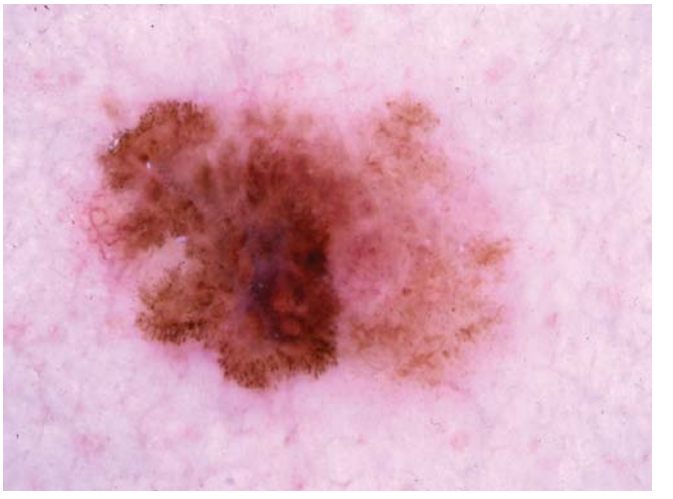
melanoma. However, some melanomas may present with relatively regular streaks and thus we recommend that at least in adults an excisional biopsy be performed on all lesions with streaks. Melanoma in childhood is rare and if it does occur the melanoma tends to be nodular and/or amelanotic, and thus they will not display any streaks. With that being said, melanoma with streaks can also be seen in children, and thus we recommend that all lesions with streaks in children be either closely monitored or excised (Figs. 6a.13 and 6a.14A, B).

Irregular Dots and Globules

Dots can be regular or irregular. Regular dots are those that are located in the center of the lesion or overlying network lines. These regular dots are usually light brown or black in color and are commonly seen in nevi. In contrast, irregular dots vary in size, color, and distribution (Argenziano et al., 1998). Irregular dots have a tendency to be located toward the periphery of the lesion and are not usually found overlying network lines. (Figs. 6a.15A, B and 6a.16A, B). Globules are larger than dots. Typical globules are of relatively uniform color, shape, and size. They can be distributed symmetrically throughout the lesion, within the center of the lesion and surrounded by a network, or around the entire perimeter of the lesion (Figs. 6a.17, 6a.18, 6a.19). Atypical globules are of different sizes, shapes and colors, distributed in an asymmetric manner (Fig. 6a.16).

Figure 6a.13 Streaks around the entire perimeter of the lesion are highly suggestive of a Spitz/reeds nevus. This is a reed nevus with only two colors (black and brown), a central blotch and peripheral streaks/globules regularly distributed at the periphery creating a starburst appearance. Dermoscopy image obtained with contact and polarized light.

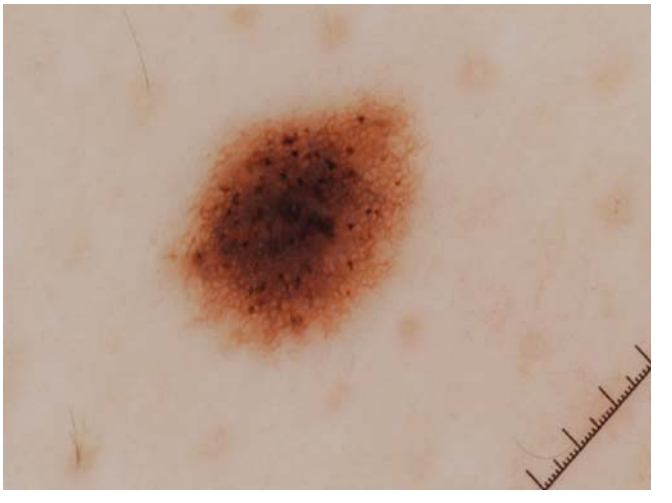
(**A**)



(**B**)

Figure 6a.14 (**A, B**) Streaks present focally should raise concern for melanoma. This lesion was a microinvasive melanoma.

(**A**)



(**B**)

Figure 6a.15 (**A, B**) This nevus has black dots distributed within the center of the lesion. In addition, the black dots are overlying the network lines. These dots are considered typical.

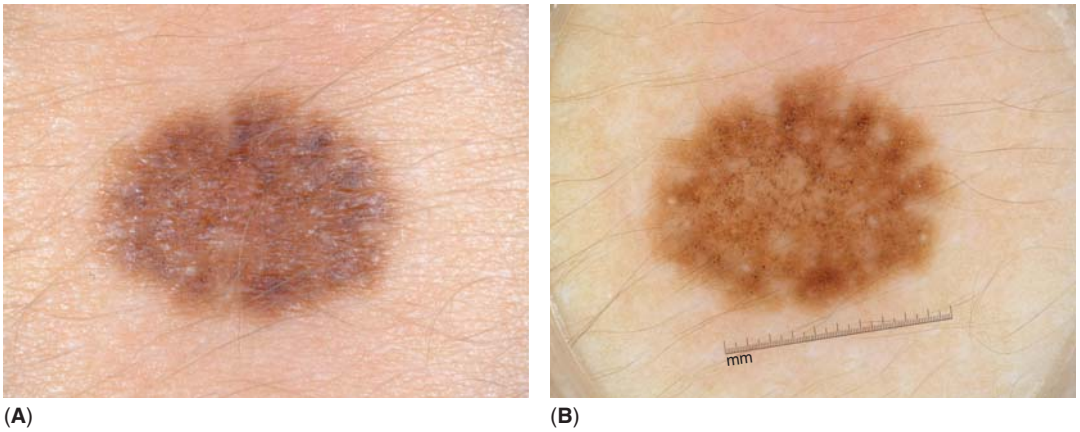
(**A**)

(**B**)

Figure 6a.16 (**A, B**) This melanoma has many atypical dots and globules.

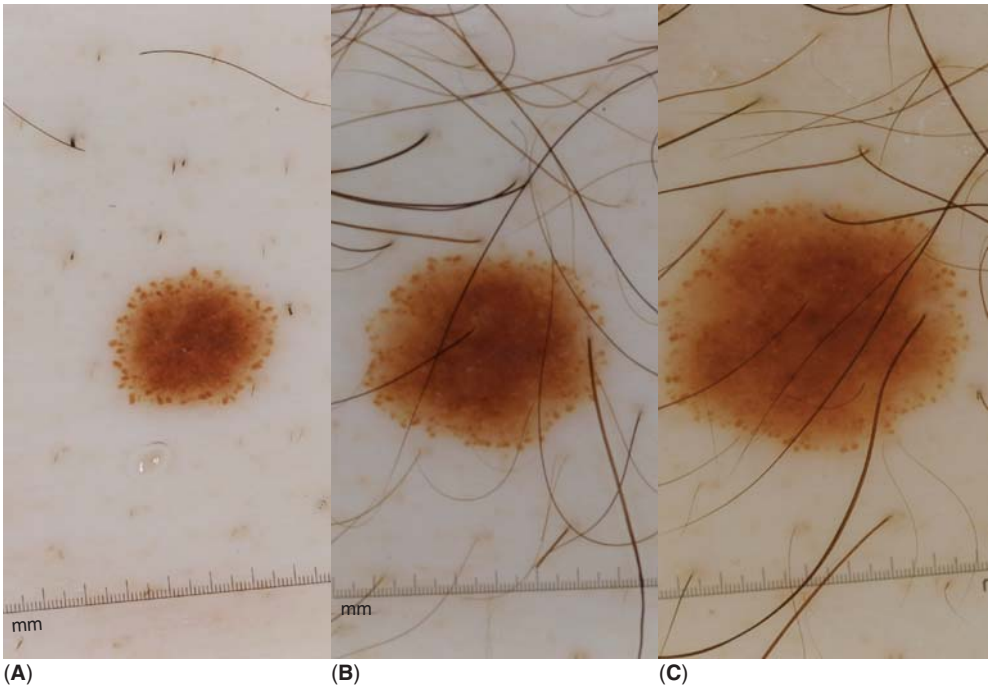
(**A**) (**B**)

Figure 6a.17 (**A, B**) This is a benign nevus with a typical globular pattern with typical globules distributed throughout the lesion.



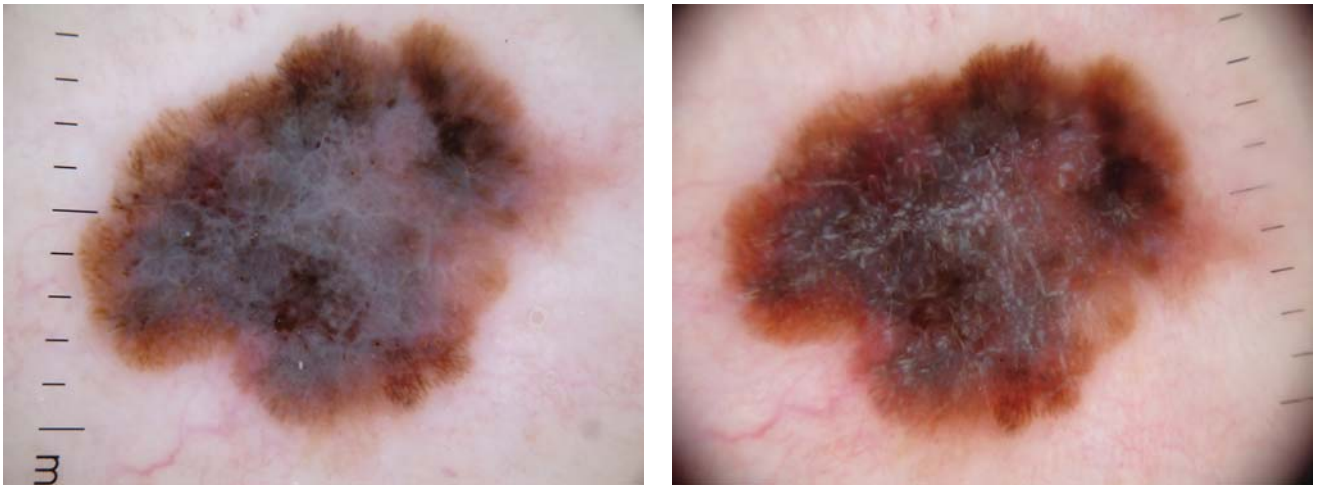
(**A**) (**B**)

Figure 6a.18 (**A, B**) This is a nevus with peripheral network and central globules. These are typical globules.



(**A**) (**B**) (**C**)

Figure 6a.19 (**A–C**) The globules present around the entire perimeter of a nevus are considered typical. The peripheral rim of globules is indicative of a growing nevus as can be seen in the three images of the same nevus taken over the course of one year.



(**A**) (**B**)

Figure 6a.20 (**A**) This melanoma has a prominent blue-white veil as seen with nonpolarized dermoscopy. (**B**) The same lesion reveals chrysalis-like structures when viewed with polarized dermoscopy. Image Courtesy of Harold Rabinovitz.

Blue-White Veil Over a Raised Portion of the Lesion
A regular blue-white veil consists of a homogenous steel blue-colored veil overlying the entire lesion surface and is characteristic of blue nevi. A homogenous blue-white veil occupying the central portion of the lesion can be seen in combined nevi and Spitz nevi. An irregular blue-white veil consists of a prominent blue-white color that has different shades, and thus appearing heterogenous. The presence of an irregular blue-white veil in a melanocytic lesion is suggestive of melanoma (Figs. 6a.1 and 6a.7).

Blue-White Veil Over a Flat Portion of the Lesion (Regression Structures)
A blue-white veil can also be seen over flat areas (nonpalpable) areas of a lesion and it corresponds with regression. Besides a blue-white veil over a flat portion of a lesion, regression structures also include peppering/granularity and scar-like depigmentation (Braun et al., 2007). The presence of focal areas of regression (peppering in <10% of the lesions) is encountered in benign lesions but the presence of large areas of regression (in >50% of the lesions) or combined areas of fibrosis (scar-like depigmentation) and melanophages (peppering) is suggestive of melanoma (Figs. 6a.5 and 6a.6).

Chrysalis-like Structures
Chrysalis-like structures consist of short white streaks that are often oriented orthogonal to each other and can only be seen with polarized light (Marghoob et al., 2009). The most common melanocytic tumors with chrysalis structures are melanomas and Spitz nevi (Fig. 6a.20). Nonmelanocytic lesions that commonly reveal chrysalis structures include basal cell carcinoma, dermatofibroma, and lichen planus-like keratosis.

Atypical Blood Vessels
The presence of comma vessels is characteristic of dermal nevi (Argenziano et al., 2004). The presence of any other vessel morphology should raise the possibility of melanoma, particularly if more than one vessel morphology is present within the lesion. Hypomelanotic and amelanotic melanomas will often manifest a polymorphous vascular pattern, most often consisting of serpentine and dotted vessels (see chap. 12 for more details).

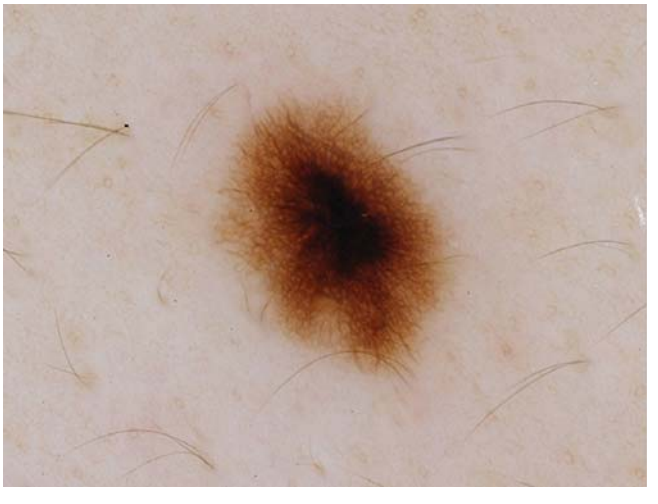
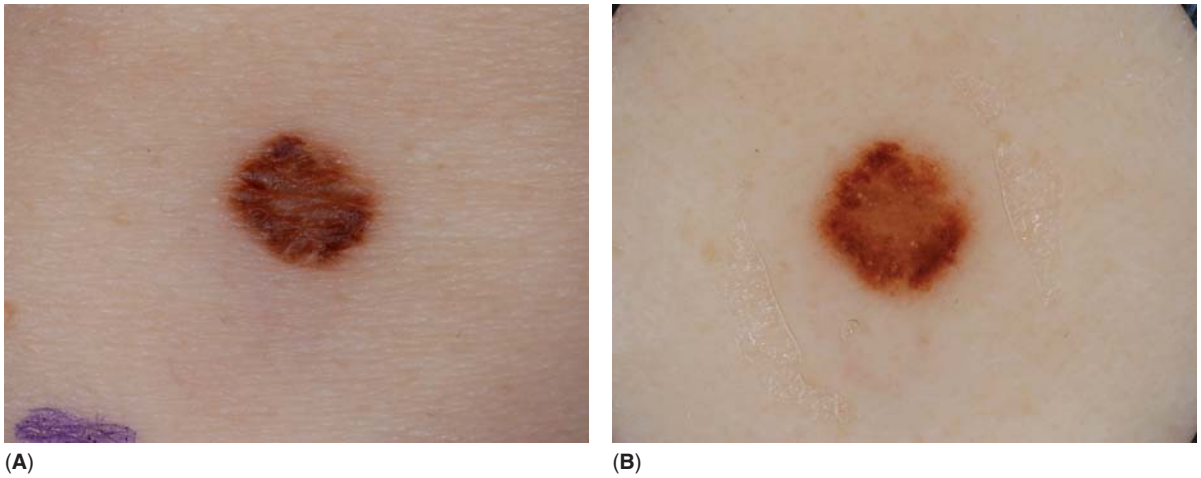


Figure 6a.21 This benign nevus has a black blotch (lamella) in the central portion of the lesion. This black blotch can be removed using tape stripping.

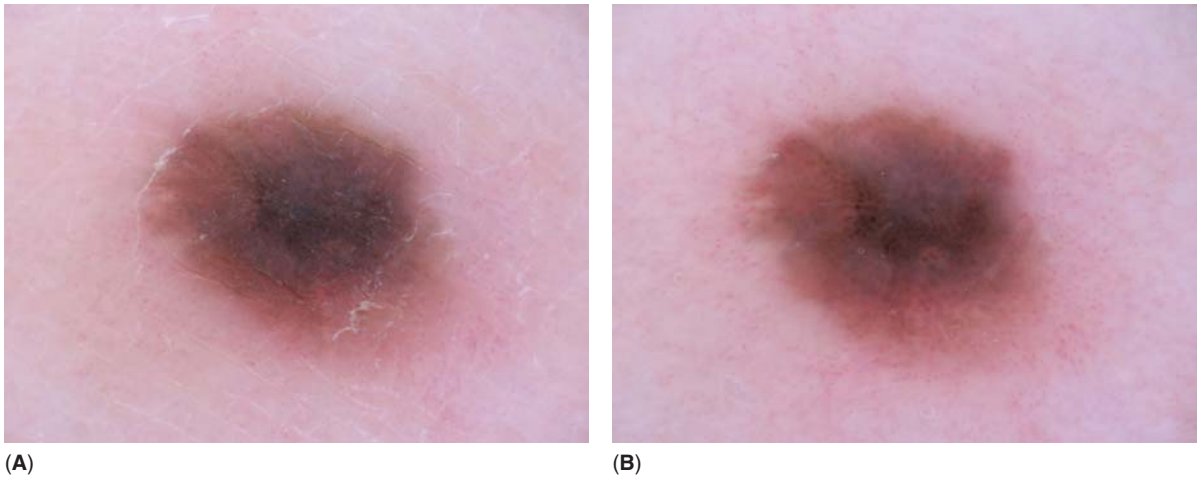
Irregular Blotches
A regular blotch consists of a blotch located symmetrically in the center of a lesion. This can be seen in benign nevi and in these lesions the central blotch often presents as a black lamella, which can be tape stripped off (junctional nevi with transepidermal elimination of melanin). An irregular blotch cannot be tape stripped off, often has a heterogenous appearance with multiple shades of color, and is located off center (asymmetric). The presence of dark and irregular blotches is associated with melanoma (Figs. 6a.1 and 6a.21).

Peripheral Brown Structureless Areas
Benign nevi can have structureless areas; however, network or globules often surround the structureless areas in benign nevi. Structureless areas located at the periphery of the lesion and not surrounded by network or globules are associated with melanoma (Annessi et al., 2007). These areas correlate with flattening of the dermoepidermal junction and with the presence of pagetoid cells Figs. 6a.22A, B and 6a.23A, B).



(**A**) (**B**)

Figure 6a.22 (**A, B**) This nevus has a brown structureless area in the central portion of the lesion.



(**A**) (**B**)

Figure 6a.23 (**A**, **B**) This melanoma has a peripheral brown structureless area.

Key Points

1. The number of colors can assist in differentiating nevi from melanoma.
   a. Nevi tend to have 1–2 colors.
   b. Melanomas often have more than two colors. A lesion with more than four colors is highly suggestive of melanoma.
   c. The presence of five or more colors is almost diagnostic of melanoma.
   d. The presence of the colors red, white, and/or blue-gray is suggestive of melanoma.
2. There are 10 dermoscopic structures associated with melanoma:
   a. atypical pigment network
   b. irregular streaks
   c. negative network
   d. chrysalis
   e. irregular dots and globules
   f. irregular blotch
   g. blue-white veil
   h. regression structures
   i. atypical vessels
   j. peripheral brown structureless areas

REFERENCES

Annessi, G., Bono, R., Sampogna, F., Faraggiana, T. & Abeni, D., 2007, Sensitivity, specificity, and diagnostic accuracy of three dermoscopic algorithmic methods in the diagnosis of doubtful melanocytic lesions: the importance of light brown structureless areas in differentiating atypical melanocytic nevi from thin melanomas. *J Am Acad Dermatol*, 56, 759–67.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140(12), 1485–9.

Braun, R.P., Gaide, O., Oliviero, M., et al., 2007, The significance of multiple blue-grey dots (granularity) for the dermoscopic diagnosis of melanoma. *Br J Dermatol*, 157, 907–13.

Braun, R.P., Rabinovitz, H.S., Oliviero, M., Kopf, A.W. & Saurat, J.H., 2005, Dermoscopy of pigmented skin lesions. *J Am Acad Dermatol*, 52, 109–21.

Marghoob, A.A., Cowell, L., Kopf, A.W. & Scope, A., 2009, Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*, 145, 618.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Yadav, S., Vossaert, K., Kopf, A., Silverman, M. & Grin-Jorgensen, C., 1993, Histopathologic correlates of structures seen on dermoscopy (epiluminescence microscopy). *Am J Dermatopathol*, 15, 297–305.

Zalaudek, I., Argenziano, G., Ferrara, G., et al., 2004, Clinically equivocal melanocytic skin lesions with features of regression: a dermoscopic-pathological study. *Br J Dermatol*, 150, 64–71.

6b Pattern analysis

Ashfaq A. Marghoob

Once the clinician has determined that the lesion under investigation is primarily of melanocytic origin using the first step of the two-step dermoscopy algorithm, then he/she needs to decide whether the melanocytic lesion is benign or whether it may represent a melanoma. Depending on the degree of suspicion for melanoma, the clinician may decide to either subject the lesion to histopathology evaluation or to short-term mole monitoring (chap. 14). In other words, the goal of the second step of the two-step dermoscopy algorithm is to assist in differentiating benign nevi from potential melanomas.

A correct interpretation of the dermoscopic view of lesions is contingent on the ability to recognize the presence or absence of specific dermoscopic colors and structures. In addition, noting the location and distribution of these colors and structures is a critically important component of the dermoscopic evaluation process. Based on the aforementioned information, multiple structured algorithms have been developed to assist clinicians in correctly identifying various benign and malignant skin lesions (chaps. 6c–6e, 6g). These algorithms may be particularly well suited for novice dermoscopists because they rely greatly on the analytic evaluation of a lesion's dermoscopic features (i.e., identifying specific structures), and thus do not require significant experience to master. However, once learned, expert dermoscopists rarely use algorithms and instead rely mainly on pattern recognition when evaluating lesions. The pattern analysis approach requires experience to master but once mastered it provides the added benefit of allowing the observer to rapidly evaluate lesions. In addition to reducing time spent evaluating lesions, pattern analysis may also yield a slightly better diagnostic accuracy as compared with analytic analysis-based algorithms (Argenziano, 2003; Annessi, 2007; Carli, 2003).

In this chapter, we instruct the reader on the fundamentals of dermoscopic pattern analysis for melanocytic lesions by the use of schematics and images. As alluded to above, reliance on pattern analysis to differentiate benign from suspect melanocytic lesions first requires the acknowledgment that the "critical element of becoming an expert is accruing the vast experience that enables experts to recognize patterns effortlessly, most of the time—and to recognize, as well, when the signs and symptoms do not fit a pattern at all" (Norman, 2006). It should be intuitively obvious to most that we rapidly gain "vast experience" in the recognition of benign nevus patterns (see chap. 7b) because we see these much more frequently than we see melanomas. Thus, lesions manifesting a "benign" nevus pattern generally do not raise concern. However, when lesions manifest a pattern that we are not accustomed to seeing, it tends to raise our level of suspicion (Marghoob, 2007). Evaluation of thousands of banal nevi has disclosed that most benign nevi manifest in 1 of the 10 patterns (Table 6b.1) (Figs. 6b.1–6b.20). These benign patterns all demonstrate symmetry of pattern, structure, and color. Thus, familiarity with the dermoscopic patterns typically exhibited by benign nevi provides assistance in distinguishing between benign and potentially malignant lesions. In contrast, melanomas consist of melanocytic lesions that deviate from the benign patterns, and thus most melanomas invariably display some degree of asymmetry of pattern, color, and structure, eliciting a sense of unease in the clinician (Figs. 6b.21–6b.41). It should be stressed that dermoscopic asymmetry by itself is not a prerequisite for the diagnosis of melanoma since some melanomas may manifest dermoscopic symmetry (Figs. 6b.42 and 6b.43). However, they will, by and large, not manifest any of the benign patterns listed in Table 6b.1. Those lesions that deviate from the benign nevus patterns and in addition manifest at least in 1 of the 10 melanoma-specific structures listed in Table 6b.2 are considered to be melanoma until proved otherwise. In other words, to correctly identify melanoma requires the utilization of both heuristic and analytic analysis, used in an interactive fashion. As stated by JL Bowen "Both nonanalytic and analytic reasoning strategies are effective and are used simultaneously, in an interactive fashion. Nonanalytic reasoning, as exemplified by 'pattern recognition,' is essential to diagnostic expertise, and this skill is developed through clinical experience. Deliberative analytic reasoning is the primary strategy when a case is complex or ill defined, the clinical findings are unusual, or the physician has had little clinical experience with the particular disease entity" (Bowen, 2006). The combination of pattern analysis and analytic analysis is also evident in two structured algorithms discussed in chapters 6f and 6h.

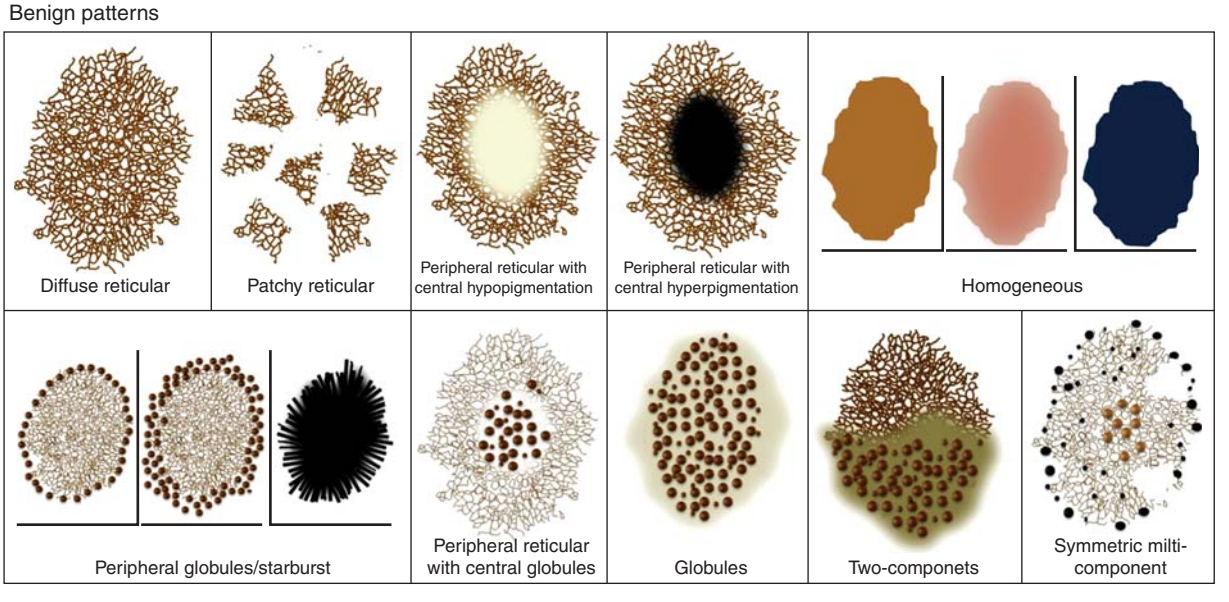
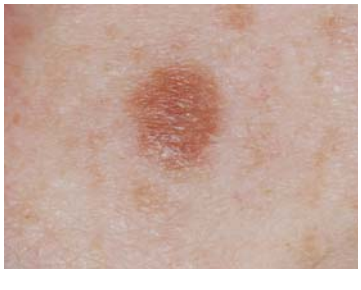


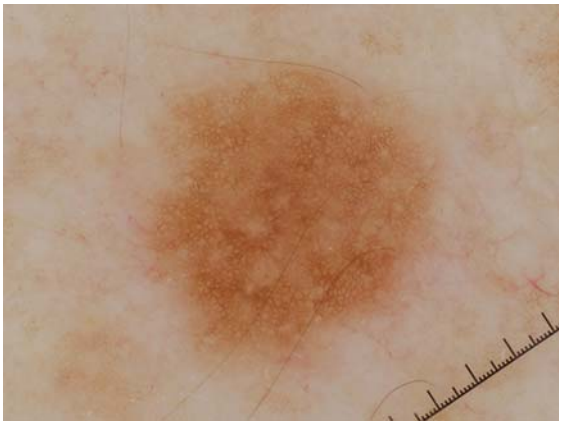
Figure 6b.1 Schematic drawings of the 10 benign nevus patterns. The homogeneous pattern and the peripheral globules/starburst pattern each have three variants. For details regarding these variants please see figure 7c.11.

Table 6b.1 The 10 Benign Nevus Patterns

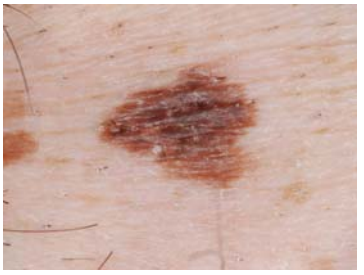
Global pattern	Definition
Reticular diffuse	Diffuse homogenous network with relatively uniform thickness and color of the network lines. The holes of the network are of relatively uniform size. The network tends to fade at the periphery. This pattern is frequently seen in acquired nevi, especially those developing in individuals with a darker phenotype. This pattern is also commonly seen in congenital nevi, especially those located on the lower extremity
Reticular patchy	Homogenous network with relatively uniform thickness and color of the network lines. The network is present in focal patches that are separated by homogenous structureless areas that are lighter in color than the network lines. The structureless areas have the same color as background skin or are slightly darker than the background skin. This pattern is commonly seen in acquired nevi located on the torso and in superficial congenital nevi, especially those located on the lower extremity
Peripheral reticular with central hypopigmentation	A relatively uniform network at the periphery of the lesion with a central homogenous and hypopigmented (relative to the color of the network) structureless area. The structureless area has the same color as background skin or is slightly darker than the background skin (but lighter in color compared with the network lines). This type of acquired nevus is more common in individuals with a fair skin phenotype
Peripheral reticular with central hyperpigmentation	A relatively uniform network at the periphery of the lesion with a central homogenous, hyperpigmented structureless area or blotch. The blotch has a darker color as compared with the network lines. This type of acquired nevus is more common in individuals with a darker skin phenotype
Homogenous tan, brown, or blue pigmentation (sometimes pink)	Primarily consists of a diffuse homogenous structureless pattern. On occasion, a few globules and/or small focal network fragments may be evident. When the nevi are tan in color they usually represent acquired nevi in individuals with fair skin phenotypes. When darker brown in color they usually represent congenital nevi. When blue in color they represent blue nevi. Nevi in very fair-skinned individuals (including redheads) can manifest a homogenous pink pattern (N.B: amelanotic and hypomelanotic melanomas can manifest in a similar manner; however, most melanomas will also reveal atypical blood vessels and/or crystalline structures)
Peripheral reticular with central globules	A relatively uniform network at the periphery of the lesion with central globules. The histopathology features of these nevi are often the same as those used to describe congenital nevi
Peripheral globules with central network or homogenous area and the starburst pattern	The central component of this type of nevus is either reticular or homogenous. When there is one row of relatively uniform brown globules surrounding the entire perimeter of the lesion, it represents an actively growing nevus (i.e., not yet undergone senescence). When the globules at the perimeter are tiered (more than one row of globules), then it is considered to be a starburst pattern, which is commonly seen in Spitz nevi. The classic starburst pattern consists of streaks (radial streaming or pseudopods) present around the entire perimeter of the lesion giving the appearance of an exploding star
Globular (includes cobblestone)	Globules of similar shape, size, and color are distributed symmetrically throughout the lesion. Globules are usually round to oval in shape. However, sometimes the globules are large and appear to be compressing each other creating angulated shapes reminiscent of cobblestones. This pattern is seen most commonly in congenital nevi
Two component	These lesions reveal two different patterns (reticular-globular, reticular-homogenous, or globular-homogenous). A half of the lesion manifests one pattern while the other half of the lesion manifests a different pattern
Multicomponent	Two definitions exist for the multicomponent pattern. N.B. only the first definition applies to benign nevi 1. Organized and/or symmetrically distributed typical dots/globules, typical network, and homogenous areas. This is the pattern associated with benign nevi. The axis of symmetry need only be in one axis. 2. Symmetrically distributed globules, network, blotches, dots, veil, regression structures, and/or structureless areas. Three or more structures are required to classify the lesion as multicomponent. N.B. Although a symmetric multicomponent pattern speaks in favor of a benign nevus, any lesion displaying a multicomponent pattern other than as described in the first definition should be viewed with caution



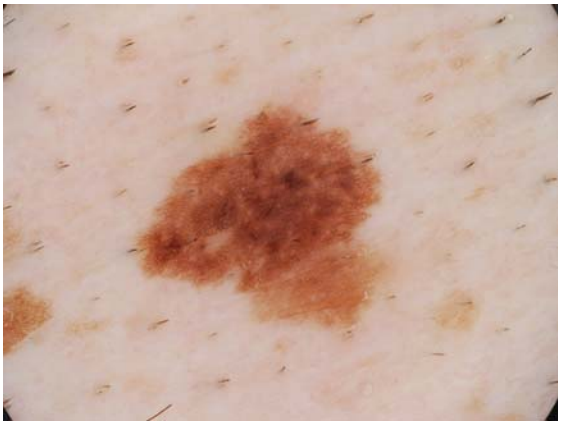
▲ **Figure 6b.2a** Clinical image.



◀ **Figure 6b.2b** Diffuse reticular pattern. This lesion was a compound dysplastic nevus.

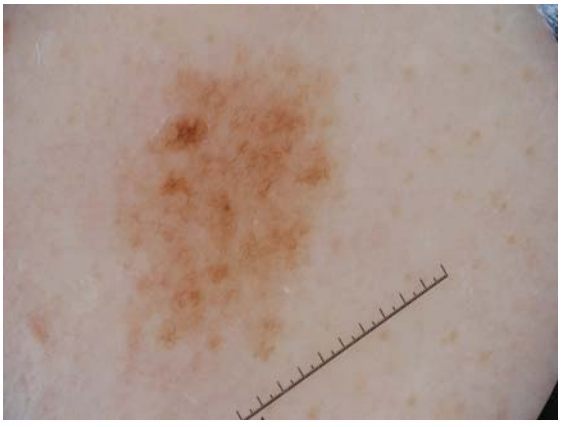


▲ **Figure 6b.3a** Clinical image.

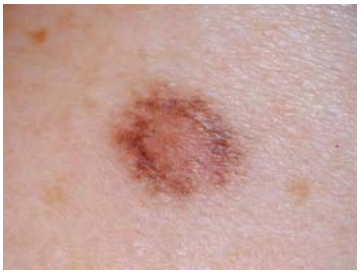


◀ **Figure 6b.3b** Although the lesion has an asymmetric silhouette, dermoscopy reveals a diffuse reticular pattern. This lesion was a junctional dysplastic nevus.

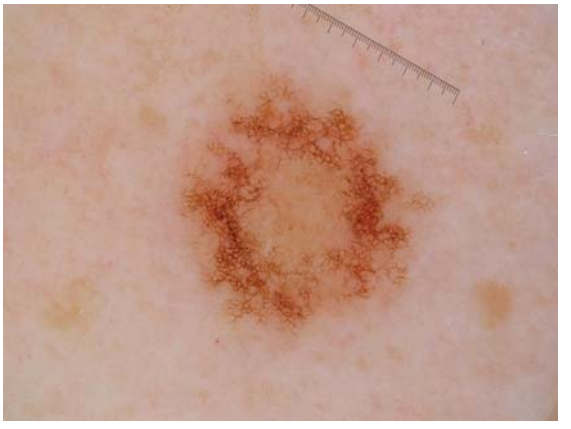
▲ **Figure 6b.4a** Clinical image.



◀ **Figure 6b.4b** This dysplastic nevus has a patch reticular pattern.



▲ **Figure 6b.5a** Clinical image.



◀ **Figure 6b.5b** This nevus manifests a peripheral network with central hypopigmentation.

▲ **Figure 6b.6a** Clinical image.

◀ **Figure 6b.6b** This nevus manifests a peripheral network with central hyperpigmentation.

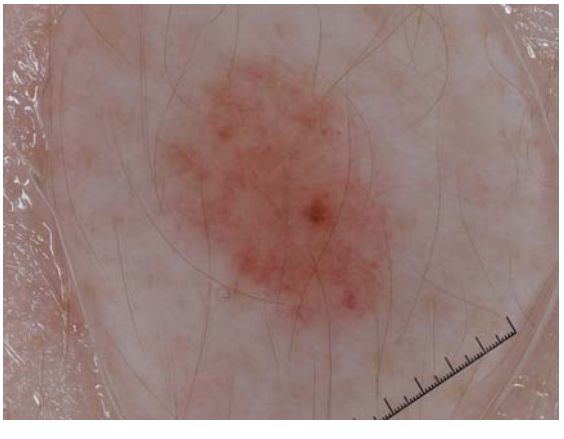
▲ **Figure 6b.7a** Clinical image.

◀ **Figure 6b.7b** This congenital nevus has a homogeneous brown pattern.

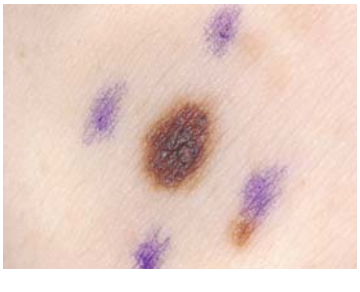
▲ **Figure 6b.8a** Clinical image.

◀ **Figure 6b.8b** This blue nevus has a homogenous blue pattern.

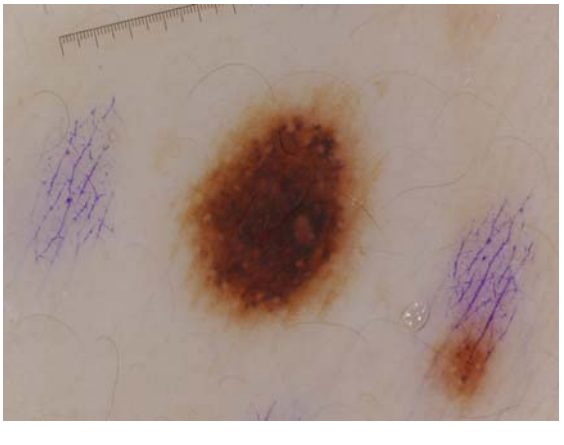
▲ **Figure 6b.9a** Clinical image.



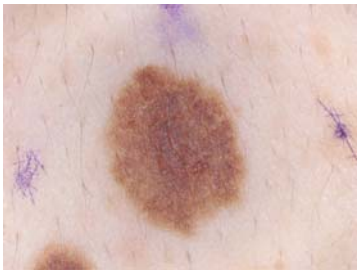
◀ **Figure 6b.9b** This dysplastic nevus has a homogenous tan to pink pattern.



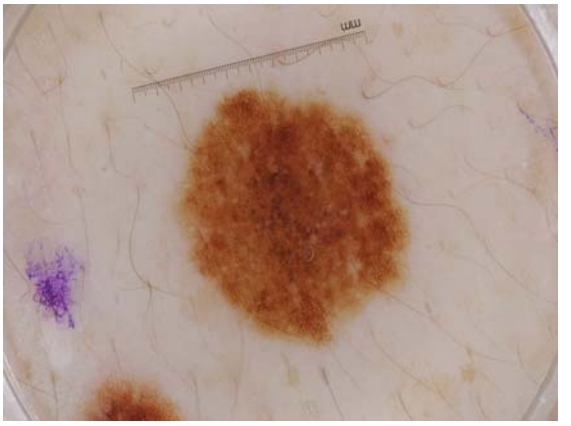
▲ **Figure 6b.10a** Clinical image.



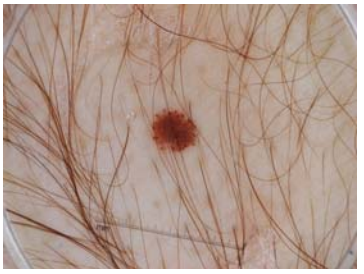
◀ **Figure 6b.10b** This congenital nevus has a homogenous brown pattern.



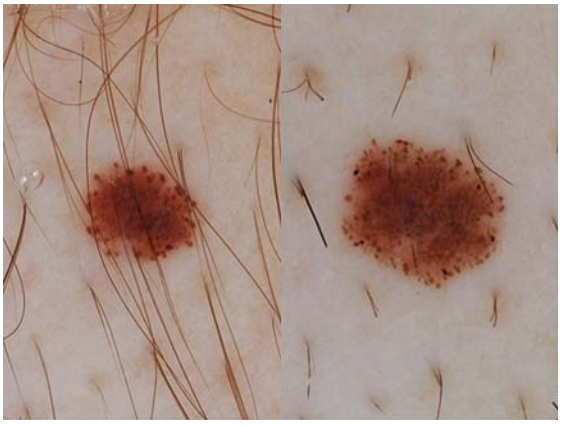
▲ **Figure 6b.11a** Clinical image.



◀ **Figure 6b.11b** This congenital nevus reveals peripheral network with central globules.

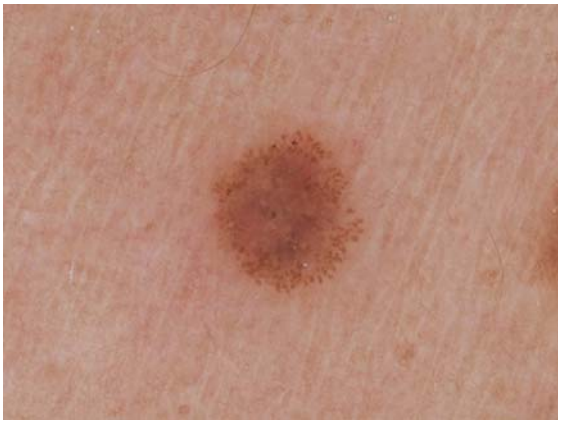


▲ **Figure 6b.12a** Clinical image.



◀ **Figure 6b.12b** This enlarging nevus has a peripheral rim of globules. This is a benign pattern and represents a growing nevus. The dermoscopic images were obtained one year apart.

▲ **Figure 6b.13a** Clinical image.

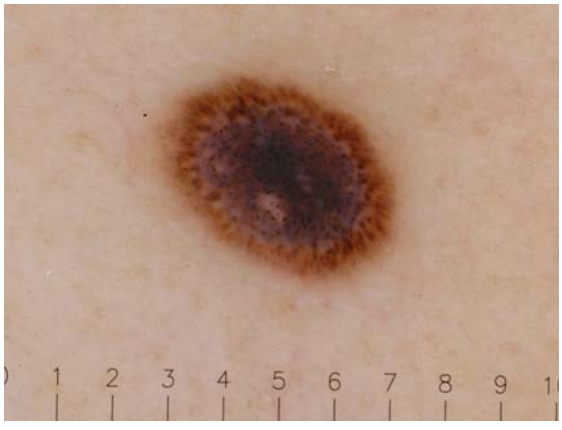


◀ **Figure 6b.13b** This Spitz nevus reveals a starburst pattern with tiered globules (multiple rows of globules).

▲ **Figure 6b.14a** Clinical image.

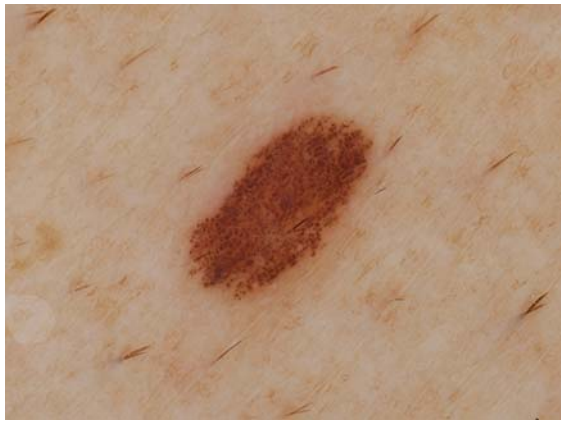
◀ **Figure 6b.14b** This Spitz nevus has a starburst pattern with streaks.

▲ **Figure 6b.15a** Clinical image.

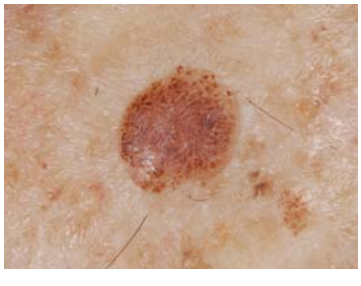


◀ **Figure 6b.15b** This Spitz nevus manifests a starburst pattern.

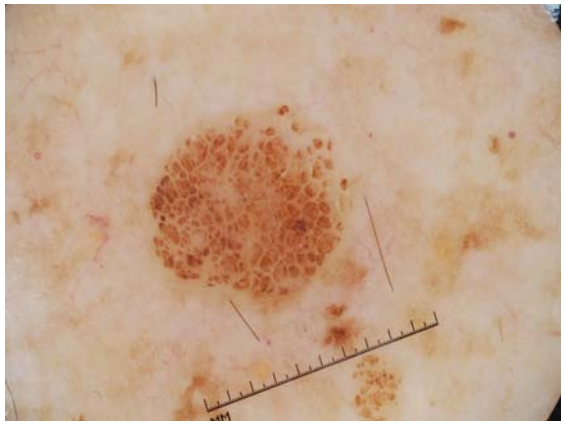
▲ **Figure 6b.16a** Clinical image.



◀ **Figure 6b.16b** This nevus has a benign globular pattern.

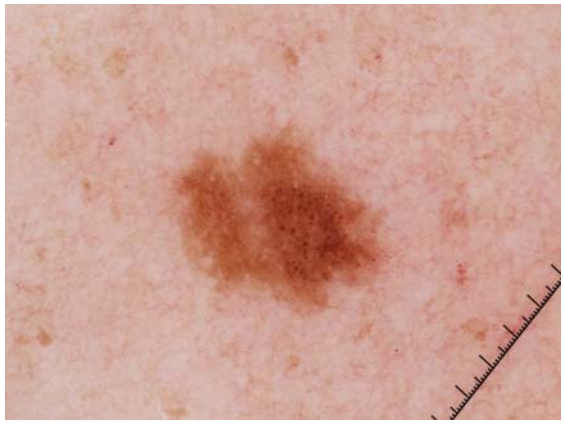


▲ **Figure 6b.17a** Clinical image.

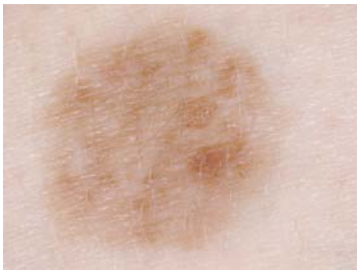


◀ **Figure 6b.17b** This congenital nevus has a cobblestone globular pattern.

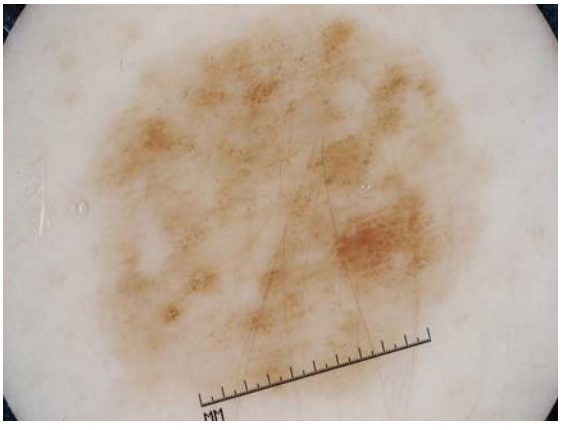
▲ **Figure 6b.18a** Clinical image.



◀ **Figure 6b.18b** This nevus reveals a benign two-component nevus pattern.

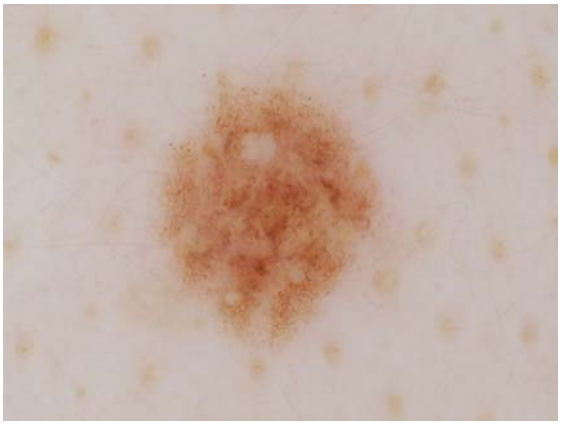


▲ **Figure 6b.19a** Clinical image.



◀ **Figure 6b.19b** This nevus reveals an organized multicomponent pattern with dots/globules, network, and homogenous areas.

▲ **Figure 6b.20a** Clinical image.



◀ **Figure 6b.20b** This nevus manifests an organized multicomponent pattern with dots/globules, network, and homogenous areas.

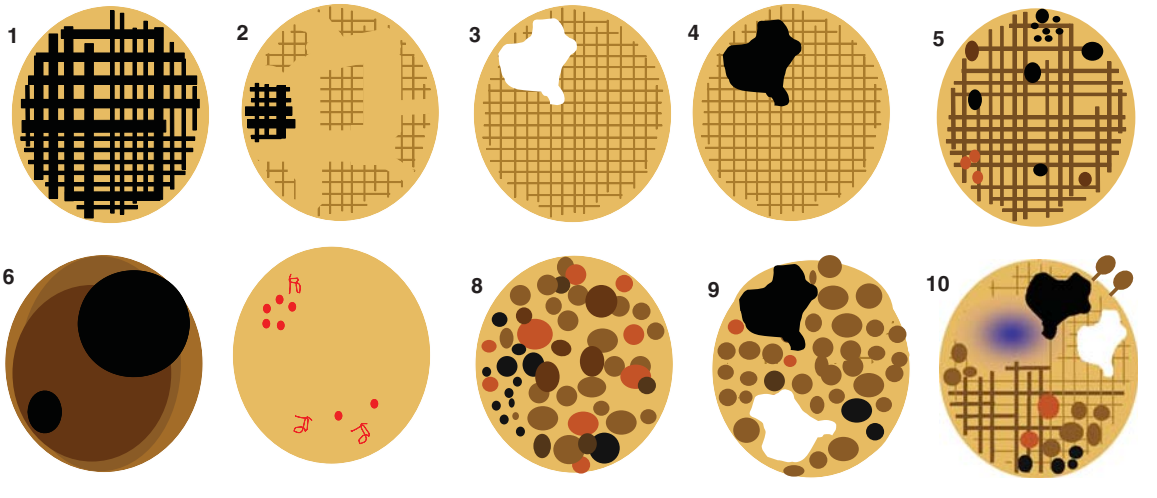
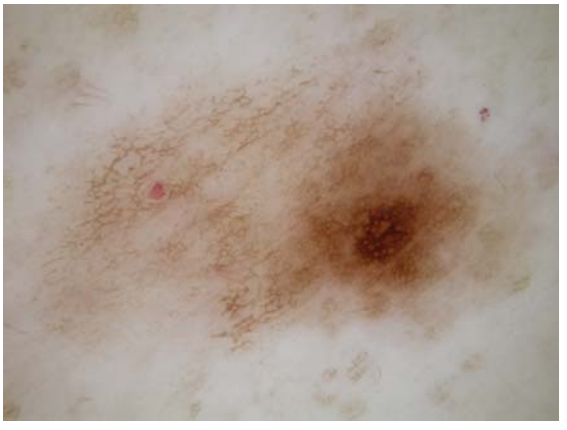
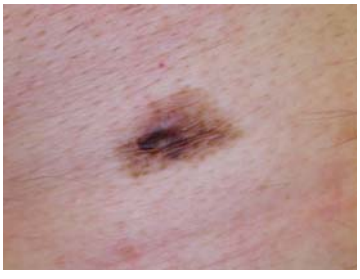


Figure 6b.21 Any pattern that deviates from the benign patterns shown in figure 6b.1 could represent a melanoma. Depicted here are Schematic drawings of a few malignant patterns.

▲ **Figure 6b.22a** Clinical image.

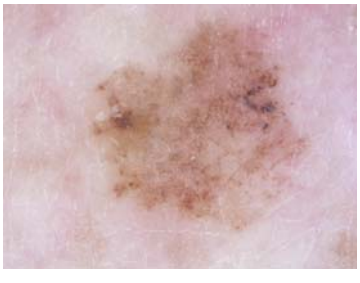


◀ **Figure 6b.22b** This melanoma in situ was diagnosed based on the presence of focal atypical network.

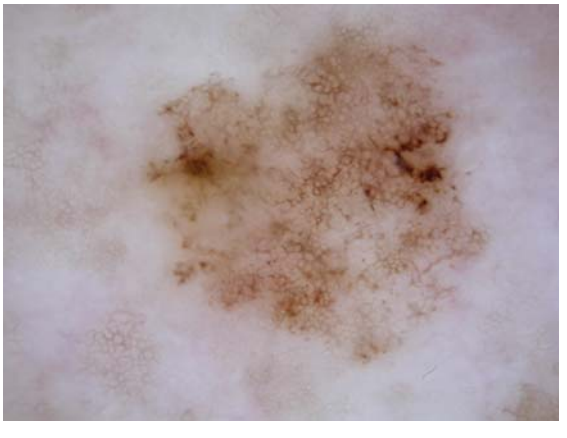


▲ **Figure 6b.23a** Clinical image.

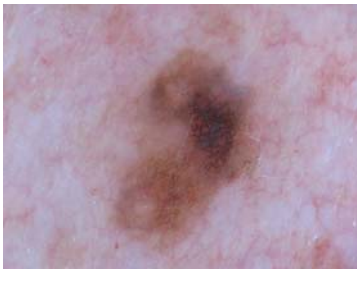
◀ **Figure 6b.23b** This 1.8 mm melanoma reveals atypical network, scar-like depigmentation, and peripheral brown structureless areas.



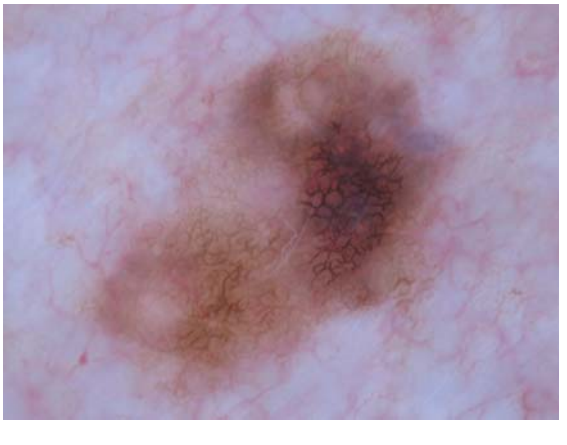
▲ **Figure 6b.24a** Clinical image.



◀ **Figure 6b.24b** This melanoma in situ has an atypical patchy network pattern.



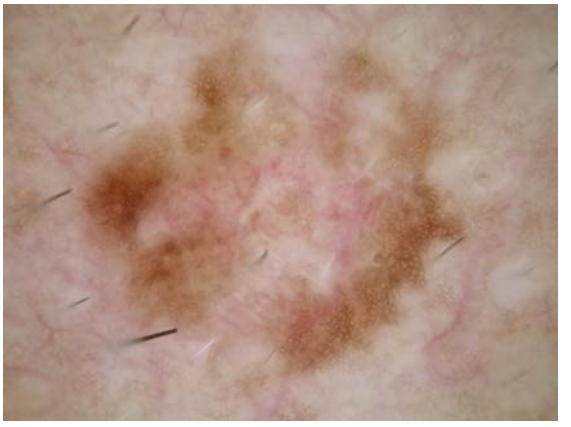
▲ **Figure 6b.25a** Clinical image.



◀ **Figure 6b.25b** This lesion does not manifest a benign nevus pattern. In addition, it has areas of atypical network and a blue-white veil. This lesion was biopsied to rule out melanoma. The pathology diagnosis was dysplastic nevus. This case highlights the limitations of dermoscopy.

▲ **Figure 6b.26a** Clinical image.

◀ **Figure 6b.26b** Nonpolarized dermoscopy reveals a peripheral patchy network and asymmetric homogenous area.



◀ **Figure 6b.26c** Polarized dermoscopy reveals crystalline structures, which are melanoma-specific structures. This lesion was biopsied and proved to be a microinvasive melanoma.

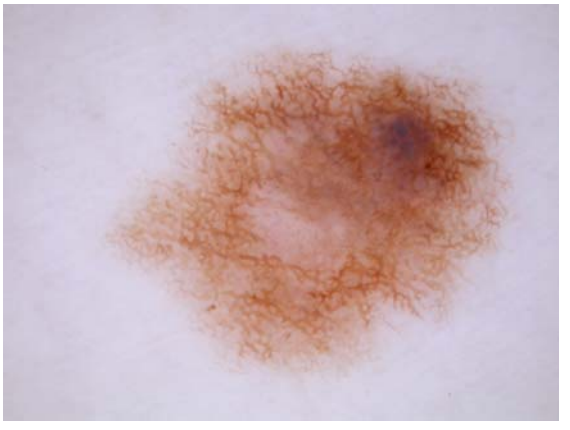
▲ **Figure 6b.27a** Clinical image.

◀ **Figure 6b.27b** This melanoma reveals a negative network, which is one of the melanoma-specific structures.

▲ **Figure 6b.28a** Clinical image.

◀ **Figure 6b.28b** This melanoma has focal network, peripheral tan structureless areas and numerous irregular linear and serpentine blood vessels.

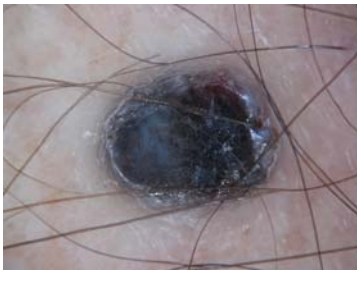
▲ **Figure 6b.29a** Clinical image.



◀ **Figure 6b.29b** This lesion has a network and eccentrically located bluish globules. On biopsy the area with the bluish globules was a melanoma with a thickness of 0.15 mm. The rest of the lesion was a dysplastic nevus.

▲ **Figure 6b.30a** Clinical image.

◀ **Figure 6b.30b** This melanoma reveals focal streaks and peripheral tan structureless areas.



▲ **Figure 6b.31a** Clinical image.

◀ **Figure 6b.31b** This 1.6 mm nodular melanoma has a disorganized homogenous pattern.

▲ **Figure 6b.32a** Clinical image.

◀ **Figure 6b.32b** Nonpolarized dermoscopy reveals regression structures, blue-white veil, irregular globules, and peripheral tan structureless areas.

◀ **Figure 6b.32c** Polarized dermoscopy reveals prominent chrysalis structures. This was a melanoma 0.5 mm in Breslow thickness.

▲ **Figure 6b.33a** Clinical image.

◀ **Figure 6b.33b** This melanoma is relatively featureless. The presence of dotted vessels is the only clue to the correct diagnosis.

▲ **Figure 6b.34a** Clinical image.

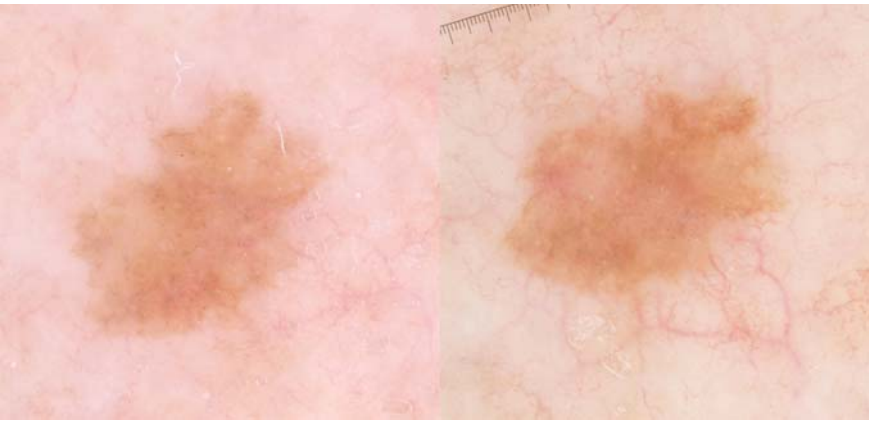
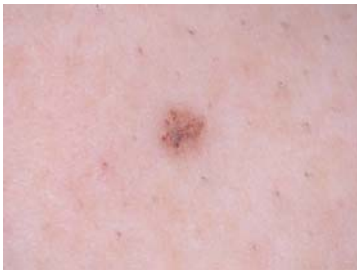
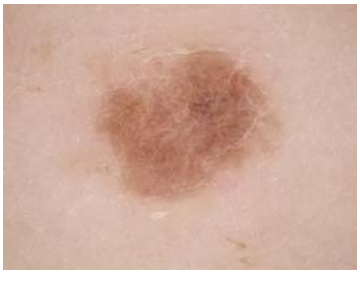


Figure 6b.34 (**B**) This homogenous structureless lesion was subjected to short-term mole monitoring over four months. Due to changes noted on followup the lesion was excised and proved to be a 0.27 mm melanoma.

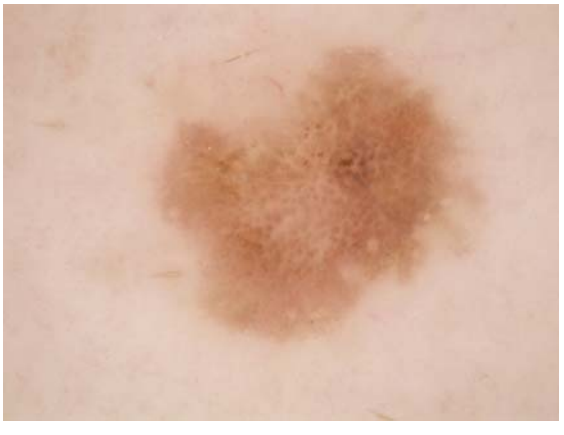


▲ **Figure 6b.35a** Clinical image.

◀ **Figure 6b.35b** This microinvasive melanoma has an atypical globular pattern.

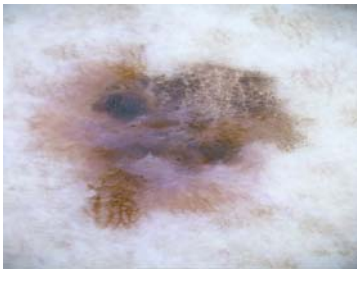


▲ **Figure 6b.36a** Clinical image.

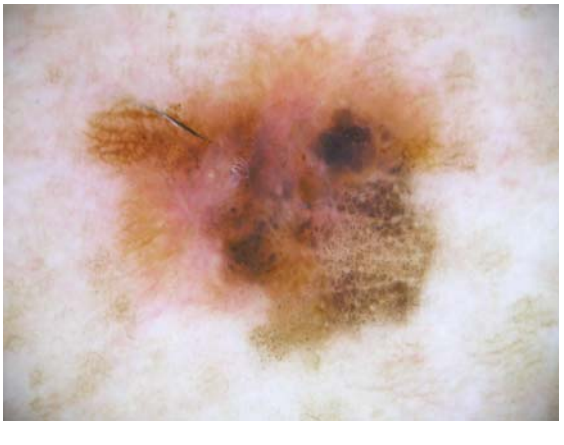


◀ **Figure 6b.36b** Nonpolarized dermoscopy of this 0.5 mm melanoma reveals a negative network with peripheral tan structureless areas.

◀ **Figure 6b.36c** With polarized dermoscopy the crystalline structures become evident.



▲ **Figure 6b.37a** Clinical image.

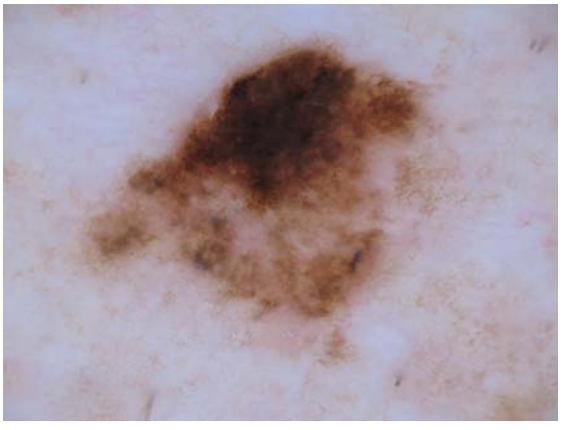


◀ **Figure 6b.37b** This melanoma reveals an asymmetric multicomponent pattern with irregular globules, peripheral structureless areas, atypical network, peripheral blotch, and blue-white veil.

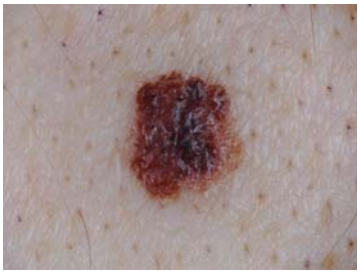
▲ **Figure 6b.38a** Clinical image.

◀ **Figure 6b.38b** This melanoma reveals an asymmetric multicomponent pattern with focal streaks, globules, dotted vessels, and structureless areas.

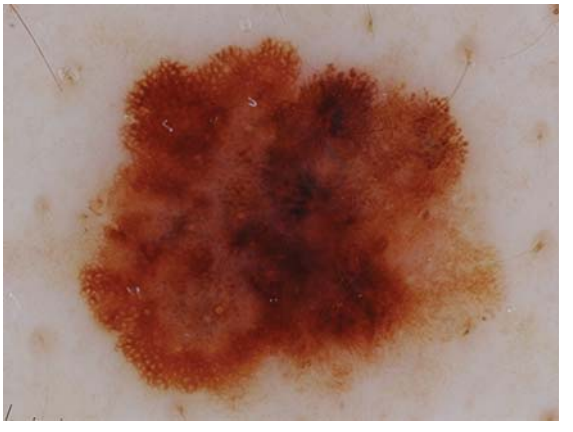
▲ **Figure 6b.39a** Clinical image.



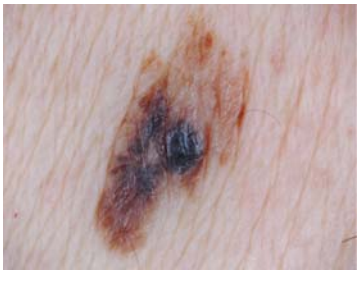
◀ **Figure 6b.39b** This disorganized homogenous melanoma has a peripheral blotch and focal regression structures.



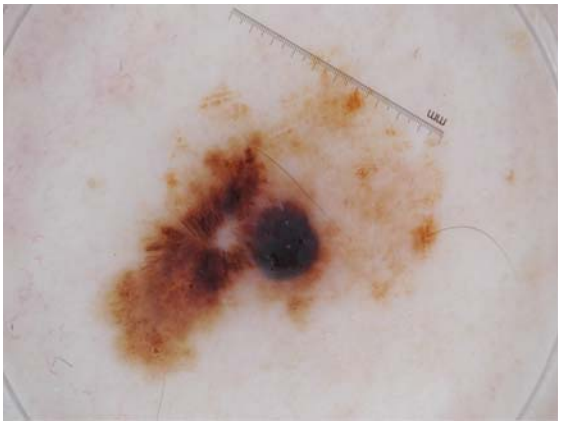
▲ **Figure 6b.40a** Clinical image.



◀ **Figure 6b.40b** This melanoma has atypical network, focal streaks, and blue-white veil.



▲ **Figure 6b.41a** Clinical image.



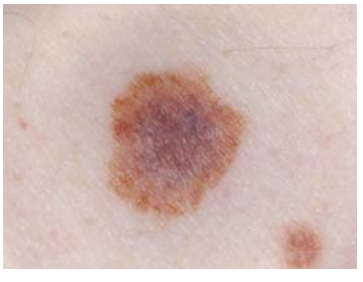
◀ **Figure 6b.41b** This melanoma has atypical network, peripheral blotch, and irregular globules.

Table 6b.2 Ten Melanoma-specific Structures

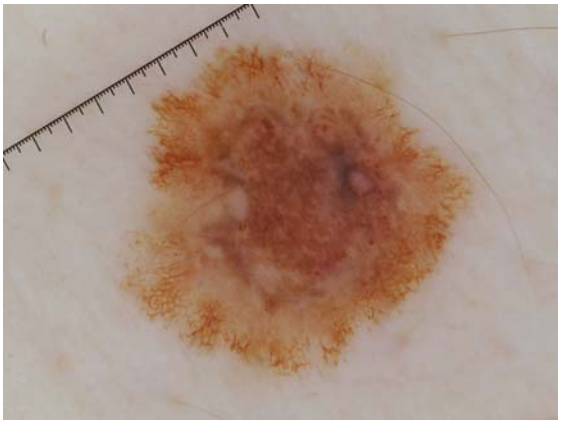
Dermoscopic structure	Description	Histopathologic correlate
Atypical pigment network	Reticulated grid of brown lines with focal broadened, thickened, or darkened areas that may end abruptly at the periphery. The network within the lesion may appear "broken-up" resulting in "Y"-shaped branched streaks. In contrast, the typical network consists of a relatively uniform and homogenous network that fades at the periphery	Atypical lentiginous or nested melanocytic proliferation along the dermoepidermal junction
Streaks (radial streaming and pseudopods)	Linear, radially oriented pigmented projections at the periphery of a lesion	Confluent junctional nests of melanocytes at the periphery. This corresponds to the radial growth phase of the melanoma
Negative pigment network	The "negative" of the pigment network consisting of hypopigmented serpiginous wide lines that appear to be surrounding brown elongated to curved globular structures	Speculation is that the negative network corresponds to either: 1. Thin elongated rete ridges together with large tubular melanocytic nests within a widened papillary dermis 2. Bridging of adjacent rete ridges 3. Nests surrounded by a fibrotic stroma
Chrysalis/crystalline	Fine, white, shiny streaks within a lesion, visible only under polarized light dermoscopy	Speculation is that this represents remodeled or new dermal collagen
Atypical dots and globules	Dark, punctate, or round-to-oval structures of varying shape, size, color, and distribution within a lesion. Whereas typical dots are located toward the center of the lesion and are situated on the network lines, atypical dots are often located toward the periphery of the lesion and they are not associated with the lines of the network. Typical globules consist of globules located in the center of the lesion, around the perimeter of the lesion, or throughout the entire lesion. In addition, globules surrounded by a network (know as target network with globules) or globules surrounded by a halo (know as halo globules) are also considered typical since they are associated with congenital nevi. All other manifestations of globules should be considered atypical. Thus, atypical globules consist of globules of varying size, shape and color that are distributed in an asymmetric fashion	Junctional or dermal nests of melanocytes; dots can also represent pagetoid nests
Irregular blotches	Dark areas of diffuse pigmentation with irregular shapes, multiple hues, sharp margins, or located eccentrically. In contrast, a regular blotch consists of a homogenous dark, symmetric area located in the center of the lesion. The presence of multiple blotches is also considered atypical.	Melanin pigmentation throughout the epidermis or dermis or both
Blue-white structures over raised areas	Blue-white color overlying raised (palpable) portions of a lesion	Compact orthokeratosis overlying melanophages, melanocytes, or free melanin in the dermis
Blue-white structures over flat areas (also known as "regression structures" and includes peppering or granularity)	White areas (scar-like) and bluish-gray areas overlying flat (nonpalpable) portions of a lesion	Fibrosis within the papillary dermis and melanosis (melanophages and free melanin "dust" within the dermis)
Atypical vascular structures	Milky red areas, dotted, linear, serpiginous, or twisted blood vessels. In contrast, typical vascular structures consist of comma vessels seen in intradermal nevi	Tumor-induced neoangiogenesis
Peripheral brown structureless areas	Peripherally arranged light brown or tan (fawn colored) areas of variable shape lacking perceptible structures	Flattening of the rete ridges with pagetoid spread of melanocytes

▲ **Figure 6b.42a** Clinical image.

◀ **Figure 6b.42b** This is a symmetric lesion. However, it does not adhere to one of the 10 benign nevus patterns. It has a central blue-white veil over a raised area. This was a 0.5 mm melanoma.



▲ **Figure 6b.43a** Clinical image.



◀ **Figure 6b.43b** This is a symmetric lesion. However, it does not adhere to one of the 10 benign nevus patterns. It has a central negative network and peripheral atypical network. This was a 0.35 mm melanoma.

Key Points

1. Nevi tend to manifest one of 10 benign patterns (figure 6b.1 & table 6b.1). The colors and structures in nevi tend to be distributed in an organized and symmetric fashion.
2. Any melanocytic neoplasm that manifest a pattern that deviates from the benign patterns shown in figure 6b.1 should be viewed with caution.
3. Any lesion that deviates from the benign patterns listed in table 6b.1 and manifests at least one of the melanoma specific structures listed in table 6b.2 should be considered a melanoma until proven otherwise.

REFERENCES

Annessi, G., Bono, R., Sampogna, F., Faraggiana, T. & Abeni, D., 2007, Sensitivity, specificity, and diagnostic accuracy of three dermoscopic algorithmic methods in the diagnosis of doubtful melanocytic lesions: the importance of light brown structureless areas in differentiating atypical melanocytic nevi from thin melanomas. *J Am Acad Dermatol*, 56, 759–67.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Bowen, J.L., 2006, Educational strategies to promote clinical diagnostic reasoning. *N Engl J Med*, 355, 2217–25.

Carli, P., Quercioli, E., Sestini, S., et al., 2003, Pattern analysis, not simplified algorithms, is the most reliable method for teaching dermoscopy for melanoma diagnosis to residents in dermatology. *Br J Dermatol*, 148, 981–4.

Marghoob, M., Korzenko, A., Changchien, L., et al., 2007, The beauty and the beast sign in dermoscopy. *Dermatol Surg*, 33, 1388–91.

Norman G., 2006, Building on experience-the development of clinical reasoning. N Engl J Med 355, 2251–2.

6c ABCD rule

Ulrike Weigert, Walter H.C. Burgdorf, and Wilhelm Stolz

The ABCD rule of dermoscopy was the first dermoscopy algorithm created to help differentiate benign from malignant melanocytic tumors. This algorithm, which was described by Stolz et al. (1994), was developed to quantitatively address the crucial question in dermoscopy of whether a melanocytic skin lesion under investigation is benign, suspicious (borderline), or malignant. Based only on four dermatoscopic criteria this method is relatively easy to learn and apply. The ABCD dermoscopy method has been extensively studied and it has been shown that it improves the diagnostic performance of clinicians evaluating pigmented skin lesions. It is the opinion of some that this method may be particularly well suited for clinicians with limited dermoscopy experience.

Using multivariate analysis, 31 dermatoscopic criteria were evaluated quantitatively in 157 benign and malignant melanocytic lesions. The criteria that combine to create the ABCD rule of dermoscopy (asymmetry, border, color, and differential structures) were found via multivariate analysis to be very important for the recognition of melanoma (Fig. 6c.1) (Stolz et al., 1994). To utilize these criteria, a scoring system was developed (Fig. 6c.2) to calculate the total dermoscopy score (TDS) using a linear equation. With this TDS, a grading of lesions is possible with respect to the probability that the lesions under investigation are malignant (Figs. 6c.3–6c.5). Binder et al. and recently Dolianitis et al. showed the usefulness of the ABCD rule of dermoscopy, especially in enabling relatively inexperienced investigators to more accurately assess melanocytic lesions (Binder et al., 1999; Dolianitis et al., 2005). In the text to follow, each criterion is explained in detail.

Dermoscopic features	Definition
A = Asymmetry	The lesion is bisected by two lines that are placed 90° to each other. The first line attempts to bisect the lesion at the division of "most symmetry" and the other line is then placed 90° to it. Symmetry takes into account the contour, colors and structures within a lesion. Lesions that are symmetric in both axes are given zero points, one axis asymmetry 1 point and biaxial asymmetry 2 points. Thus, the points range from 0 to 2
B = Border sharpness	First, the lesion is divided into eight equal pie-shaped pieces. Next, one counts the number of segments that have an abrupt perimeter cutoff. Thus, the points range from 0 to 8
C = Colors	Number of following colors present: light brown, dark brown, black, red, white, blue-gray. Thus, the points range from 1 to 6
D = Dermoscopic structures	Number of following 5 structures: dots, globules, structureless (homogeneous) areas, network and branched streaks. Thus, the points range from 1 to 5
NB Structureless areas can be either hypopigmented or hyperpigmented (blotch). Branched streaks include streaks, pseudopods, radial streaming and branched streaks, as defined in Chapter 1.	

Figure 6c.1 Definitions for the ABCD rule of dermoscopy.

Feature	Points	Weight factor	TDS score
Asymmetry	0–2	× 1.3	0–2.6
Border sharpness	0–8	× 0.1	0–0.8
Colors	1–6	× 0.5	0.5–3.0
Dermoscopic structures	1–5	× 0.5	0.5–2.5
Total dermoscopy score (TDS range)			1.0–8.9

Figure 6c.2 Formula and coefficients utilized in multivariate analysis for determination of total dermoscopy score.

ASYMMETRY

In judging asymmetry, the lesions should be bisected by two 90° axes that are positioned in such a manner as to bisect the lesion in its most symmetric plane, thereby yielding the lowest possible asymmetry score. It is important to acknowledge that the asymmetry criterion in the ABCD rule incorporates both contour asymmetry and the asymmetry in the distribution of dermoscopic colors and structures. In other words, asymmetry has to be evaluated by taking into account the distribution of colors and structures on either side of each axis, as well as the contour of the lesion. If asymmetry is absent with respect to both axes within the lesion then the asymmetry score is 0. If there is asymmetry in only one axis then the asymmetry score is 1. If there is asymmetry in both axes, then the asymmetry score is 2. The analysis of the data from the original ABCD-rule study revealed that 96% of melanomas had an asymmetry score of 2 as compared with only 24% of benign melanocytic nevi. Of the remaining melanocytic nevi 61% had an asymmetry score of 1, and 15% had a score of 0. Figure 6c.6 demonstrates melanocytic lesions with asymmetry scores of 0, 1, and 2, respectively. It is important to realize that many lesions appearing clinically symmetric may be dermoscopically quite asymmetric by revealing asymmetric distribution of colors and structures (Fig. 6c.7).

BORDER

The evaluation of the border score is predicated upon whether there is a sharp, abrupt cutoff of pigment pattern at the periphery of the lesion or a gradual, indistinct cutoff. For the purpose of analysis, the lesions are divided

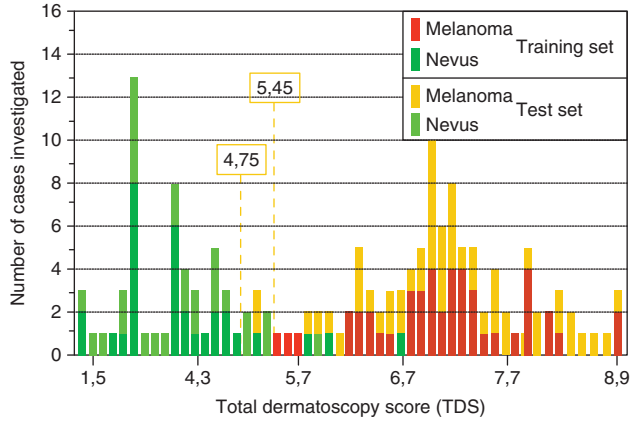


Figure 6c.3 TDS obtained by the ABCD rule in 157 melanocytic lesions was retrospectively investigated. The lesions were randomly and evenly divided into a test and training set. Diagnostic accuracy was 92% in the test set at a threshold of 5.45 for the TDS (all lesions with a TDS higher than 5.45 were diagnosed as malignant). Corresponding sensitivity was 98% and specificity was 90%. Because melanoma can occasionally have a TDS between 4.75 and 5.45, all lesions in this range must be regarded as potentially malignant unless they belong to the group of lesions with special patterns, which represent exceptions to the ABCD rule. Melanocytic lesions presenting with a TDS higher than 5.45 must be regarded as malignant if they do not fall under the same exceptions mentioned above. *Abbreviation*: TDS, total dermoscopy score.

into eight. The maximum border score of eight is given when the entire border (i.e., all eight segments) of the lesion reveal a sharp cutoff. If the border of the lesion in all eight quadrants has an indistinct cutoff then the minimum score of 0 is given (Fig. 6c.8). The original ABCD-rule study data revealed that 60% of nevi have a border score of 0 and only 10% of nevi have a border score greater than 4. In contrast, the border score in melanoma was predominately between 3 and 8. Figure 6c.8 demonstrates examples of the calculation of border scores. The main limitation of the border score is the subjective nature of what is considered a sharp cutoff and what is not. Thus, it should come as no surprise that the reproducibility of the border score is lower as compared with the other criteria used in the ABCD rule.

COLOR

In determining the color score, the following six colors are considered important: white, red, light brown, dark brown, blue-gray, and black. Four colors correspond with melanin distribution (i.e., light and dark brown reflect melanin localized mainly in the epidermis and/or superficial dermis, black represents melanin in the upper granular layer or stratum corneum or all layers of the epidermis, and blue-gray corresponds with melanin in the papillary dermis). White color corresponds with areas of regression and red color reflects the degree of inflammation or neovascularization. The color white is considered to be present only if the area in question is lighter (whiter) in color than the adjacent color of normal skin. The values for the color score range from 1 to 6 (Fig. 6c.9). As was the case with asymmetry, the dermoscope reveals a wider range of colors than can be seen with the naked eye (Fig. 6c.7). In the original ABCD-rule data, 56% of melanocytic nevi had two colors, 29% had three colors, and only 10% had more than three colors. In contrast, 85% of melanomas manifested three or more colors, and 40% of melanomas revealed five to six colors.

DERMOSCOPIC STRUCTURES

For evaluation of dermoscopic (also known as differential) structures, five main features are considered: structureless areas, pigment network, branched streaks, dots, and globules (Fig. 6c.10). In general, melanomas display more dermoscopic structures as compared with nevi. Ninety percent of melanocytic nevi reveal three or fewer structural components. In contrast, 73% of melanomas reveal four or more structural components.

It is important to be aware of a few caveats regarding the ABCD rule. First, dots and globules of any color (including red) are considered significant. Second, structureless areas are considered present if they encompass at least 10% of the lesion's surface area. These structureless areas can be hypo- or hyperpigmented. Third, dots and branched streaks are counted if there are more than two of each, and globules are counted if there is at least one present within the lesion.

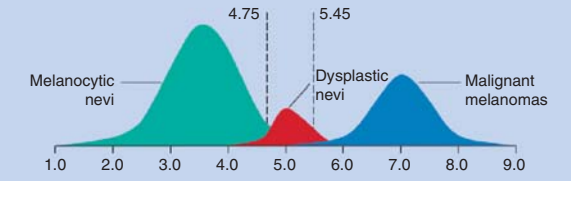


Figure 6c.4 Total dermoscopy score for melanocytic neoplasms. *Source*: From Stolz et al. (2002).

Category	Score range
Benign	<4.75
Suspicious	4.75 to 5.45
Malignant	>5.45

Figure 6c.5 Scoring system for melanocytic neoplasms.

COMBINATION OF CRITERIA: DETERMINATION OF TOTAL DERMOSCOPY SCORE

An accurate distinction between benign and malignant melanocytic lesions can be made if the individual scores of asymmetry, border, color, and dermoscopic structures (the components of the ABCD rule of dermoscopy) are multiplied by the coefficients 1.3, 0.1, 0.5, and 0.5, respectively (Fig. 6c.2), yielding a TDS.

To calculate a formula for a TDS that would reliably discriminate between benign and malignant melanocytic lesions, 157 histologically proven cases were equally and randomly divided between a training and test set. Using the training set, the criteria and coefficients were selected as shown in the formula of Figure 6c.2. The reliability of these criteria and coefficients were tested on the test set of cases. As shown in Figures 6c.3 and 6c.4, at a threshold of 5.45 (Fig. 6c.5), a diagnostic accuracy of 94% was obtained. The diagnostic accuracy measures the number of correct diagnoses of melanoma compared with all cases of melanoma and all cases falsely diagnosed as melanoma. In the training set, the specificity was 90% and the sensitivity was 100%, which indicates that all melanomas in the training set had a dermoscopy score greater than 5.45, and only approximately 10% of melanocytic nevi were falsely classified as malignant. In the test set, the diagnostic accuracy was 92%, sensitivity was 98%, and specificity was 90%, confirming the high diagnostic value of the ABCD rule of dermoscopy.

In an effort to maintain the highest sensitivity for diagnosing melanoma, the ABCD rule was further refined by classifying as suspicious for malignancy all lesions whose dermoscopy score falls between 4.75 and 5.45 (Figs. 6c.3–6c.5). These suspicious lesions should be excised or monitored very closely with a low threshold for excision should any changes develop.

As with all investigative and diagnostic techniques in medicine, it is important that the investigators have sufficient experience with the technique. This can be achieved by attending training courses in dermoscopy and reviewing the relevant literature. However, the best method for becoming

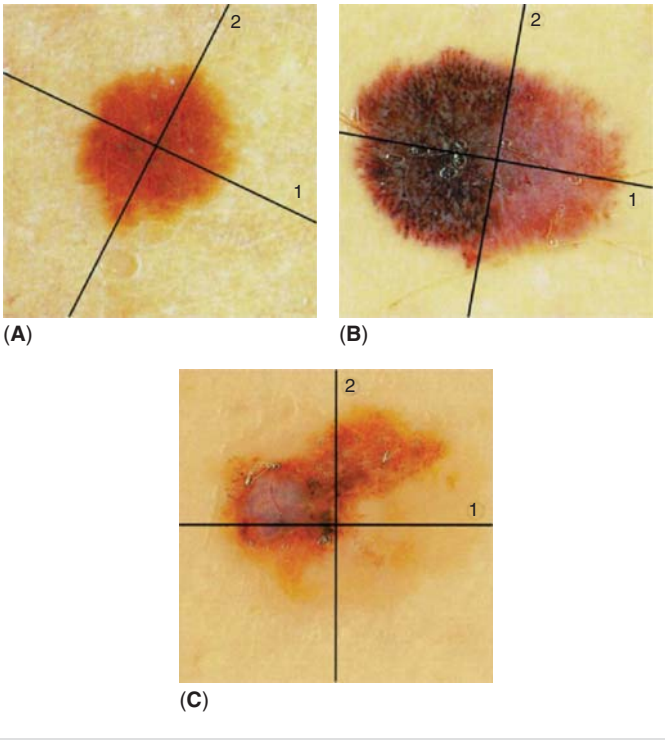


Figure 6c.6 If asymmetry is absent with regard to both axes, as seen in (**A**), the score is 0. If as in (**B**) the lesion is asymmetric in one axis (axis 2) the score is 1. If there is asymmetry in both axes, as in (**C**), the score is 2. Diagnoses: (**A**) melanocytic nevus, compound type; (**B**) superficially spreading melanoma (0.65 mm); and (**C**) superficially spreading melanoma (0.7 mm). *Source*: From Stolz et al. (2002).

proficient in dermoscopy is by the regular use of this instrument in daily practice and by correlating the macroscopic image with the dermoscopic image and then correlating those images with histopathology.

Reliability of the ABCD rule of dermoscopy in the daily practice routine was evaluated in a prospective study by Nachbar et al. (1994). In this study the TDS was calculated and recorded immediately at the time of the patient encounter. The study evaluated 172 melanocytic lesions (69 melanomas and 103 melanocytic nevi). Based on the TDS, the specificity was calculated to be 90% and the sensitivity was 93%. Furthermore, by using dermoscopy the diagnostic accuracy increased by over 15% when compared with the diagnostic accuracy of conventional clinical examination. The mean TDS for melanomas was 6.79, and this score was significantly greater than the TDS score of nevi, which was 4.27. No melanomas in the study had a TDS of less than 4.75. The usefulness of the ABCD rule of dermoscopy was also

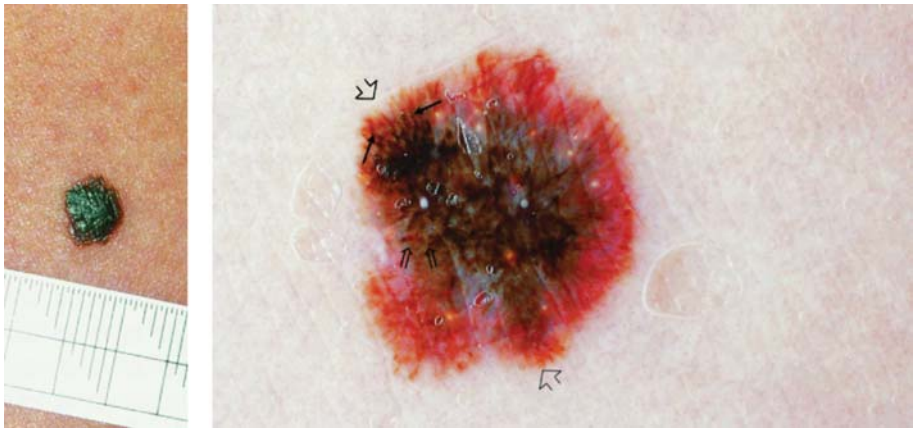


Figure 6c.7 Comparison between the naked eye evaluation of the clinical ABCD criteria of Friedman et al. (1985) (asymmetry, border irregularity, color variegation, and diameter >6.0 mm) and the ABCD rule of dermoscopy. According to Friedman's rule this lesion (clinical view) is symmetric, has a regular border, has no significant color variegation, and has a diameter of 6.0 mm, which thus would be the only criterion for melanoma. Using the ABCD rule of dermoscopy the lesion is asymmetric with regard to color and differential structure along both axes. In addition, an abrupt pigment pattern cutoff at the periphery is present in two segments (=>), four different colors can be seen (red, light and dark brown, and blue-gray) and three structural components [branched streaks (→), dots (➔), and structureless areas]. According to the ABCD rule, this yields a total dermoscopy score of 6.3 (A2, B2, C4, and D3), which indicates that the lesion is malignant. Diagnosis: superficially spreading melanoma (0.65 mm). *Source*: From Stolz et al. (2002).

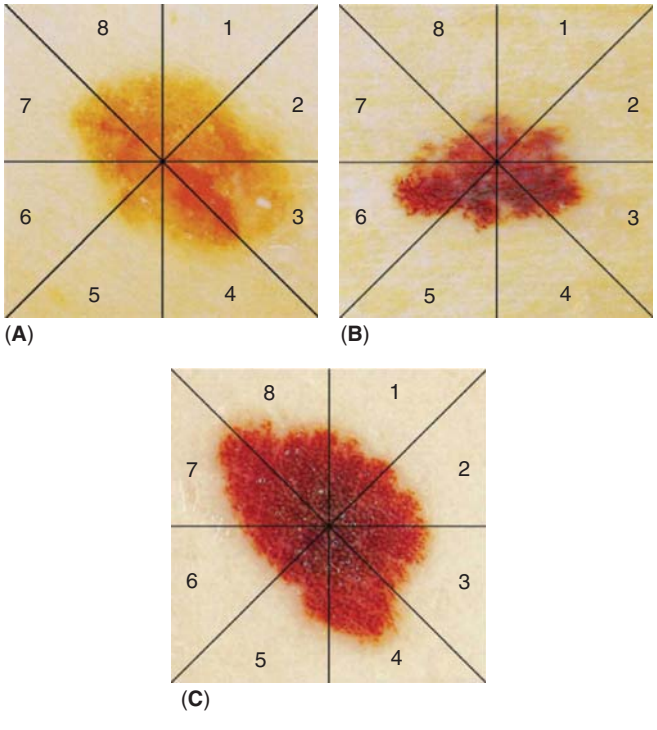


Figure 6c.8 For semi-quantitative analysis the lesions are divided into eight. If no segment shows an abrupt cutoff (**A**), the border score is 0. In (**B**) an abrupt border cutoff is present in segments 3–6, whereas in segments 7, 8, 1, and 2 the pigment pattern gradually thins out toward the periphery. Thus, the border score for lesion (**B**) is 4. All eight segments in (**C**) exhibit an abrupt pigment pattern cutoff, yielding a score of 8. Diagnoses: (**A**) melanocytic nevus, compound type; (**B**) melanoma in situ; (**C**) dysplastic nevus, compound type. *Source*: From Stolz et al. (2002).

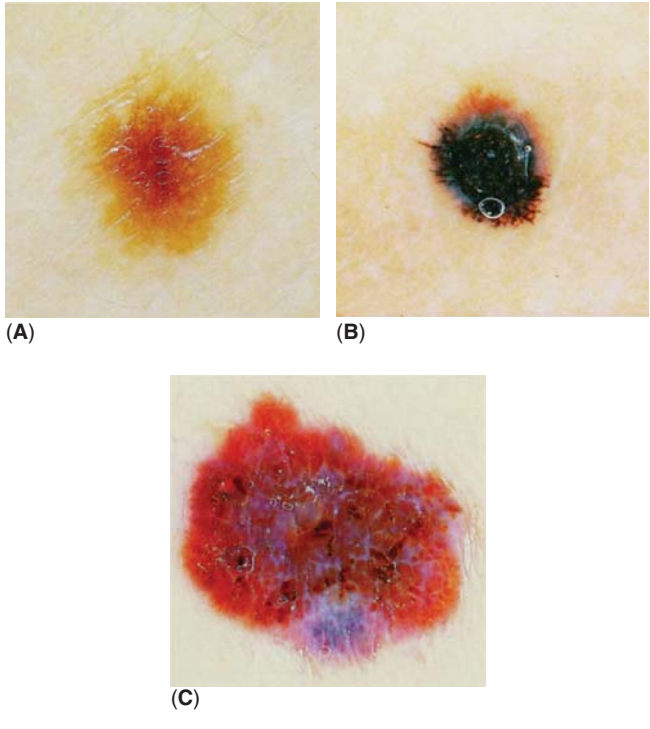


Figure 6c.9 In determining the color score, one needs to search for the presence of any of the following colors: white, red, light brown, dark brown, blue-gray, and black. Depending on the number of colors seen the resulting color score can range from 1 to 6. In (**A**) only light and dark brown colors are present, therefore the score is 2. In (**B**) four different colors can be identified (light and dark brown, blue-gray, and black). All six possible colors, leading to a color score of 6, are seen in (**C**). Diagnoses: (**A**) melanocytic nevus, junctional type; (**B**) melanoma in situ; (**C**) superficial spreading melanoma (1.0 mm). *Source*: From Stolz et al. (2002).

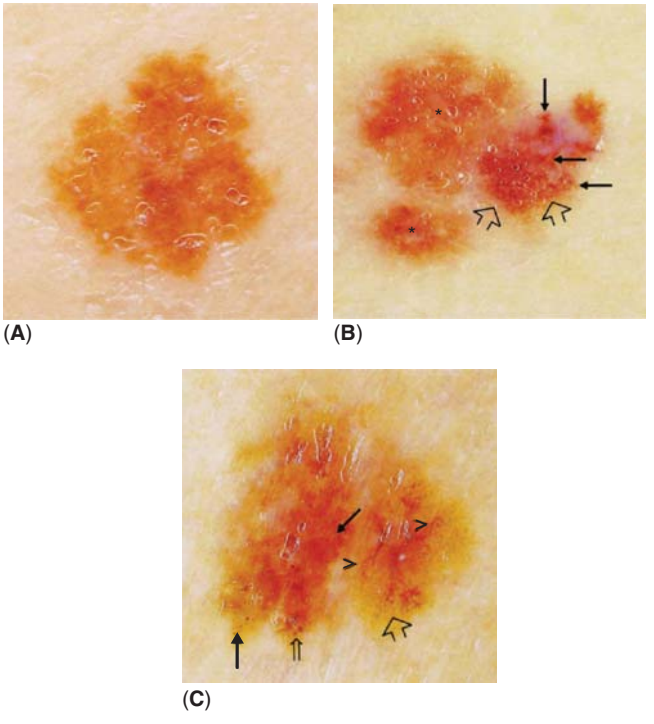


Figure 6c.10 At least one of the following five different structural components must be present for the lesion to be considered a melanocytic lesion. The five structures are network, branched streaks, dots, globules, and structureless/homogenous areas. The resulting score for differential structure ranges from 1 to 5. In (**A**) only structureless area is present, therefore the score is 1. In (**B**), due to three different components [structureless areas (*), areas with network (=>), and branched streaks (→)] a score of 3 is calculated. All five possible structural components are observed in (**C**) [structureless areas, network (=>), branched streaks (>), dots (➔), and pigmented globules (→)). Diagnoses: (**A**) melanocytic nevus, compound type; (**B**) superficial spreading melanoma (0.3 mm); (**C**) superficial spreading melanoma (0.65 mm). *Source*: From Stolz et al. (2002).

1. Certain melanocytic nevi are diagnosed dermoscopically by "Gestalt" (overall impression) and not by the ABCD dermoscopy scoring system:
   - Blue nevus
   - Intradermal nevus (globular; papillomatous)
   - Spitz/Reed nevus
   - Congenital nevus
   - Recurrent nevus
   - Nevus spilus
2. Additional dermoscopic clues:
   clues for melanoma not included in the ABCD dermoscopy scoring system include:
   - Melanin peppering (regression structures)
   - Vessels (dot-like; irregular linear)
   - Red dots/globules
   - Milky-red areas
3. Indeterminate lesions:
   - Indeterminate dermoscopic patterns can be seen in both benign and malignant melanocytic neoplasms
   - The ABCD rule fails in the detection of some early small (<3–4mm in diameter) malignant melanomas because these lesions can be symmetric. Thus, such lesions cannot be dermoscopically differentiated by this method
4. Featureless melanomas:
   - Clinically and dermoscopically they lack melanoma-specific features. They also lack features and patterns of benign lesions
   - Clue: dermoscopically atypical vascular patterns (dotted and irregular linear) in a pink lesion
   - LOOK FOR PIGMENTED REMNANTS!

Figure 6c.11 The exceptions to the ABCD rule are listed in this table.

confirmed in another study of 500 melanocytic skin lesions conducted in Austria (Feldmann et al., 1998).

Binder et al. (1993) observed a decrease in diagnostic accuracy as compared with clinical assessment when less experienced dermoscopy investigators applied pattern analysis to discriminate between benign and malignant pigmented skin lesions. However, participation in didactic dermoscopy training sessions did lead to an increase in the clinician's diagnostic accuracy. In addition, it was determined that clinicians with limited dermoscopy exposure performed better with the ABCD rule of dermoscopy than they did with pattern analysis, presumably because pattern analysis requires experience to master (Binder et al., 1999). Pagnanelli et al. (2003) showed that after participating in a web-based training program clinicians significantly improved their sensitivity and diagnostic accuracy of lesions analyzed using the ABCD rule. In another study, the positive effect of training on diagnostic accuracy was also confirmed (Stanganelli & Bucchi, 1998). Based on the above literature and our own experience we are of the opinion that simple algorithms and criteria may be the best method to introduce dermoscopy to practitioners with limited dermoscopy experience. During our training courses we have observed that some less-experienced clinicians have a tendency to be stricter regarding their judgments of asymmetry of colors and dermoscopic structures, which, when taken to the extreme, will almost always lead to asymmetry scores of 2 and consequently to false-positive TDS resulting in lower specificity. Experience has taught us that pigmented skin lesions with an overall symmetric appearance under dermoscopy should be considered symmetric. In other words, minor dermoscopic variations in the distribution of colors and structures with respect to the axes should not be taken to represent asymmetry. Although the specificity for novice dermoscopists may be lower, the sensitivity remains high for novices using the ABCD dermoscopy rule. This is important since it is imperative that clinicians not miss the diagnosis of melanoma when using the ABCD rule.

As with any rule, there can be exceptions to the ABCD rule of dermoscopy (Fig. 6c.11). Melanocytic nevi with a lentiginous component may not be reliably classified via clinical or dermoscopic examination and these lesions often look suspicious under dermoscopy. False-positive TDS are also common when evaluating melanocytic nevi with globules or nevi with a papillomatous surface. In addition, Spitz/Reed nevus, congenital melanocytic nevus, nevus spilus, agminated nevus, recurrent melanocytic nevus, and ink spot lentigo can have a high TDS score. In these cases the typical "Gestalt" view and diagnosis is superior to the diagnosis based on the calculated TDS. Lesions located on the face, palms, soles, and mucosa, cannot reliably be analyzed using the ABCD rule. Lesions on these locations have their own unique set of diagnostic criteria (see chapter 9, "Special locations") (Stolz et al., 2002).

Unfortunately, using the ABCD rule of dermoscopy does not guarantee that all melanomas will be correctly identified. In particular, it is not uncommon for amelanotic melanomas or deep nodular melanomas to have dermoscopy scores lower than 5.45. In these cases the presence of additional dermoscopic clues, such as regression structures, milky-red areas, and atypical blood vessels can assist in their diagnosis. These criteria are also helpful in the diagnosis of early, small, or so-called featureless melanomas (Skvara et al., 2005).

An extension to the ABCD rule of dermoscopy was proposed by Kittler et al. They suggested including the presence of morphologic change (E) as a fifth parameter (Kittler et al., 1999). Either subjective evidence of change based on the patient's history or objective evidence of change (i.e., comparison of lesion to baseline images) was considered significant. They found that this modification produced a slight but significant increase in diagnostic accuracy.

The ABCD score can also be useful in the preoperative assessment of melanomas to predict their thickness. Carli et al. showed that the TDS score increased with increasing melanoma thickness. They showed that most melanomas with a TDS that was at least 6.8 had a Breslow thickness greater than 0.75 mm with a sensitivity of 80%, a specificity of 84%, and a diagnostic accuracy of 82% (Carli et al., 2000).

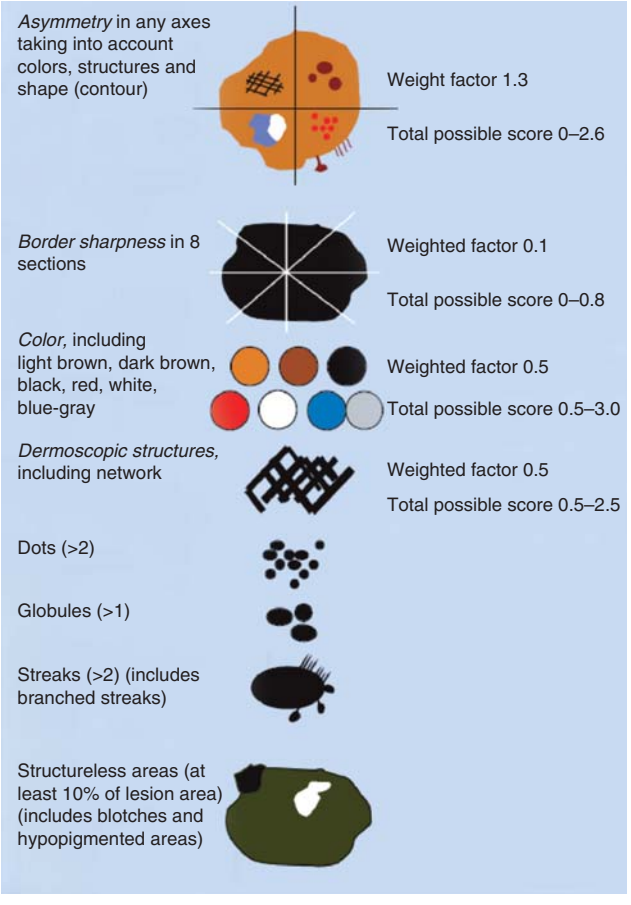


Figure 6c.12 This schematic summarizes the ABCD rule of dermoscopy.

In conclusion, after more than a decade of research and development of numerous other algorithms besides the ABCD rule discussed in this chapter, one fact remains clear, namely, that three features are extremely important in differentiating melanoma from benign nevi. These three features are degree of symmetry/asymmetry, number of colors and number of dermoscopic structures present in the lesion. Benign nevi tend to be symmetric, having few colors and structures. In contrast, melanomas tend to be asymmetric, having many colors and structures.

Key Points (Fig. 6c.12)

- The ABCD rule of dermoscopy is an algorithm based on four criteria: asymmetry, border sharpness, colors, and differential structures.
- A scoring system for each criterion allows for the calculation of the total dermoscopy score (TDS): Asymmetry × 1.3 + Border × 0.1 + Color × 0.5 + Differential structures × 0.5 = TDS.
- A TDS higher than 5.45 indicates melanoma with high specificity and sensitivity.
- Lesions with a TDS between 4.75 and 5.45 are considered suspicious for malignancy and should be excised or monitored closely.
- Some lesions cannot be properly assessed with the ABCD rule, for example, papillomatous melanocytic nevus, Spitz nevus or congenital melanocytic nevus as well as lesions on the face, palms, soles, and mucosa. In addition, small diameter melanomas also cannot be adequately be evaluated via the dermoscopy ABCD rule.
- The presence of regression structures, milky-red areas, or atypical vessels, independent from the TDS, should heighten suspicion that the lesion may be a melanoma.

REFERENCES

Binder, M., Kittler, H., Steiner, A., et al., 1999, Reevaluation of the ABCD rule for epiluminescence microscopy. *J Am Acad Dermatol*, 40, 171–6.

Binder, M., Schwarz, M., Winkler, A., et al., 1993, Application of epiluminescence microscopy in the diagnosis of pigmented skin lesions is a questionable tool for not specifically trained dermatologists. *J Invest Dermatol*, 101, 475.

Carli, P., de Giorgi, V., Palli, D., Giannotti, V. & Giannotti, B., 2000, Preoperative assessment of melanoma thickness by ABCD score of dermoscopy. *J Am Acad Dermatol*, 43, 459–66.

Dolianitis, C., Kelly, J., Wolfe, R. & Simpson, P., 2005, Comparative performance of 4 diagnostic algorithms by nonexperts for the diagnosis of melanocytic lesions. *Arch Dermatol*, 141, 1008–14.

Feldmann, R., Fellenz, C. & Gschnait, F., 1998, Die ABCD-Regel in der dermatoskopie: Analyse von 500 melanozytären Läsionen. *Hautarzt*, 49, 473–6.

Friedman, R., Rigel, D.S. & Kopf, A.W., 1985, Early detection of malignant melanoma: the role of physician examination and self-examination of the skin. *Cancer CA*, 35, 130–51.

Kittler, H., Seltenheim, M., Dawid, M., et al., 1999, Morphologic changes of pigmented skin lesions: a useful extension of the ABCD rule for dermoscopy. *J Am Acad Dermatol*, 40, 558–62.

Nachbar F, Stolz W, Merkle T., & et al., 1994, The ABCD rule of dermoscopy. High prospective value in the diagnosis of doubtful melanocytic skin lesions. *J Am Acad Dermatol*, 30, 551–9.

Pagnanelli, G., Soyer, H.P., Argenziano, G., et al., 2003, Diagnosis of pigmented skin lesions by dermoscopy: web-based training improves diagnostic performance of non-experts. *Br J Dermatol*, 148, 698–702.

Skvara, H., Teban, L., Fiebiger, M., Binder, M. & Kittler, H., 2005, Limitations of dermoscopy in the recognition of melanoma. *Arch Dermatol*, 141, 155–60.

Stanganelli, I. & Bucchi, L., 1998, Epiluminescence microscopy versus clinical evaluation of pigmented skin lesions: effects of operator's training on reproducibility and accuracy. *Dermatology*, 196, 199–203.

Stolz, W., Riemann, A., Cognetta, A.B., et al., 1994, ABCD rule of dermoscopy: a new practical method for early recognition of malignant melanoma. *Eur J Dermatol*, 4, 521–7.

Stolz, W., Braun-Falco, O., Bilek, P., et al., 2002, *Color Atlas of Dermoscopy*. 2nd ed. Oxford, Blackwell.

6d Menzies method

Scott W. Menzies

INTRODUCTION

Since reliance on pattern analysis to evaluate lesions requires significant expertise, we embarked on creating a simplified dermoscopy method for diagnosing melanomas. This method, known as the Menzies method, (Menzies et al., 1996) gives a sensitivity of 92% and specificity of 71% for the diagnosis of melanoma (Argenziano et al., 2003; Henning et al., 2007; Dolianitis et al., 2005). This method has been repeatedly shown to have an increased sensitivity for the diagnosis of melanoma (incorporating both invasive and in situ lesions) compared with other published methods both in expert and nonexpert settings. In contrast to other methods (Carli et al., 2003), it also improves the sensitivity for the diagnosis of small diameter melanoma (Bono et al., 2006). The Menzies method is simple, with 11 features being used to create the model. All features can be visualized with standard 10× magnification handheld surface microscopes and are scored as categorical (present or absent), which reduces the intra- and interobserver errors seen when features are graded. Finally, an atlas has been produced that allows even inexperienced clinicians to learn the method. This enabled primary care physicians to increase their sensitivity for the diagnosis of melanoma by 38% compared with standard clinical visualization (Westerhoff et al., 2000).

To develop the method, a training set of 62 invasive melanomas and 159 clinically atypical pigmented nonmelanomas were scored for 72 surface microscopic features. Unlike in some other methods, the nonmelanoma set included nonmelanocytic lesions, such as seborrheic keratoses, hemangiomas, and dermatofibromas. To create the model, individual features were selected with low sensitivity (0%) for melanoma, defining the two "negative features" for melanoma; or high specificity (>85%) for melanoma, defining the 9 "positive features." Here, "sensitivity" equals the percentage of melanomas with a particular feature and "specificity" the percentage of nonmelanomas without that feature, for example, blue-white veil, which has a sensitivity of 51% and specificity of 97% for the diagnosis of melanoma, meaning that it is present in 51% of melanoma and only 3% of nonmelanoma. This diagnostic method was tested on an independent set comprising 45 invasive melanomas (median Breslow thickness <0.7 mm) and 119 atypical nonmelanomas. The model gave a sensitivity of 92% and specificity of 71% for invasive melanoma. It should be emphasized that most of the nonmelanomas used to determine specificity were clinically atypical, leading to the decision to perform a biopsy. The use of the model would have avoided excision of 71% of those lesions. Clearly, the true specificity of the method in the field is likely to be much greater.

THE METHOD

For a melanoma to be diagnosed, it must have neither of the two morphologic negative features and must have at least 1 of the 9 positive features. The following sections describe each feature in detail. A comprehensive description of these features has been published.

Negative Features: Both Features Must be Absent

Symmetry of Pigmentation Pattern

This is symmetry of all pattern structures, including color along any axis through the center (of gravity) of a lesion. It does not require symmetry of shape (Figs. 6d.1–6d.4). The presence of symmetry of the pigmentation pattern is often the immediate defining feature of benign pigmented lesions.

Single Color

The colors scored are black, gray, blue, red, dark brown, and tan. White is not scored. A single color excludes the diagnosis of melanoma. Melanomas usually manifest more than one color because malignant melanocytes often retain cellular melanin and can be found at varying depths in the skin. Melanin at the level of the stratum corneum appears black and at the level of the midepidermis it appears dark brown. Both black and dark brown

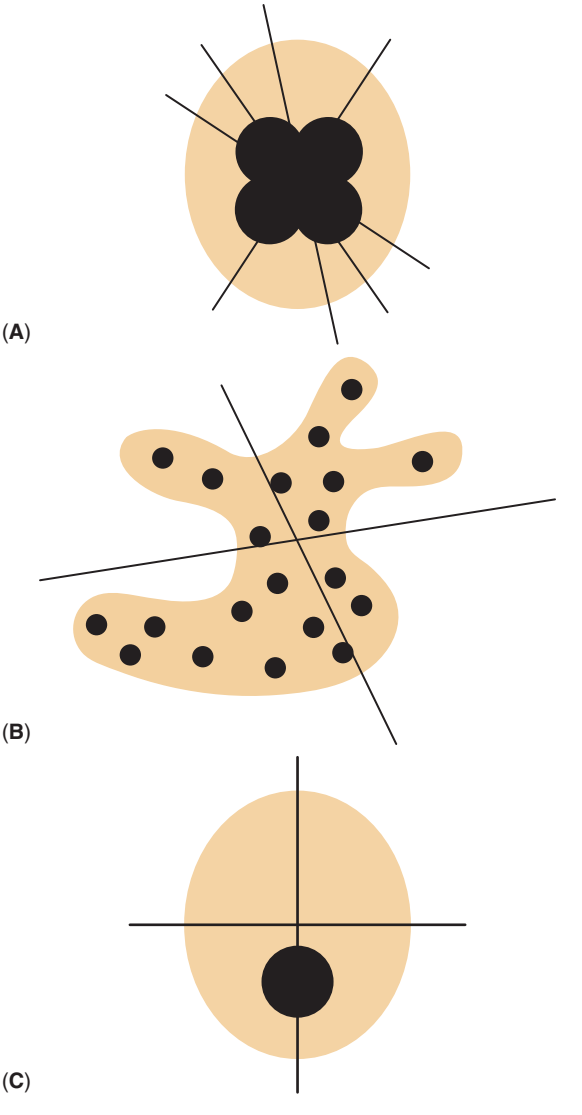


Figure 6d.1 Pattern symmetry definitions. (**A**) Symmetrical pigmentation pattern (symmetry of pattern/texture over *all* axes through the center (of gravity) of a lesion. It does *not* require symmetry of shape. Here, the schematic lesion has mirror symmetry across any axis through its center, and hence it has a symmetrical pigmentation pattern. (**B**) Here, although the lesion lacks symmetry of shape, its repeated pattern results in a symmetrical pigmentation pattern. (**C**) While this lesion has symmetry of pattern over its long axis, it lacks symmetry over its short axis. Hence the lesion has an asymmetric pigmentation pattern. *Source*: From Menzies SW, Crotty KA, Ingvar C, McCarthy WH. Dermoscopy: An Atlas. 3rd Edition, McGraw-Hill Book Co., Sydney, 2009 with permission.

colors are often seen in melanoma with pagetoid invasion of the epidermis. Melanin at the dermoepidermal junction (DEJ) appears as tan, melanin in the upper dermis as gray, and melanin in the middermis as blue.

In summary, most melanomas are asymmetric and have more than one color.

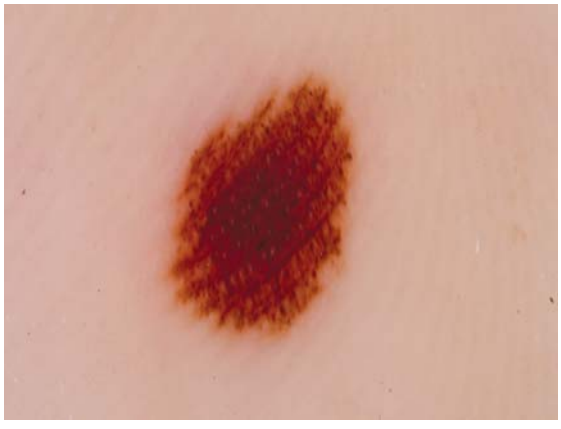


Figure 6d.2 Symmetrical pigmentation pattern. Diagnosis: acral junctional nevus.

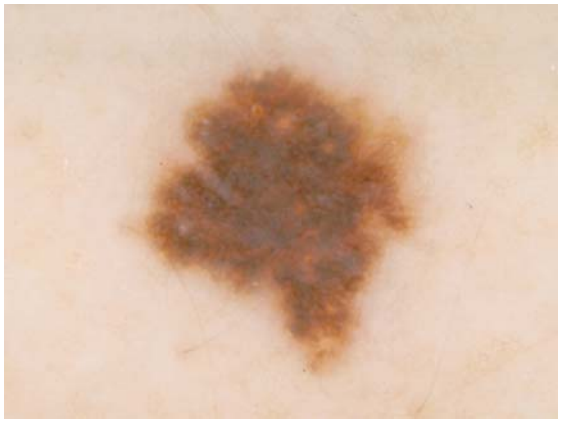


Figure 6d.3 Symmetrical pigmentation pattern. While this lesion has asymmetry of shape it has a repeated pattern throughout the surface of the lesion (similar to the schematic lesion in Fig. 6d.1B). Hence it has a symmetrical pigmentation pattern. It should be emphasized that biological material never has precise symmetry, but rather approximates the situation. Diagnosis: dysplastic nevus.

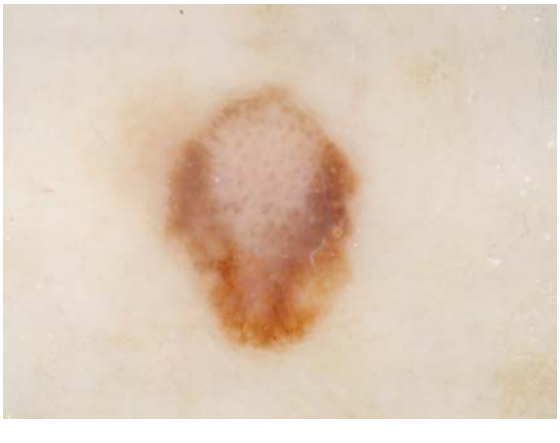


Figure 6d.4 Asymmetric pigmentation pattern. While this lesion has symmetry of pattern over its long axis, it fails symmetry over its short axis, hence it lacks symmetry of pigmentation pattern. Diagnosis: melanoma.

Positive Features: At Least One Feature Must be Found

Blue-White Veil

This is an irregular confluent blue pigmentation with an overlying "ground glass" white film or "veil" (Fig. 6d.5). Histologically it represents melanin in the middermis (melanoma cells, dense collections of melanophages, or free melanin) with compact orthokeratosis of the overlying epidermis. It cannot be associated with red-blue lacunae found in hemangiomas or well-defined structures, such as large ovoid nests seen in pigmented basal cell carcinomas. It can never occupy the entire lesion, as occurs with many blue nevi. Blue-white veil is found in 51% of invasive melanoma and has a specificity of 97%.

Multiple Brown Dots

These are focal aggregations of dark brown dots, which histopathologically represent intraepidermal (suprabasal) melanoma cells (Fig. 6d.6). They should be distinguished by their small size (dots rather than globules) and should be multiple and focal rather than scattered sparsely. They are found in 30% of melanoma and have a specificity of 97%.

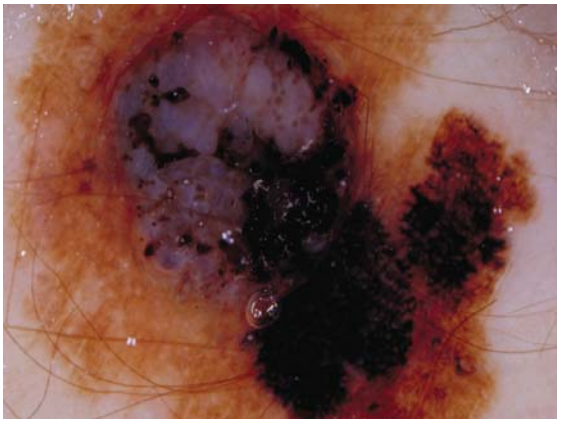


Figure 6d.5 Blue-white veil. Blue-white veil is seen as an irregular confluent blue pigmentation with an overlying "ground glass" white film or "veil." It cannot be associated with red-blue lacunae found in hemangiomas or well-defined structures, such as large ovoid nests seen in pigmented basal cell carcinomas. It can never occupy the entire lesion, as occurs with many blue nevi. It is seen here in the central nodular component of this melanoma. Diagnosis: melanoma 2.15 mm Breslow thickness.

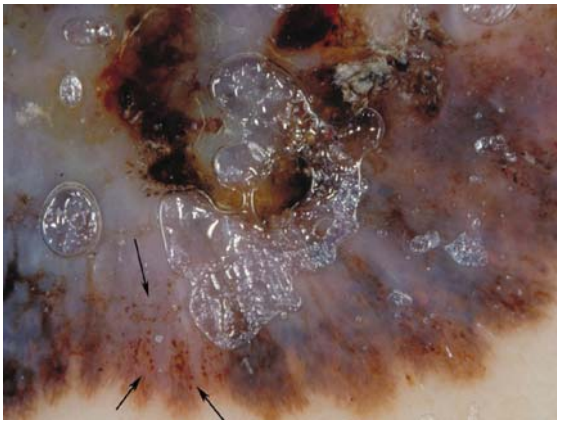


Figure 6d.6 Multiple brown dots, focal aggregations of dark brown dots. They should be distinguished by their small size (dots rather than globules) and should be multiple and focal rather than scattered sparsely (*arrows*). Diagnosis: melanoma 1.8 mm Breslow thickness.

Radial Streaming
This consists of finger-like projections at the edge of the lesion. These projections include linear extensions emanating from an existing network or, more often, they arise from a solid tumor (Figs. 6d.7 and 6d.8). Histologically they represent confluent radial nests of melanoma at an intraepidermal or DEJ position, which is classically seen in some superficial spreading melanomas. Radial streaming is found in 18% of melanoma and has a 96% specificity.

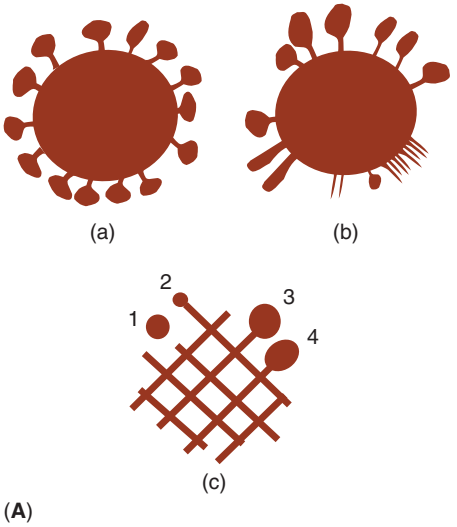
Pseudopods
These are bulbous "foot-like" projections present at the edge of a lesion. They can arise from a pigmented network or from the border of a solid pigmented tumor (Fig. 6d.9A). They are morphologically highly variable (Figs. 6d.9B and 6d.10). They have the same histologic correlate as radial streaming. Pseudopods are found in 23% of invasive melanoma and have a specificity of 97%. Pseudopods should never occupy a uniform circumferential position in melanoma, as seen in Spitz nevi (Fig. 6d.11).

Scar-Like Depigmentation
The final phase of regression may be seen as scarring. Scar-like depigmentation is seen as well-defined areas that are pure white in color (Fig. 6d.12). It is seen in 36% of invasive melanomas and has a specificity of 93%. Scar-like depigmentation should be distinguished from hypomelanotic areas commonly found in nevi; the former's pure white color and well-defined irregularly shaped borders helps in distinguishing it from benign hypopigmented areas.

Peripheral Black Dots/Globules
These are found at or near the edge of the lesion (Fig. 6d.13). They are truly black in color in contrast to brown globules commonly found in benign lesions. They should also be distinguished from central black dots/globules, which are found in some dysplastic nevi. They are found in 42% of invasive melanoma and have a specificity of 92%. Histologically they represent accumulation of pigment in the stratum corneum, arising from pagetoid spread of malignant melanocytes.

Figure 6d.7 Radial streaming, finger-like projections focally present at the edge of the lesion (*arrows*). Diagnosis: melanoma 0.5 mm Breslow thickness.

Figure 6d.8 Radial streaming. Here, more subtle areas are found (*arrows*). Diagnosis: melanoma 0.5 mm Breslow thickness.



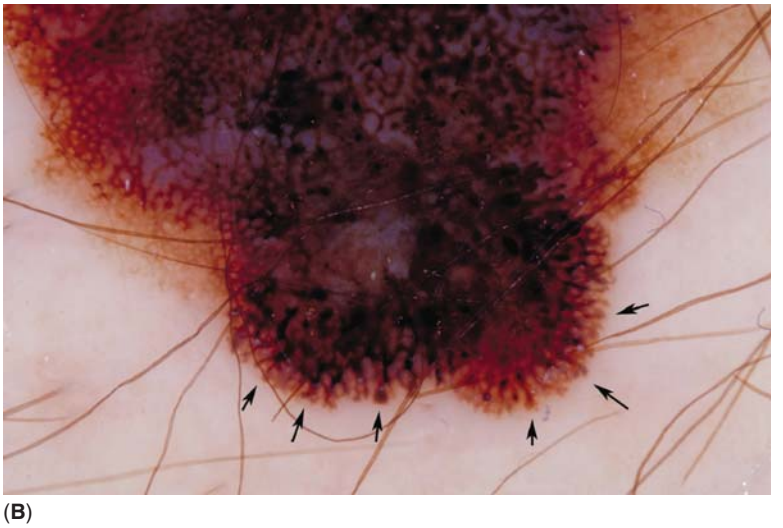


Figure 6d.9 (**A**) Schematic drawing of pseudopods in melanocytic lesions. Pseudopods have small knobs at their tips, and are connected to either a central pigment network or central pigmented blotch. (a) Regular distribution at the periphery; (b) irregular distribution; (c) to be considered pseudopods the bulbous knobs must be directly connected to the tumor and must have a maximum diameter that is larger than the atypical network from which it originates (3 and 4); 1, 2 are not considered pseudopods. (**B**) Pseudopods, bulbous "foot-like" projections at the edge of a lesion. They can arise from a pigmented network (*arrows*) or solid pigmented border. Diagnosis: melanoma 1.2 mm Breslow thickness.

Multiple (Five to Six) Colors

In invasive melanoma melanin is often found at different levels from the stratum corneum to the middermis. Due to the melanin distribution in melanoma and due to the presence of increased vasculature in melanoma, most melanomas display multiple colors. To be a significant positive feature there must be at least five colors from a possible total of six (red, tan, dark brown, black, gray, and blue) (Fig. 6d.14). Multiple (five to six) colors are found in 53% of invasive melanoma and have a specificity of 92%.

Multiple Blue-Gray Dots

In areas of regression of melanocytic lesions, melanin-laden macrophages (melanophages) can be found in the acute phase. These are seen as partly aggregated blue-gray dots often described as "pepper-like" in morphology (Fig. 6d.15). When abundant, melanophages may form areas of blue-white veil. Because regression is a common feature of superficial spreading melanoma, multiple blue-gray dots are found in 45% of invasive melanoma and have a specificity of 91%. They are also a common feature of lentigo maligna (in situ melanoma).

Broadened Network

This is an increase in the width of the "grids" or "cords" of the pigmented net found in melanocytic lesions. This broadening of the network is usually found focally in melanoma, rather than uniformly throughout the lesion. It is found in 35% of invasive melanoma with a specificity of 86%.

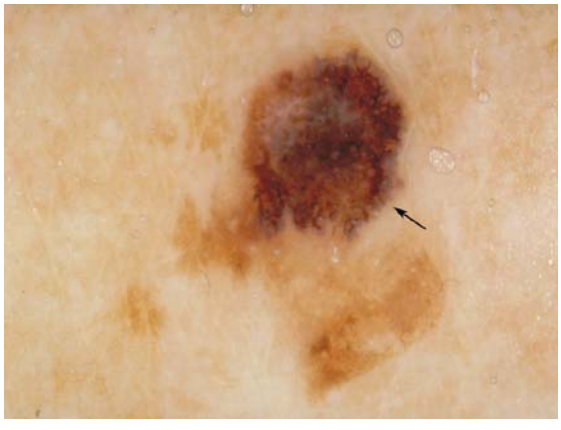


Figure 6d.10 Pseudopods. Diagnosis: melanoma.

Figure 6d.11 Pseudopods in a Spitz nevus. Pseudopods should never occupy a uniform circumferential position in melanoma, unlike that commonly found in Spitz nevi. Diagnosis: Spitz nevus.

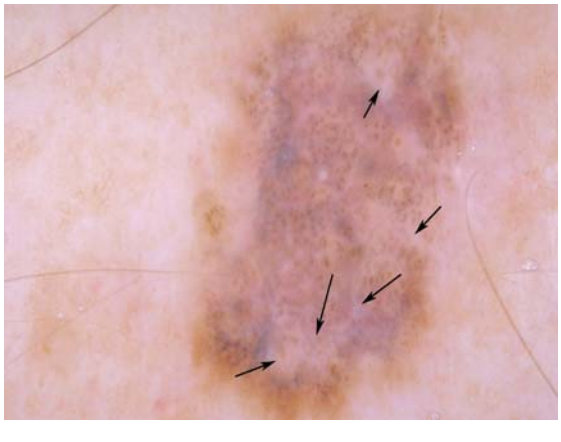


Figure 6d.12 Scar-like depigmentation, seen as areas of pure white well-defined irregular extensions (*arrows*). Scar-like depigmentation should be distinguished from hypomelanotic areas commonly found in lesions, because of the former's pure white color and well-defined irregularly shaped borders.

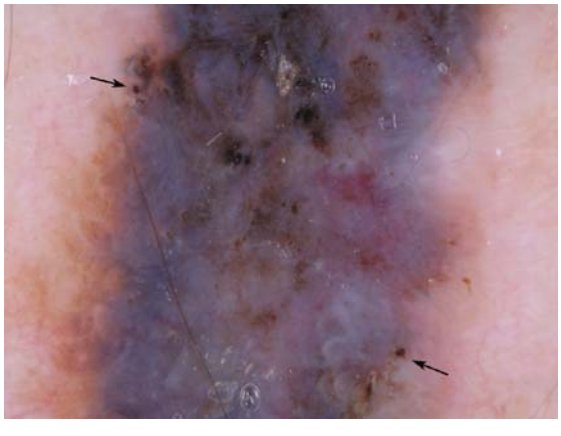


Figure 6d.13 Peripheral black dots/globules, found at or near the edge of the lesions (*arrows*). They are truly black in color, in contrast to brown globules commonly found in benign lesions. They should also be distinguished from central black dots/globules found in some dysplastic nevi. Diagnosis: melanoma 1.4 mm Breslow thickness.

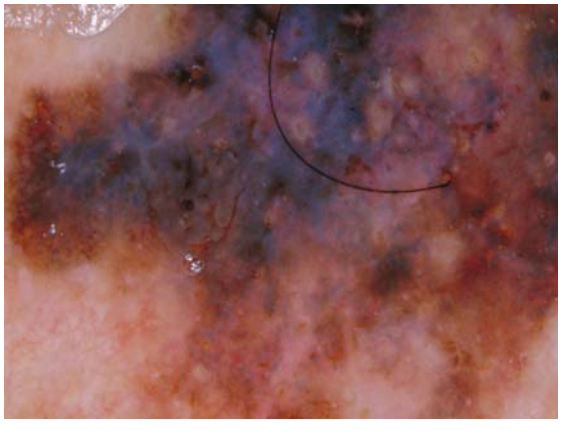


Figure 6d.14 Multiple (five to six) colors. Invasive melanoma often has melanin found from the stratum corneum to the middermis. This and the presence of increased vasculature can lead to multiple colors. To be a significant positive feature there must be at least five colors from a possible total of six (tan, dark brown, black, gray, blue, and red). This lesion has all six colors. Diagnosis: melanoma 0.25 mm Breslow thickness.

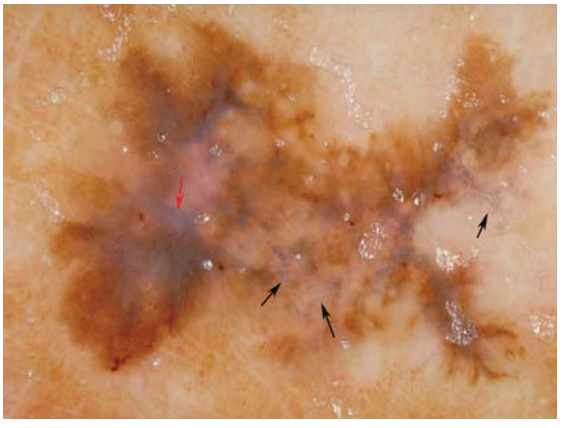


Figure 6d.15 Multiple blue-gray dots. In areas of early to intermediate regression of melanocytic lesions melanin-laden macrophages (melanophages) can be found. These are seen as partly aggregated blue-gray dots often described as "pepper-like" in morphology (*black arrows*). When melanophages are found in abundance they can form areas of blue-white veil (*red arrow*). Diagnosis: melanoma.

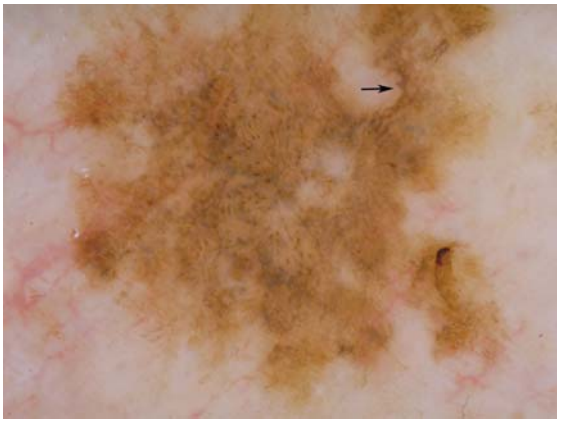


Figure 6d.16 Broadened network, an increase in the width of the "grids" or "cords" of the pigmented net found in melanocytic lesions. This broadening of the network is usually focally found in melanoma (*arrow*), rather than uniformly throughout the lesion. Broadened network is also a common feature of lentigo maligna, as found here. Diagnosis: lentigo maligna.

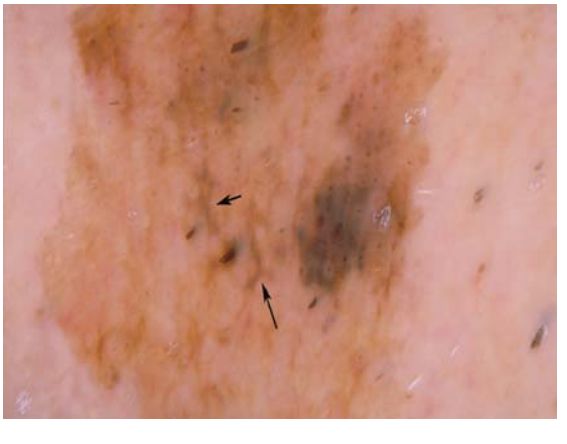


Figure 6d.17 Focal areas of broadened network are found in this lentigo maligna (*arrows*).

Figure 6d.18 Menzies method. This lesion lacks the two negative features of symmetry of pigmentation pattern and a single color. In addition, it has two positive features of blue-white veil (*black arrow*) and focal broadened network (*red arrow*). Diagnosis: superficial spreading melanoma 0.4 mm Breslow thickness.

Figure 6d.19 Menzies method. This lesion has one of the two negative features (symmetrical pigmentation pattern), and therefore is immediately diagnosed as benign. Note that symmetry of shape is not necessary for symmetrical pigmentation pattern (Fig. 6d.1). Diagnosis: compound nevus.

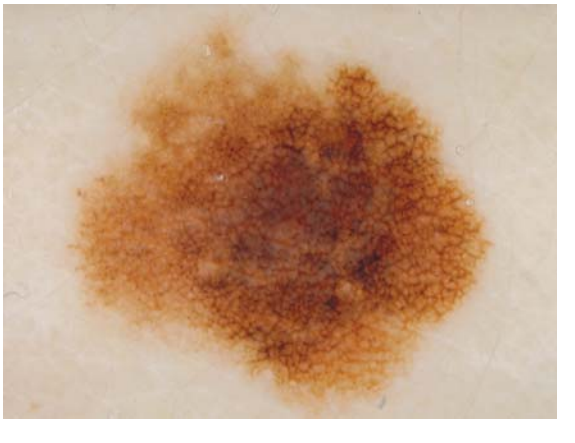


Figure 6d.20 Menzies method. This lesion has neither of the two negative features (symmetry of pigmentation pattern and a single color) but has none of the 9 positive features of melanoma either. Diagnosis: dysplastic nevus.

Broadened network is also a common feature of lentigo maligna. It correlates histologically with expansion of melanocytic nests found at the dermo-epidermal junction (DEJ) (Figs. 6d.16 and 6d.17).

Examples of Menzies method in use are shown in Figures 6d.18–6d.22. Many other examples are illustrated in the chapters on superficial spreading melanoma (chap. 9a) and nodular melanoma (chap. 9c). Finally, although the model development did not include in situ melanomas, the common features of broadened network and multiple blue-gray dots in both in situ superficial spreading melanoma and lentigo maligna allow this method to detect the majority of these lesions.

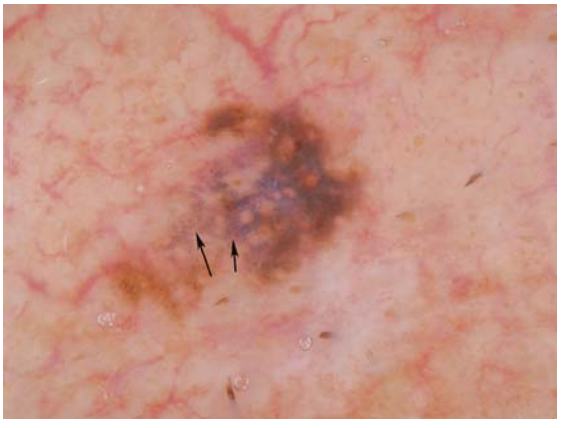


Figure 6d.21 Menzies method. This lesion has neither of the two negative features (symmetry of pigmentation pattern and a single color) but has one of the positive features of melanoma—multiple blue-gray dots (*arrows*). Diagnosis: lentigo melanoma.

Figure 6d.22 Menzies method. This lesion has neither of the two negative features but has none of the positive features of melanoma either. Diagnosis: dysplastic nevus.

Key Points (Fig. 6d.23)

- Menzies method gives a sensitivity of 92% and specificity of 71% for the diagnosis of melanoma.
- For lesions to be considered suspect for melanoma they must possess more than one color and they must reveal asymmetry. Suspect lesions displaying any of the 9 positive features for melanoma are considered to be melanoma unless proved otherwise.
- The positive feature for melanoma are blue-white veil, multiple brown dots, focal pseudopods, focal radial streaming, scar-like depigmentation, peripheral black dots/globules, five to six colors, multiple blue-gray dots/peppering, and a focally broadened network.

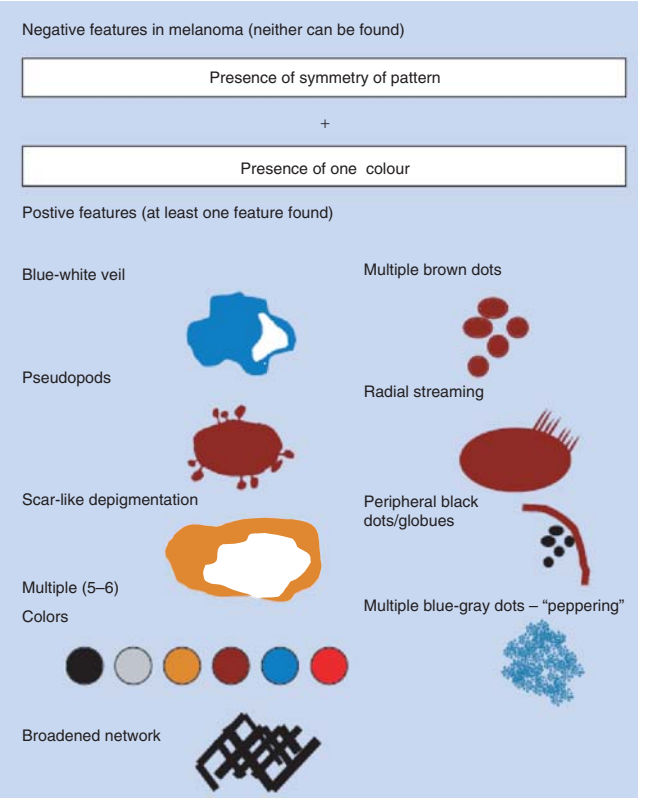


Figure 6d.23 Menzies method.

REFERENCES

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Bono, A., Tolomio, E., Trincone, S., et al., 2006, Micro-melanoma detection: a clinical study on 206 consecutive cases of pigmented skin lesions with a diameter < or = 3 mm. *Br J Dermatol*, 155, 570–3.

Carli, P., Quercioli, E., Sestini, S., et al., 2003, Pattern analysis, not simplified algorithms, is the most reliable method for teaching dermoscopy for melanoma diagnosis to residents in dermatology. *Br J Dermatol*, 148, 981–4.

Dolianitis, C., Kelly, J., Wolfe, R. & Simpson, P., 2005, Comparative performance of 4 dermoscopic algorithms by nonexperts for the diagnosis of melanocytic lesions. *Arch Dermatol*, 141, 1008–14.

Henning, J.S., Dusza, S.W., Wang, S.Q., et al., 2007, The CASH (color, architecture, symmetry, and homogeneity) algorithm for dermoscopy. *J Am Acad Dermatol*, 56, 45–52.

Menzies, S.W., Ingvar, C., Crotty, K., McCarthy, W.H., 1996, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features, *Arch Dermatol*,132, 1178–82.

Westerhoff, K., McCarthy, W.H., Menzies, S.W., 2000, Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy, *Br J Dermatol*, 143, 1016–20.

6e Seven-point checklist and the seven rules not to miss melanoma incognito

Giuseppe Argenziano

The classic approach for rendering a diagnosis using dermoscopy is the so-called pattern analysis method originally published by Pehamberger and colleagues in 1987 (Pehamberger et al., 1987). However, the pattern analysis method requires experience to master. Analytical methods based on scored algorithms have been introduced over the past few years aimed at increasing sensitivity for detecting melanoma, with results that are reliable and reproducible even in the hands of nonexpert dermoscopists (Stolz et al., 1994; Menzies et al., 1996; Argenziano et al., 1998).

For all these analytically based scored algorithms, a given pigmented lesion must first be classified as melanocytic or nonmelanocytic. Only when the diagnosis of a nonmelanocytic lesion is ruled out and the lesion in question is determined to be of melanocytic origin can these methods be utilized.

The seven-point checklist is one of the analytically based diagnostic algorithms that provides a quantitative scoring system requiring the observer to identify a limited number of structures (Argenziano et al., 1998). This method was developed for the dermoscopic diagnosis of melanoma based on the evaluation of 342 melanocytic skin lesions (117 melanomas and 225 clinically atypical nevi).

DEFINITION OF THE SEVEN CRITERIA

In the original manuscript describing the seven-point checklist the dermoscopic images of melanocytic skin lesions were studied to evaluate the frequency of seven criteria. The following features were selected due to their frequent association with melanoma (Table 6e.1). Most of these features were also described in the guidelines of the first consensus meeting on dermoscopy held in Hamburg in 1989 (Bahmer et al., 1990).

Major Criteria

Atypical Pigment Network

In contrast to the terminology in the first consensus paper on dermoscopy (Argenziano, 2003), we used the term "atypical" pigment network to define a black, brown, or gray network with focal thick lines that are distributed irregularly within the lesion.

Blue-White Veil

Dermoscopically this feature appears as an irregular, structureless area of confluent blue pigmentation with an overlying white "ground-glass" haze. The pigmentation cannot occupy the entire lesion, as would be seen in a blue nevus, and usually corresponds to a clinically elevated portion of the lesion. The blue-white veil correlates with an acanthotic epidermis with focal hypergranulosis above sheets of heavily pigmented melanocytes in the dermis. It must be differentiated from gray-blue areas (i.e., blue pepper-like granules, peppering, multiple blue-gray dots), which are commonly associated with white scar-like areas, corresponding histopathologically to the presence of melanophages and fibrosis (i.e., regression).

Atypical Vascular Pattern

A vascular pattern may be observed in any melanoma but atypical vessels are most commonly seen in focally hypo pigmented melanomas, completely hypopigmented melanomas and in pure amelanotic melanomas. Atypical vascular pattern is defined as vascular structures that are irregularly distributed within the melanocytic lesion and are not clearly associated with regression structures (i.e., areas of regression). The following morphologic variations of atypical vascular pattern can be distinguished:

1. Linear–irregular vessels, which presumably reflect melanoma neovascularization with vessels oriented parallel to the skin surface.
2. Dotted vessels, which represent blood vessels oriented perpendicular to the skin surface.

Minor Criteria

Irregular Streaks

Although radial streaming and pseudopods (irregular extensions) were described independently, they are evaluated as a single criterion in the seven-point checklist. This is due to the fact that, although morphologically distinct, they both correspond histopathologically with confluent radial junctional nests of melanocytes (Menzies et al., 1995). To be scored, streaks must be irregularly or focally distributed at the edge of the lesion.

Table 6e.1 Seven-Point Checklist for the Dermoscopic Differentiation Between Benign Melanocytic Lesions and Melanoma.*

Dermoscopic criterion	Definition	Score
Major criteria		
1. Atypical pigment network	Black, brown, or gray network with irregular holes and thick lines	2
2. Blue-white veil	Irregular, structureless area of confluent blue pigmentation with an overlying white "ground-glass" film. The pigmentation cannot occupy the entire lesion and usually corresponds to a clinically elevated part of the lesion	2
3. Atypical vascular pattern	Linear–irregular or dotted vessels, which cannot be present within areas revealing regression structures	2
Minor criteria		
4. Irregular streaks	Brown to black, bulbous or finger-like projections irregularly distributed at the edge of a lesion. They may arise from network structures but more commonly do not	1
5. Irregular dots/globules	Black, brown, round to oval, variously sized structures irregularly distributed within the lesion	1
6. Irregular blotches	Black, brown and/or gray structureless areas asymmetrically distributed within the lesion	1
7. Regression structures	White scar-like depigmentation and/or blue pepper-like granules usually corresponding to a clinically flat part of the lesion. Atypical vascular structures are not visible within areas revealing regression structures.	1

*By simple addition of the individual scores a minimum total score of 3 is required for the diagnosis of melanoma, whereas a total score of less than 3 is indicative of a nevus.

Irregular Dots/Globules
Dots and globules are considered as a single criterion in the seven-point checklist. Although dots and globules are distinguished by their size (a globule being larger than a dot), both may have a black or brown coloration and both may represent nests of melanocytes. To be scored, dots/globules must be irregularly distributed within the lesion.

Irregular Blotches
Irregular blotches consist of black, brown, and/or gray structureless areas asymmetrically distributed within the lesion.

Regression Structures
On the basis of their similar histopathologic significance we included white (scar-like) depigmentation and gray-blue areas (blue pepper-like granules) in a single criterion called regression structures, the former being related to the presence of fibrosis and the latter corresponding to melanosis.

THE SEVEN-POINT SCORE

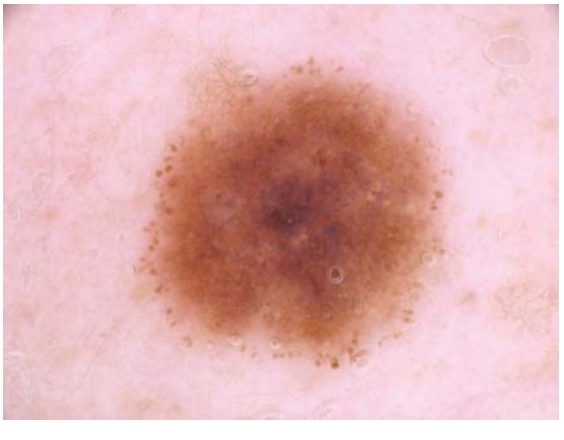
The differences between melanomas and nevi were evaluated by a univariate statistical test and the significant variables were then used for stepwise logistic regression analysis to determine their significance, which was expressed by odds ratios. Using the odds ratios calculated by multivariate analysis, a score of 2 was assigned to the three criteria with an odds ratios of >5. These structures became known as the "major" criteria and consisted of atypical network, blue-white veil, and atypical vascular pattern. A score of 1 was assigned to the four criteria with odds ratios <5. These structures became known as the "minor" criteria consisting of irregular streaks, irregular dots/globules, irregular blotches, and regression structures. By simply adding together the individual assigned scores, a total score of 3 or more allowed classification of melanoma with a sensitivity of 95% and a specificity of 75%. In total, 82% of melanocytic lesions were correctly diagnosed using the seven-point checklist method (Figs. 6e.1–6e.7).

SIMPLIFIED SCORED SEVEN-POINT CHECKLIST

The seven-point checklist method can be simplified by eliminating the division of structures into major and minor categories. In the simplified method the presence of any one of the seven criteria is sufficient to consider the diagnosis of melanoma. This simplified algorithm has been shown to be reproducible and reliable in the hands of nonexpert dermatologists, who were able to classify a high percentage of melanomas (sensitivity range: 85–93%). However, the specificity rates of nonexperts were low in the range of 45–48%. This low specificity can, in part, be explained by the fact that most of the nevi in the test set were clinically atypical, easily leading to the decision of performing a biopsy. Clearly, the true specificity of the method in the daily routine practice should be much greater.

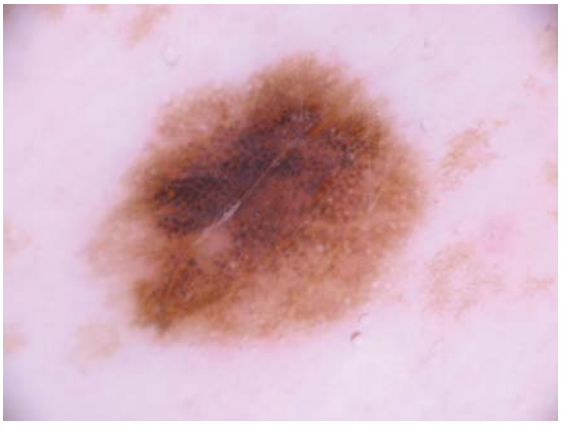
In a re-evaluation of dermoscopic algorithms (Pagnanelli et al., 2003), the seven-point checklist was found to allow the highest sensitivity for diagnosing melanoma in the hands of nonexperts. In this study, 16 clinicians not yet familiar with dermoscopy were asked to evaluate dermoscopic images of 20 pigmented skin lesions using different diagnostic methods (pattern analysis, the ABCD rule, Menzies method, and the seven-point checklist), before and after an Internet-based training course on dermoscopy. The results revealed a considerable improvement in the dermoscopic diagnosis of melanoma after the Web-based training compared with the situation before training. Remarkably, the pre- and posttraining test sensitivity significantly improved for pattern analysis, the ABCD rule and Menzies method; however, it did not change significantly for the seven-point checklist due to the fact that the seven-point checklist maintained a high sensitivity both in the pre- and posttraining course test. In this study, use of the seven-point checklist by 16 nonexperts in dermoscopy showed a

▲ **Figure 6e.1a** Melanocytic nevus, clinical image.



◀ **Figure 6e.1b** Dermoscopy of this nevus does not reveal any of the seven-point checklist criteria. Globules are regularly distributed at the periphery and a thin pigment network is seen in the center.

▲ **Figure 6e.2a** Melanocytic nevus, clinical image.

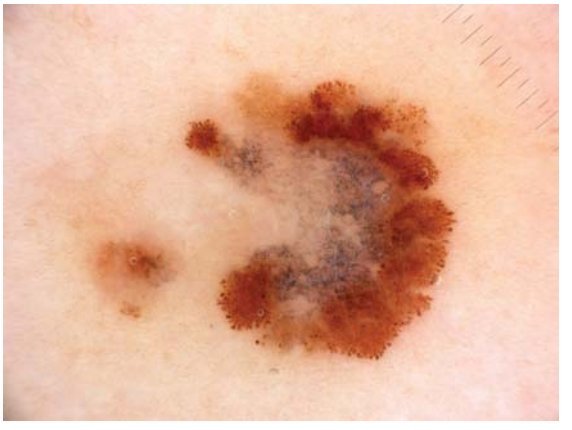


◀ **Figure 6e.2b** This is a nevus with irregular dots/globules. The total seven-point score is 1, thus within the range of a benign lesion.

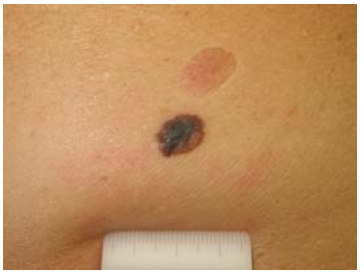
▲ **Figure 6e.3a** Early melanoma simulating a seborrheic keratosis on clinical inspection.

◀ **Figure 6e.3b** In this melanoma there is atypical pigment network (2 points) together with regression features (1 point). The total score is 3, thus indicating that the lesion is suspicious for melanoma.

▲ **Figure 6e.4a** Early melanoma, clinical image.



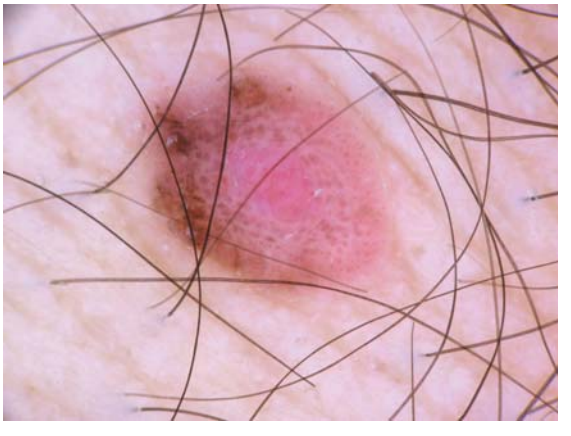
◀ **Figure 6e.4b** This is a melanoma with pronounced regression features (pepper-like granules especially seen in the center; 1 point). Other melanoma-specific criteria include atypical network (2 points), irregular dots/globules (1 point) and irregular streaks (1 point). The total score is 5, indicating that the lesion is a melanoma.



▲ **Figure 6e.5a** Melanoma, clinical image.

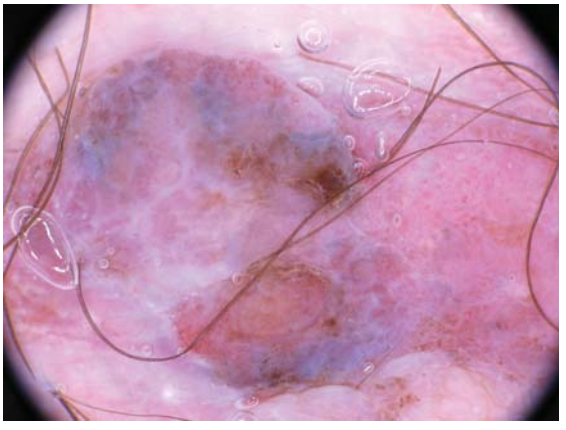
◀ **Figure 6e.5b** Blue-white veil (2 points) is the most striking feature of this lesion. Together with an atypical pigment network (2 points), and focal white scar-like area of regression (1 point), the total score reaches 5 points, which is indicative of melanoma.

▲ **Figure 6e.6a** Melanoma, clinical image.



◀ **Figure 6e.6a** This is a 1.1 mm thick, hypomelanotic melanoma showing atypical vascular structures with dotted vessels at the periphery and linear–irregular vessels in the center. In addition, this lesion also has irregular dots/globules. The final total score for this lesion is 3, which is in the suspicious range.

▲ **Figure 6e.7a** Nodular melanoma, clinical image.



◀ **Figure 6e.7b** In this relatively large nodular melanoma that is arising in a pre-existing congenital nevus there is a combination of blue-white veil and atypical vascular pattern, including dotted vessels at the right pole and linear–irregular vessels at the upper pole of the lesion. There are also small focal irregular black dots/globules. The total score for this lesion is thus 5.

sensitivity of 100% with a 70% specificity after a short Web-based training period, with a good kappa value for interobserver agreement.

In the publication from the Consensus Net Meeting on Dermoscopy the value of the seven-point checklist in diagnosing melanoma was confirmed (Argenziano et al., 2003). The seven-point checklist had sensitivity for diagnosing melanoma that was similar to that calculated for pattern analysis, the ABCD rule, and the Menzies method. It is interesting to note, however, that in the hands of dermoscopy experts the use of pattern analysis allowed better specificity (up to 10% increased specificity) compared with the analytically based scored algorithms.

In the seven-point checklist the usual cutoff value at which point the lesion is considered suspicious for melanoma is three. In other words, at minimum, two dermoscopic features must be present for a lesion to be classified as a potential melanoma (one major and one minor criterion). As a general rule in dermoscopy, there is no single criterion allowing for the diagnosis of melanoma, but rather a combination of multiple criteria is required. However, one exception to this general rule applies when lesions exhibit regression structures as a single predominant feature. Such lesions should be managed carefully because of the possibility that they may represent melanomas that are undergoing regression. In a recent study (Zalaudek et al., 2004), approximately 15% of melanocytic lesions revealing dermoscopic features of regression (in the absence of the other criteria listed in the seven-point checklist) were considered histopathologically equivocal with at least one out of four pathologists diagnosing any given lesion as melanoma. Most of these histopathologically equivocal lesions exhibited significant regression structures under dermoscopy with more than 50% of the lesion area involved with blue and/or white structures. Therefore, for this particular group of lesions, not only is the careful evaluation for the presence of criteria listed in the seven-point checklist required, but also a quantitative evaluation of the area within a lesion involved by dermoscopic features of regression is necessary.

Other clinical situations where additional clues for the diagnosis of melanoma are often required are the following:

1. Lesions on the face. In this location special dermoscopic features should be considered for the diagnosis of early melanoma, such as rhomboidal structures for lentigo maligna (Schiffner et al., 2000) (see chapter 8d and 9c).
2. Lesions on the palms and soles. In these locations special dermoscopic features should be considered for the diagnosis of melanoma including the parallel-ridge pattern (Saida et al., 2004) (see chapter 8b, "Acrolentiginous melanoma" and chapter 9a, "The palms and soles").
3. Lesions with spitzoid features. Independent from the seven-point score, lesions with Spitzoid features should generally be excised and diagnosed histopathologically (Argenziano et al., 1999) (see chapter 7e, "Spitz and Reed nevi").

MELANOMA INCOGNITO

Possible scenarios resulting in the failure to diagnose melanoma creates much anxiety in clinicians dealing with pigmented skin lesions. A small series of difficult-to-diagnose melanomas, which have been termed "melanoma incognito," has been published. Although these melanomas were difficult to diagnose, the dermoscopic examination did in fact play a valuable diagnostic role by increasing the index of suspicion to biopsy these lesions (Argenziano et al., 2007). The evaluation of these melanoma incognitos resulted in the creation of seven lesion management rules, whose aim is to help correctly identify these otherwise difficult to diagnose melanomas.

Rule #1: Dermoscopy Should not be Used Only for Clinically Suspicious Skin Lesions (Fig. 6e.8a,b)

Melanoma may mimic a wide range of benign melanocytic and nonmelanocytic skin lesions. In particular, some early and small melanomas may lack the classic clinical ABCD criteria and can resemble a benign nevus. On the other hand, thick melanoma such as nodular melanomas may mimic an intradermal nevus, a pyogenic granuloma, or a dermatofibroma, to name but a few examples. In all these cases dermoscopy may add useful information to the clinical assessment, allowing the raising of the red flag. Some dermoscopists even recommend the examination of all melanocytic lesions and not only the suspicious ones with dermoscopy (Seidenari, 2006). Opponents of the technique argue that examining all melanocytic lesions in all patients is a very time-consuming and cost-ineffective way to find melanoma. Proponents of examining all nevi with dermoscopy claim that examining nevi with dermoscopy is not a very time-consuming endeavor, especially if a polarized-light hand-held instrument is used since such an instrument eliminates the need to apply a liquid to the skin, and thereby facilitates the rapid viewing of many nevi (Zalaudek et al., 2008).

Rule #2: Biopsy Lesions that Lack Clinical–Dermoscopic Correlation

The index of suspicion for melanoma can sometimes only be raised when the dermoscopic features do not confirm the clinical impression. To minimize the risk of missing melanoma, clinically centered diagnoses should be based on correlating the clinical naked eye findings with the dermoscopic findings. For example, in the context of clinically banal lesions, what is seen via dermoscopy should fit with the clinical impression, and a red flag should be raised when unexpected features are observed (Zalaudek et al., 2005).

Rule #3: Biopsy Lesions with a Non-Specific Pigment Pattern

In the case series mentioned previously (Argenziano et al., 2007), one of the cases was a desmoplastic melanoma revealing clinical features of a nonpigmented, benign, inflammatory lesion. Unexpectedly, dermoscopic examination revealed nonspecific pigment pattern that was not diagnostic of melanoma yet was atypical enough to warrant a biopsy. The observation that a nonspecific pigment pattern should increase one's suspicion for melanoma has been published previously (Argenziano et al., 2003). This rule is especially relevant when evaluating clinically amelanotic or hypopigmented skin tumors.

Rule #4: Biopsy Lesions Revealing Spitzoid Features (Figs. 6e.9a,b)

The accuracy in diagnosing Spitz nevi, especially the pigmented variant, has improved dramatically with the use of dermoscopy (Steiner et al., 1992; Peris

et al., 2002; Ferrara et al., 2005). We owe this improved diagnostic accuracy to the fact that many Spitz nevi display a strikingly characteristic starburst pattern. By contrast, the clinical recognition of Spitz nevi is often difficult due to their often heterogenous morphologic features. However, it has also been documented that although the starburst pattern is usually associated with the diagnosis of a Spitz nevus, it may on rare occasions be seen in melanoma (Argenziano et al., 1999). Thus, especially in adult patients a biopsy should be performed on lesions displaying spitzoid features under dermoscopy.

Rule #5: Biopsy Lesions with Extensive Regression Features (Figs. 6e.10a,b)

As mentioned above, the presence of regression structures is another dermoscopic clue that should prompt the observer to consider the diagnosis of melanoma, especially if occurring in patients with multiple acquired melanocytic nevi. White scar-like areas (corresponding to fibrosis) and/or blue pepper-like granules (corresponding to melanophages) represent regression areas and can be seen in melanoma and in so-called Clark nevi, especially those located on the back of fair skin individuals. In the absence of other melanoma-specific criteria, the risk for a lesion being melanoma is directly correlated with the extent of regression seen with dermoscopy (Zalaudek et al., 2004). Therefore, lesions exhibiting extensive areas of regression should always be biopsied even in the absence of any other dermoscopic criteria suggestive for melanoma.

Rule #6: Lesions that Reveal Changes on Short-Term Monitoring Should be Biopsied

Many clinicians believe that performing a biopsy on all clinically atypical lesions is the only safe way to avoid missing a melanoma. However, this approach may not be practical for patients that harbor numerous atypical melanocytic nevi. Another strategy endorsed by some is to excise all clear-cut or outlier atypical lesions, while simultaneously capturing digital images of all lesions deemed to be only slightly atypical and subjecting them to

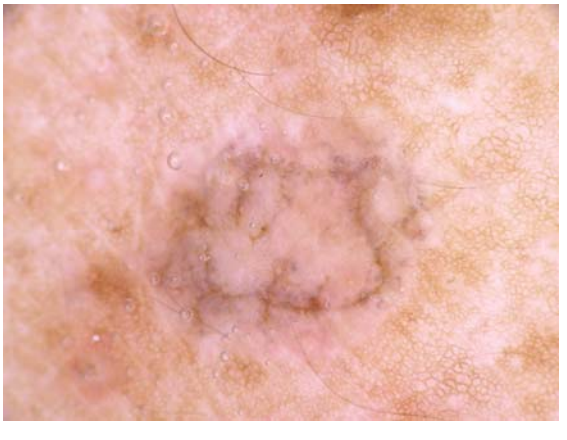
▲ **Figure 6e.8a** Early melanoma simulating a nevus clinically.

◀ **Figure 6e.8b** Dermoscopically this lesion is suspicious for melanoma based on the presence of irregular dots/globules (1 point) and blue-white veil (2 points). Total score for this lesion is thus 3.

▲ **Figure 6e.9a** Early melanoma, clinical image.

◀ **Figure 6e.9b** The overall appearance of this melanoma is reminiscent of the starburst pattern. Although the starburst pattern is commonly associated with Spitz nevi, it can also be seen in melanoma as exemplified by this case.

▲ **Figure 6e.10a** Early melanoma, clinical image.



◀ **Figure 6e.10b** This lesion is characterized almost exclusively by regression structures under dermoscopy. In such instances, a reliable differentiation between a benign lesion and a melanoma is virtually impossible and all such lesions should be biopsied.

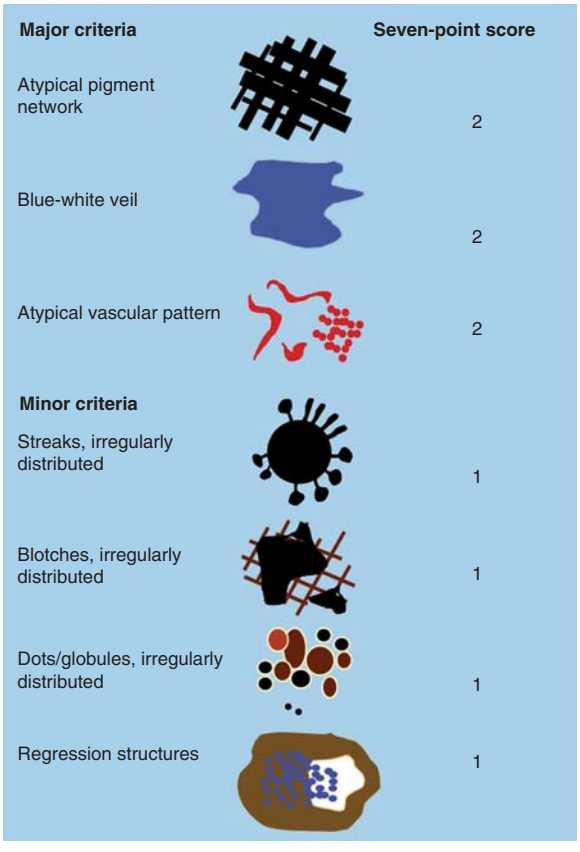


Figure 6e.11 Seven-point checklist.

short-term followup (i.e., digital monitoring). The rationale behind short-term monitoring is that melanomas that cannot be diagnosed clinically or dermoscopically on initial inspection can be diagnosed based on dermoscopic changes observed during followup monitoring (Altamura et al., 2008; Argenziano et al., 2008; Kittler et al., 2006; Haenssle et al., 2006; Skvara et al., 2005). Short-term monitoring experience has shown that lesions displaying dermoscopic changes observed after an average followup of three months have an 11% probability of being early and thin melanoma (Menzies et al., 2001). Thus, short-term monitoring appears to be an acceptable strategy that maximizes both sensitivity and specificity for melanoma diagnosis, which helps avoid missing a melanoma while at the same time minimizes the excision of benign lesions. It should be emphatically emphasized that monitoring protocols should only be applied to lesions that are moderately atypical, flat, or only slightly raised, without a history of change or dermoscopic evidence of melanoma, or for mildly atypical lesions with a history of change (Menzies et al., 2001). Nodular lesions should never ever be subjected to short-term monitoring because a delay in the treatment of nodular melanoma of as little as a few months can negatively impact prognosis. Thus, in the case of atypical nodular lesions the best strategy is "if in doubt, cut it out!"

Rule #7: Biopsy Pink Lesions that Manifest an Atypical Vascular Pattern

There is mounting evidence that dermoscopy can be helpful in evaluating hypopigmented and amelanotic tumors. This is primarily because one can better visualize vascular patterns within a lesion with the use of dermoscopy. Several different morphologic types of vascular structures have been associated with melanocytic and nonmelanocytic skin tumors (Argenziano et al., 2004). In hypopigmented and amelanotic melanoma, an atypical vascular pattern can frequently be observed. One such example is the presence of dotted and linear–irregular telangiectatic vessels (see chapter 8e, "Amelanotic and hypomelanotic melanoma"). (Menzies et al., 2008).

Key Points

- The seven-point checklist is an analytically based diagnostic algorithm that provides a quantitative scoring system based on the presence or absence of only seven features. These seven criteria are divided into three major and four minor criteria (Fig. 6e.11).

Major criteria (2 Points)
Atypical pigment network
Blue-white veil
Atypical vascular pattern
Minor criteria (1 Point)
Irregular streaks
Irregular dots and globules
Irregular blotches
Regression structures

- By simply adding together the individual assigned scores, a total score of 3 or more allowed classification of melanoma with a sensitivity of 95% and a specificity of 75%.
- Additional management rules that are important so as to avoid missing melanoma are the following:
  1. Dermoscopy should not only be used for clinically suspicious skin lesions
  2. Biopsy lesions that lack clinical-dermoscopic correlation
  3. Biopsy lesions with nonspecific pigment pattern
  4. Biopsy lesions revealing spitzoid features
  5. Biopsy lesions with extensive regression features
  6. Biopsy lesions that reveal changes on short-term monitoring
  7. Biopsy pink lesions that manifest an atypical vascular pattern.

REFERENCES

Altamura, D., Avramidis, M. & Menzies, S.W., 2008. Assessment of the optimal interval for and sensitivity of short-term sequential digital dermoscopy monitoring for the diagnosis of melanoma. *Arch Dermatol*, 144, 502–6.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Mordente, I., Ferrara, G., et al., 2008, Dermoscopic monitoring of melanocytic skin lesions: clinical outcome and patient compliance vary according to follow-up protocols. *Br J Dermatol*, 159, 331–6.

Argenziano, G., Scalvenzi, M., Staibano, S., et al., 1999, Dermatoscopic pitfalls in differentiating pigmented Spitz naevi from cutaneous melanomas. *Br J Dermatol*, 141, 788–93.

Argenziano, G., Soyer, H.P., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Argenziano, G., Zalaudek, I., Ferrara, G., et al., 2007, Dermoscopy features of melanoma incognito: indications for biopsy. *J Am Acad Dermatol*, 56, 508–13.

Bahmer, F.A., Fritsch, P., Kreusch, J., et al., 1990, Terminology in surface microscopy. Consensus meeting of the committee on analytical morphology of the arbeitsgemeinschaft dermatologische forschung, Hamburg, Federal Republic of Germany, Nov. 17, 1989. *J Am Acad Dermatol*, 23, 1159–62.

Ferrara. G., Argenziano, G., Soyer, H.P., et al., 2005, The spectrum of Spitz nevi: a clinicopathologic study of 83 cases. *Arch Dermatol*, 141, 1381–7.

Haenssle, H.A., Krueger, U., Vente, C., et al., 2006, Results from an observational trial: digital epiluminescence microscopy follow-up of atypical nevi increases the sensitivity and the chance of success of conventional dermoscopy in detecting melanoma. *J Invest Dermatol*, 126, 980–5.

Kittler, H., Guitera, P., Riedl, E., et al., 2006, Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. *Arch Dermatol*, 142, 1113–19.

Menzies, S.W., Crotty, K.A. & McCarthy, W.H., 1995, The morphologic criteria of the pseudopod in surface microscopy. *Arch Dermatol*, 131, 436–40.

Menzies, S.W., Gutenev, A., Avramidis, M., Batrac, A. & McCarthy, W.H., 2001, Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. *Arch Dermatol*, 137, 1583–9.

Menzies, S.W., Ingvar, C., Crotty, K.A. & McCarthy, W.H., 1996, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. Arch Dermatol, 144, 1120–7.

Pagnanelli, G., Soyer, H.P., Argenziano, G., et al., 2003, Diagnosis of pigmented skin lesions by dermoscopy: web-based training improves diagnostic performance of non-experts. *Br J Dermatol*, 148, 698–702.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

Peris, K., Ferrari, A., Argenziano, G., Soyer, H.P. & Chimenti, S., 2002, Dermoscopic classification of Spitz/Reed nevi. *Clin Dermatol*, 20, 259–62.

Saida, T., Miyazaki, A., Oguchi, S., et al., 2004, Significance of dermoscopic patterns in detecting malignant melanoma on acral volar skin: results of a multicenter study in Japan. Arch Dermatol, 140, 1233–8.

Schiffner, R., Schiffner-Rohe, J., Vogt, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42, 25–32.

Seidenari, S., Longo C., Giusti F. & Pellacani G., 2006, Clinical Selection of Melanocytic Lesions for Dermoscopy Decreases the Identification of Suspicious Lesions in Comparison with Dermoscopy Without Clinical Preselection. *Br J Dermatol,* 154, no. 5: doi:10.1111/j.1365-2133.2006.07165.x.

Skvara, H., Teban, L., Fiebiger, M., Binder, M. & Kittler, H., 2005, Limitations of dermoscopy in the recognition of melanoma. *Arch Dermatol*, 141, 155–60.

Steiner, A., Pehamberger, H., Binder, M. & Wolff, K., 1992, Pigmented Spitz nevi: improvement of the diagnostic accuracy by epiluminescence microscopy. *J Am Acad Dermatol*, 27, 697–701.

Stolz, W., Riemann, A. & Cognetta, A.B., 1994, ABCD rule of dermatoscopy: a new practical method for early recognition of malignant melanoma. *Eur J Dermatol*, 4, 521–7.

Zalaudek, I., Argenziano, G., Ferrara, G., et al., 2004, Clinically equivocal melanocytic skin lesions with features of regression: a dermoscopic-pathological study. *Br J Dermatol*, 150, 64–71.

Zalaudek, I., Ferrara, G., Di Stefani, A. & Argenziano, G., 2005, Dermoscopy for challenging melanoma; how to raise the 'red flag' when melanoma clinically looks benign. *Br J Dermatol*, 153, 200–2.

Zalaudek, I., Kittler, H., Marghoob, A.A., et al., 2008, Time required for a complete skin examination with and without dermoscopy: a prospective, randomized multicenter study. *Arch Dermatol*, 144, 509–13.

6f CASH algorithm

Jennifer A. Stein and Alfred W. Kopf

The CASH (color, architecture, symmetry, homogeneity) algorithm is a new dermoscopic method designed as a simplified form of pattern analysis that can be used even by a novice dermoscopist. It assesses many of the features used in the ABCD dermoscopy algorithm; however, it adds an element not found in any other algorithm, namely, architecture.

Architectural order refers to the overall organization of the lesion in terms of dermoscopic structures and colors. Melanomas are generally architecturally disorganized, whereas benign melanocytic lesions tend to be orderly and organized. CASH is aimed at teaching novices the important skill of being able to diagnose melanomas with the use of dermoscopy. CASH has been demonstrated to have good sensitivity, specificity, and diagnostic accuracy in diagnosing melanoma (Henning, 2007). In a second study that compared the performance of the CASH algorithm to the ABCD, Menzies, and seven-point checklist methods, the sensitivity and specificity of the CASH algorithm was found to be comparable to these other well-recognized methods (Henning, 2008).

The CASH algorithm is simple to use. The user assigns the lesion a given number of points based on its number of colors (range 1–6), architectural order/disorder (range 0–2), symmetry (range 0–2), and level of homo-/heterogeneity (range 0–7) (Table 6f.1). The user simply sums up the points and a total score is determined. If the total CASH score is less than eight, the lesion is classified as "probably benign nevus." A total score of eight or higher classifies the lesion as "suspicious for melanoma."

Below is an explanation of each of the components of the CASH algorithm.

COLOR

Benign lesions tend to have few colors, whereas melanomas often have many. The six colors recognized in the CASH algorithm are light brown, dark brown, black, red, white, and blue. Each of these colors in a lesion is assigned one point. For an explanation of what causes each of these colors within a melanocytic lesion, see chapter 3. The color point score will range from one to six.

ARCHITECTURE

When evaluating the architecture of a lesion, the user assesses its overall orderliness. This is achieved by a process called "Gestalt" (global perception of the order *vs* disorder of the lesion). Melanomas tend to be disorderly in their contour and/or content, whereas benign lesions tend to be orderly. In the CASH algorithm, architecture is scored on a scale of zero to two points. A lesion with no or mild architectural disorder is assigned a score of zero. If a lesion is moderately disordered it is assigned a score of one, and if markedly disordered, a score of two.

SYMMETRY

The lesion is bisected by two lines that are at 90° to each other. The first line bisects the lesion across the diameter, which has the greatest symmetry. The second line is placed perpendicular to the first line at a point to divide the lesion so that it again has the greatest symmetry in that axis. Symmetry is evaluated based on the contour and the content of the lesion. If the lesion has biaxial symmetry of contour and content, it is assigned a score of zero (i.e., it has no asymmetry). If the lesion has monoaxial symmetry in which only half the lesion is a mirror image of the other in terms of contour and content, it receives one point. If there is no symmetry across either axis, the lesion is assigned two points.

HOMOGENEITY/HETEROGENEITY

This component of the CASH algorithm is a measure of how many specific dermoscopic structures are present in the lesion. The lesion is assigned one point for each of the structures present. The dermoscopic structures recognized in the CASH algorithm are: 1. network, 2. dots/globules, 3. blotches, 4. regression, 5. streaks, 6. blue-white veil, and 7. polymorphous blood vessels. Benign lesions tend to have one or two of these seven dermoscopic structures (described below), whereas melanomas often have three or more structures.

Network refers to any kind of pigment network, typical or atypical.

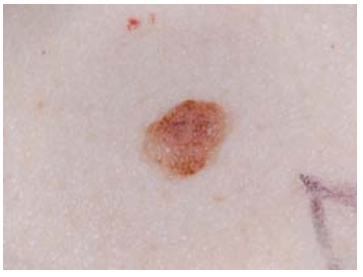
Dots and globules are considered a single structure; the lesion is assigned one point if either or both are present.

Blotch is defined as a structureless area of any color. If there are several blotches, the areas of the blotches are added together. One point is assigned if the sum of the blotch areas is 10% or greater of the entire area of the lesion.

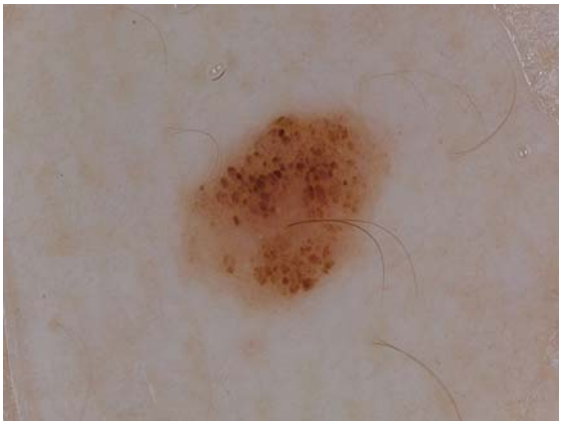
Regression structure is a hypopigmented, depigmented, or white scar-like area with peripheral blue-grey hue with or without granularity. This

Table 6f.1 Summary of Point Scoring for the CASH Algorithm

Feature	Suspicion for melanoma			
	Low	Medium	High	
Colors	Few colors	Moderate number of colors	Many colors	Colors
	1–2	3–4	5–6	Light brown
				Dark brown
Architecture disorder	No/mild	Moderate	Marked	Black
	0	1	2	Red
Symmetry	Biaxial	Monoaxial	None	White
	0	1	2	Blue
Homo-/heterogeneity	Structure	Structures	Structures	Structures
	1	2	3–7	Network
Total CASH score (range 2–17: cutoff point ≥8)				Dots/globules
				Blotches
				Regression
				Streaks
				Veil (blue)
				Polymorphous vessels



▲ **Figure 6f.1a** Congenital nevus, clinical image: abdomen, 21-year-old woman.

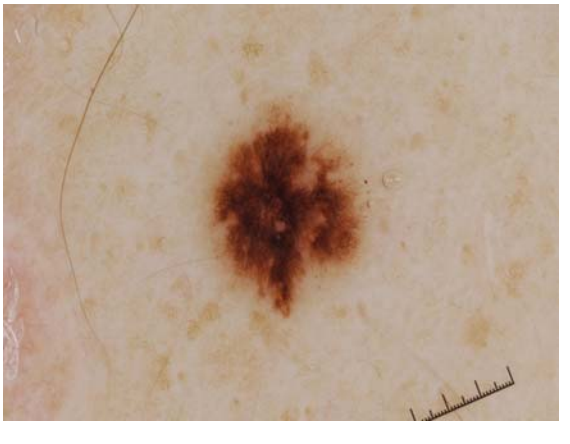


◀ **Figure 6f.1b** Congenital nevus on dermoscopy. Total CASH score = 4. Colors: light brown, dark brown. Architecture: mild disorder. Symmetry: one axis of symmetry. Homogeneity: dots/globules.

▲ **Figure 6f.2a** Spitz nevus, clinical image: thigh, 36-year-old man.

◀ **Figure 6f.2b** Spitz nevus on dermoscopy. Total CASH score = 4. Colors: dark brown, black. Architecture: no disorder. Symmetry: biaxial. Homogeneity: blotch, streaks.

▲ **Figure 6f.3a** Dysplastic nevus, clinical image: back, 51-year-old man.



◀ **Figure 6f.3b** Dysplastic nevus on dermoscopy. Total CASH score = 7. Colors: light brown, dark brown, black. Architecture: mild disorder. Symmetry: none. Homogeneity: network, dots/globules.

latter feature is also known as "peppering" and has been shown to correlate histologically with free melanin and/or melanophages in the dermis.

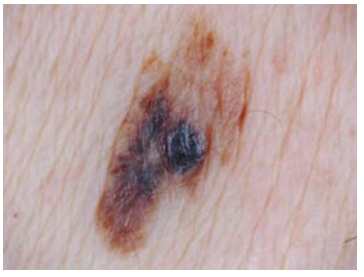
The term "streaks" includes both radial streaming and pseudopods and the lesion is assigned one point if either or both are present.

Blue-white veil is defined as irregularly marginated, confluent, blue-white pigmentation with an overlying translucent, ground glass-like haze.

Polymorphous blood vessels are defined as blood vessels of varying sizes and shapes.

TOTAL CASH SCORE

The four components of the CASH score are summed giving a total score that ranges from 2 to 17 (Table 6f.1). The higher the total CASH score, the more likely the lesion is a melanoma. A total CASH score of ≥8 was found to give the optimal sensitivity (98%) and specificity (68%) for separating melanomas from benign nevi. Examples of the application of the CASH algorithm are shown in Figures 6f.1–6f.4.



▲ **Figure 6f.4a** Melanoma 0.76 mm, clinical image: left arm, 27-year-old woman.

◀ **Figure 6f.4b** Melanoma 0.76 mm, dermoscopy. Total CASH score = 11. Colors: light brown, dark brown, black, blue. Architecture: marked disorder. Symmetry: none. Homogeneity: network, dots/globules, blotch.

Key Points

- The CASH algorithm incorporates both analytic and simplified pattern analysis in one method.
- The CASH acronym stands for: Colors, Architecture, Symmetry, Homogeneity.
- Colors: light brown, dark brown, black, red, white, blue
- Architecture: architectural disorder ranging from: no/mild (0 points), moderate (1 point), marked (2 points)
- Symmetry: judged as biaxial (0 points), monoaxial (1 point), and none (2 points) taking into account both the contour of the lesion and the distribution of colors and structures within the lesion.
- Homo-/Heterogeneity: the number of dermoscopic specific structures (network, dots/globules, blotches, regression, streaks, blue-white veil, polymorphous blood vessels)
- Each color and structure is assigned one point. All the CASH points are then summed together resulting in the CASH score.
- The cutoff for the total CASH score is eight. Eight or greater classifies the lesion as "suspicious for melanoma." Seven or less classifies the lesion as "probably benign nevus."

REFERENCES

Henning, JS., Dusza, SW., Wang SQ., et al., 2007, The CASH (color, architecture, symmetry, and homogeneity) algorithm for dermoscopy. *J Am Acad Dermatol,* 56, 45–52.

Henning, JS., Stein, JA., Yeung, J., et al., 2008, CASH algorithm for dermoscopy revisited. *Arch Dermatol*, 144, 554–5.

6g Three-point checklist

Giuseppe Argenziano

THE CONSENSUS NET MEETING ON DERMOSCOPY

Based on the results of a internet-based study on dermoscopy (Argenziano et al., 2003), known as Consensus Net Meeting on Dermoscopy (CNMD), a set of dermoscopic criteria deemed necessary for correctly differentiating pigmented skin lesions (PSL), with emphasis placed on criteria to correctly diagnose melanoma, were redefined (see also www.dermoscopy.org). Results of this CNMD study showed that three criteria were especially important in distinguishing malignant [i.e., melanotic melanoma and pigmented basal cell carcinoma (BCC)] from benign PSL. These three criteria are the presence of (*i*) asymmetry, (*ii*) atypical pigment network, and (*iii*) blue-white structures, which includes any blue or white color, including blue-white veil, scar-like depigmentation, and regression structures, such as peppering. Not only were these three criteria strongly associated with malignancy, but they also had a good interobserver agreement with a kappa value of 0.41 for asymmetry, a kappa value of 0.45 for atypical pigmented network, and a kappa value of 0.51 for blue-white structures. Preliminary analysis revealed that the presence of any two of these criteria was associated with a high likelihood that the lesion under investigation is malignant. Applying this new three-point checklist to a group of unknown lesions resulted in sensitivity and specificity values comparable to those achieved using other algorithms.

Three-Point Checklist: Definition

1. *Asymmetry:* This is defined as asymmetry in the distribution of dermoscopic colors and/or structures in one or two perpendicular axes. The shape or contour of the lesion does not factor into determining whether the lesion is symmetric or not.
2. *Atypical network:* This is defined as pigmented network lines that are focally thickened and distributed in an irregular or disorganized manner.
3. *Blue-white structures:* This includes any blue and/or white color visible within the lesion.

The presence of more than one of the above three criteria is suggestive of a malignancy (basal cell carcinoma or melanoma).

THE PILOT STUDY

Based on these three critera a retrospective pilot study was designed to verify the reproducibility and validity of this new simplified dermoscopic method, called the three-point checklist, which, based on its simplicity, may in turn serve well as a screening procedure for melanoma by nonexperienced observers (Soyer et al., 2004). Six nonexperienced dermoscopists were given a 1-hour introduction to the three-point checklist, after which they were asked to evaluate 231 clinically suspicious PSL using the three-point checklist. Using this method the nonexperts were able to correctly classify 96.3% of melanomas as suspicious, with a specificity of 32.8%. This level of specificity was comparable to the specificity of experts regarding their decision to biopsy the lesion or not. In other words, the nonexperts considered suspicious 2/3 of benign lesions, whereas the experts, on face-to-face evaluation, recommended biopsy of 2/3 of benign lesions.

THE WEB-BASED STUDY

The promising results obtained from the above-mentioned pilot study on the three-point checklist prompted a subsequent larger web-based study, designed to test the sensitivity and specificity for melanoma diagnosis in a larger number of observers, irrespective of their specialty and expertise in dermoscopy (Zalaudek et al., 2006). After a short web-based tutorial, the participants evaluated dermoscopic images of 165 (116 benign and 49 malignant) PSLs (15 training cases and 150 test lesions). For each lesion the participants scored for the presence or absence of asymmetry, atypical network, and blue-white structures. Kappa values, odds ratios, sensitivity, specificity, and likelihood ratios were calculated. Overall, 150 participants joined the study. The three-point checklist showed good interobserver reproducibility with a kappa value of 0.53. The sensitivity for skin cancer (melanoma and BCC) was 91.0% and this value was not influenced by the observers' professional profile. Only 20 participants, all of whom lacked any experience in dermoscopy, performed significantly worse as compared with the rest of the group; however, even these 20 observer's sensitivity was remarkably high at 86.7%. The specificity for the entire group was 71.9% and this value was significantly influenced by the observers' professional profile, with dermatologists performing best. In conclusion, this study confirmed that the three-point checklist may be a feasible, simple, and reproducible skin cancer screening algorithm.

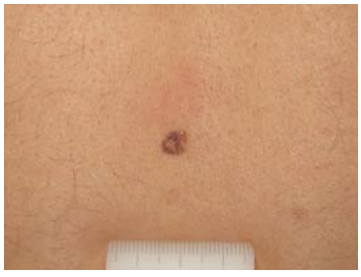
THE RANDOMIZED PROSPECTIVE STUDY

Since many primary care physicians (PCPs) are willing to engage in skin cancer screening efforts, a randomized study was designed to determine whether the adjunct of dermoscopy three-point checklist to the standard clinical examination improves the accuracy of PCPs to triage lesions suggestive of skin cancer (Argenziano et al., 2006). PCPs in Barcelona, Spain, and Naples, Italy, were given a one-day training course in skin cancer detection and dermoscopic evaluation, and were randomly assigned to the dermoscopy evaluation arm or naked-eye evaluation arm. During a 16-month period, 73 PCPs evaluated 2522 patients with skin lesions who attended their clinics. All the lesions evaluated were scored as benign or suggestive of skin cancer using the three-point checklist. All the patients were re-evaluated by expert dermatologists at clinics for pigmented lesions. Referral accuracy of both PCP groups was calculated by their scores, which were compared with those tabulated for dermatologists. Referral sensitivity, specificity, and positive, and negative predictive values for the PCPs in the naked-eye examination arm of the study were 54.1%, 71.3%, 11.3%, and 95.8%, respectively. The corresponding values for the PCPs in the dermoscopy arm of the study were 79.2%, 71.8%, 16.1%, and 98.1%, respectively. Significant differences were found in terms of sensitivity and negative predictive value ($P = 0.002$ and $P = 0.004$, respectively). In other words, PCPs using dermoscopy performed 25% better triage of skin lesions suggestive of skin cancer compared with naked-eye examination alone, with a low risk (1.9%) for patients with lesions suggestive of skin cancer not being referred by PCPs for a second expert opinion. Histopathologic examination of equivocal lesions revealed 23 malignant skin tumors missed by PCPs performing naked-eye observation and only six by PCPs using dermoscopy ($P = 0.002$). In conclusion, the use of dermoscopy improved the ability of PCPs to triage lesions suggestive of skin cancer without increasing the number of unnecessary expert consultations.

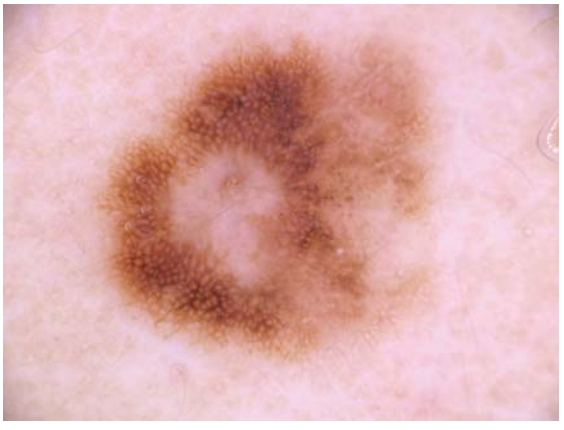
Typical findings are illustrated in Figures 6g.1–6g.5.

CAVEATS

The three-point checklist was designed to triage PSLs. Since its development a few new dermoscopic insights, especially for the identification of amelanotic/hypomelanotic melanomas and amelanotic BCCs have arisen. Structures such as negative pigment network, atypical blood vessels and chrysalis may be important additional clues to the diagnosis of some skin cancers. Research efforts are under way to determine the significance of these structures in diagnosing skin cancer. The results of these studies will dictate whether modifications to the three-point checklist will be required.

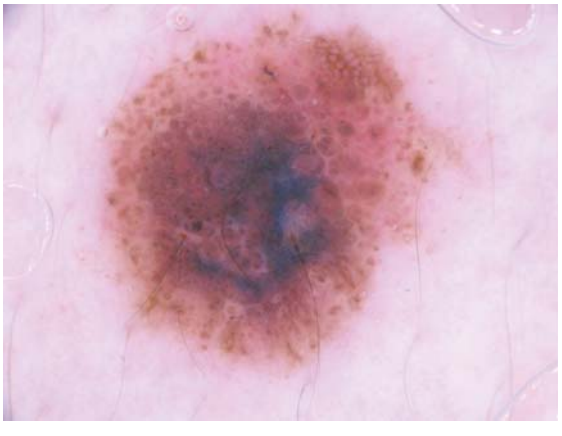


▲ **Figure 6g.1a** Melanoma. Clinical image.



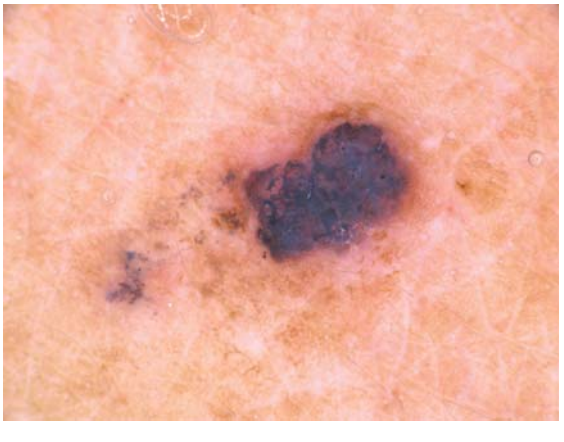
◀ **Figure 6g.1b** All three dermoscopic criteria of the three-point checklist are seen, namely, asymmetry of color and structure, atypical network, and (blue)-white structures.

▲ **Figure 6g.2a** Melanoma. Clinical image.



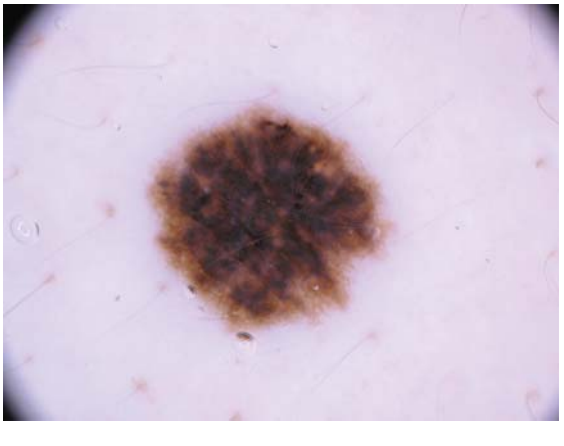
◀ **Figure 6g.2b** More pronounced blue-(white) structures are visible together with asymmetry of color/structure. The pigment network is irregularly distributed but not thickened, thus the total score is 2.

▲ **Figure 6g.3a** Basal cell carcinoma.

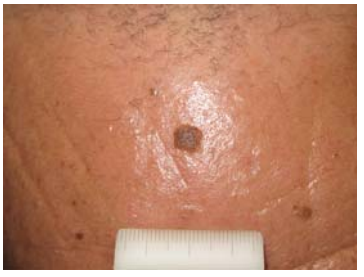


◀ **Figure 6g.3b** There are pronounced blue-white structures together with asymmetry of color and structures. The total score is 2, and thus it is a suspicious lesion.

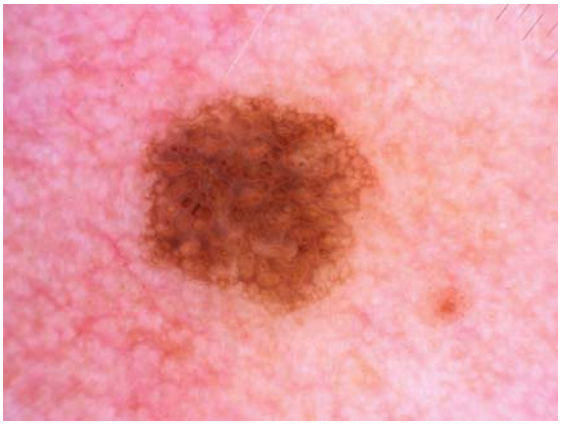
▲ **Figure 6g.4a** Benign nevus. Clinical image.



◀ **Figure 6g.4b** Although heavily pigmented this nevus is symmetric and shows regular and thin network at the periphery and structureless black pigmentation interrupted by multiple hair follicles. The total score is thus 0.



▲ **Figure 6g.5a** Seborrheic keratosis. Clinical image.



◀ **Figure 6g.5b** This seborrheic keratosis is symmetric in color and structure and shows neither atypical network nor blue-white structures. The total score is thus 0.

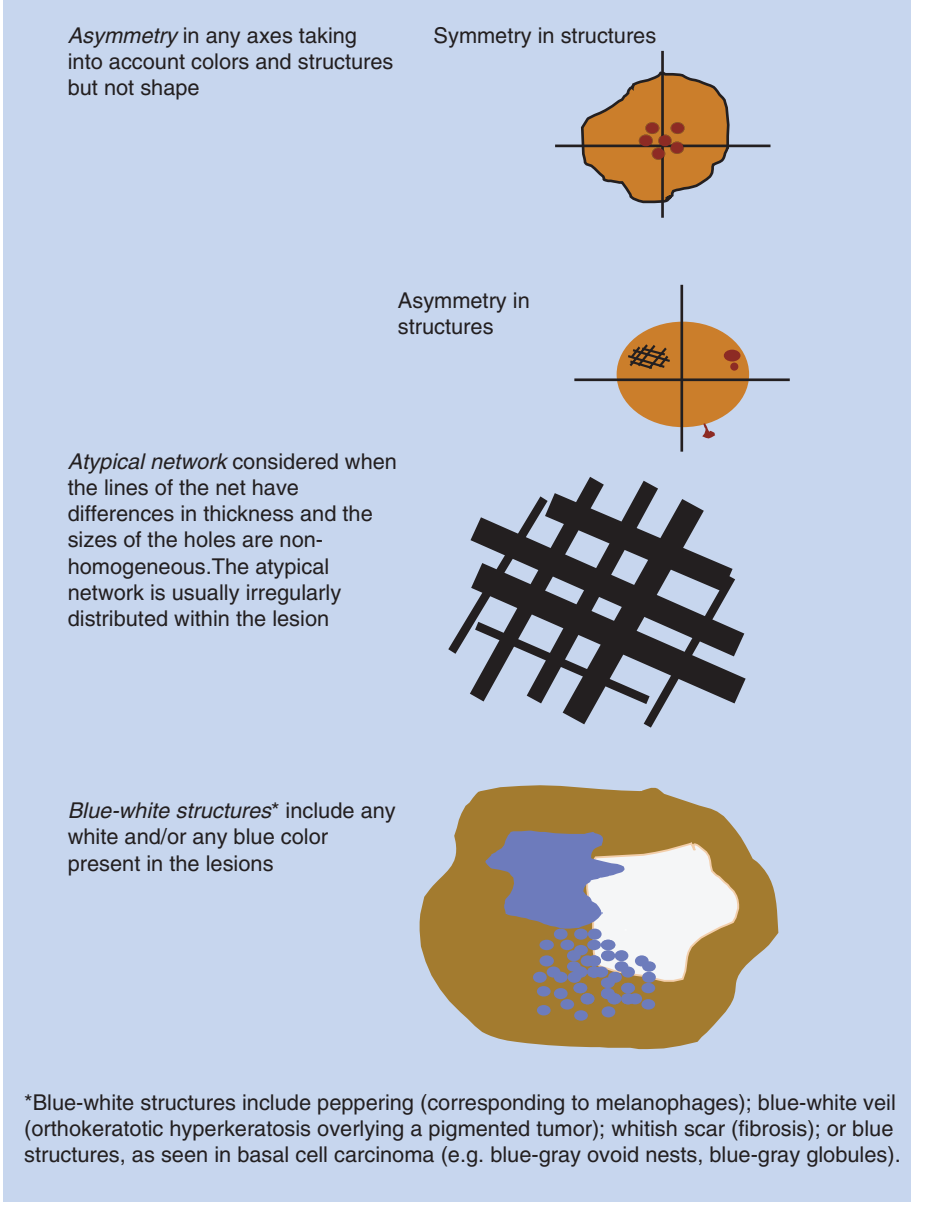


Figure 6g.6 Criteria of the three-point checklist.

Key Points (Fig. 6g.6)

- The primary purpose of dermoscopy is to determine which lesions require a biopsy and which lesions can be monitored safely.
- Results of the Consensus Net Meeting on Dermoscopy revealed that the following three criteria were especially important in distinguishing malignant from benign PSLs: (*i*) asymmetry, (*ii*) atypical network, and (*iii*) blue-white structures.
- In a web-based study the three-point checklist showed good interobserver reproducibility and also revealed a good sensitivity of 91.0% and specificity of 71.9% for skin cancer.
- In a randomized study, primary care physicians using dermoscopy improved their triage ability by 25% of PSLs suggestive of skin cancer compared with naked-eye examination alone, resulting in a low risk (1.9%) for patients with lesions suggestive of skin cancer not being referred for a second expert opinion. In other words, the use of dermoscopy improved their ability to triage lesions suggestive of skin cancer without increasing the number of unnecessary expert consultations.

REFERENCES

Argenziano, G., Puig-Butille, S., Zalaudek I., et al., 2006, Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *J Clin Oncol* 24, 1877–82.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: Results of a consensus meeting via the internet. *J Am Acad Dermatol*, 48, 679–93.

Soyer, H.P., Zalaudek, I., et al., 2004, Three-point checklist of dermoscopy: A new screening method for early detection of melanoma. *Dermatology*, 208, Available from: doi:10.1159/000075042.

Zalaudek, I., Argenziano, G., Soyer H.P., et al., 2006, Three-point checklist of dermoscopy: An open Internet study. *Br J Dermatol*, 154, Available from: doi:10.1111/j.1365-2133.2005.06983.x.

6h Revised version of pattern analysis

Harald Kittler, Cliff Rosendahl, and Alan Cameron

Pattern analysis is known as the most powerful tool to analyze pigmented skin lesions by dermoscopy (Pehamberger et al., 1987). It is regarded as the method of experts, in contrast to simplified algorithms that are said to be more suitable for beginners (Binder et al., 1999; Binder et al., 1995; Argenziano et al., 2003). Pattern analysis as originally formulated has developed organically as the field of dermoscopy has progressed. The lack of an overall structured logical approach to act as a basis for these additions makes it difficult to define exactly what now constitutes "pattern analysis."

This lack of clarity makes teaching beginners more difficult. Beginners in dermoscopy often are confused by opaque terminology and by the lack of precise, repeatable criteria. This language does not encourage the observer to formulate a precise description of lesions, and on occasion encourages or even requires the post hoc construction of a description to fit the diagnosis.

We propose a revised system of pattern analysis to offer this logical framework. It uses simple geometric terms and avoids subjective, metaphoric language. It is neither just a diagnosis by "Gestalt" nor justification of a diagnosis established at first glance. It is a way to take advantage of our human ability to recognize patterns, and by formalizing the observation of these patterns, to interpret them in a meaningful way. This requirement of well-defined criteria expressed in simple language is not just a linguistic matter; it is a prerequisite for consistent logical analysis. Revised pattern analysis is a system based on terms defined clearly, precisely, and lucidly, that can be used for every morphologic aspect of dermoscopy (Kittler, 2007). It is designed to establish a standardized description language common to all diagnostic algorithms, to enhance communication and to reduce errors. It is applicable to every pigmented lesion of the skin, melanocytic, and nonmelanocytic, and on every anatomic site of the skin. It is also designed to reach the most specific diagnosis possible and not just classify lesions as "benign" or "malignant."

DESCRIPTION OF THE METHOD

Basic Elements

All patterns observed in dermoscopy are composed of five simple geometric elements. These basic elements are lines, pseudopods, circles, clods, and dots (Fig. 6h.1).

They are defined as follows: (*i*) Line—a two-dimensional continuous object with length greatly exceeding width, extending in one direction; (*ii*) pseudopod—a line with a bulbous end; (*iii*) circle—a curved line equidistant from a central point; (*iv*) clod—any well circumscribed, solid object larger than a dot. Clods may take any shape; and (*v*) dot—an object too small to have a discernable shape. The morphology of vessels is described using the same objective geometric terms as pigmented structures (Kittler et al., 2010). Additional line types (looped, serpentine, helical, and coiled) are defined for vessels as these are rarely seen in pigmented structures (Fig. 6h.2).

Patterns Formed by Basic Elements

Every basic element may be part of a pattern (Fig. 6h.3). A pattern is built up of multiple repetitions of the same single basic element. There is also a pattern "structureless," an area characterized by the absence of any of the basic elements, or at least with no basic element dominating. Lines can be arranged to form five different patterns: reticular, branched, parallel, radial, and curved (Fig. 6h.4). Straight lines crossing each other in an angle of 90° forming a grid are termed "reticular," straight lines crossing each other in different angles are termed "branched," straight lines that do not cross each other are "parallel," and straight lines that converge to the center of the lesion or to a central dot or clod are called "radial." Lines that bend are not straight but "curved." One or two repetitions of a basic element are not sufficient to form a pattern; furthermore, a pattern has to cover a significant part of the lesion (25%). This means a pattern can be discerned by scanning the overall appearance of a lesion.

Exceptions to this principle are (*i*) any pseudopods or two or more radial lines are sufficient to constitute a pattern, and (*ii*) any lines reticular not due to collision with another lesion also constitutes a pattern. The same term is applied to patterns that are composed of the same type of basic element, regardless of color or diagnosis. For example, "brown globules" are brown clods, "red lacunes" are red clods, "blue ovoid nests" are blue clods, and "cobblestones" are large polygonal clods (Fig. 6h.5). Every metaphoric expression can be replaced by simple terms (Table 6h.1).

Variations of basic patterns may be based either on morphologic appearance, for example, lines reticular may be thin or thick, or on variation in distribution of basic elements. For example, on acral skin, parallel lines may lie on ridges, in furrows, or cross the ridges and furrows. Pigmented skin lesions may consist of a single pattern or of two or more patterns. Two or more patterns can be combined in a symmetric or asymmetric fashion (Fig. 6h.6).

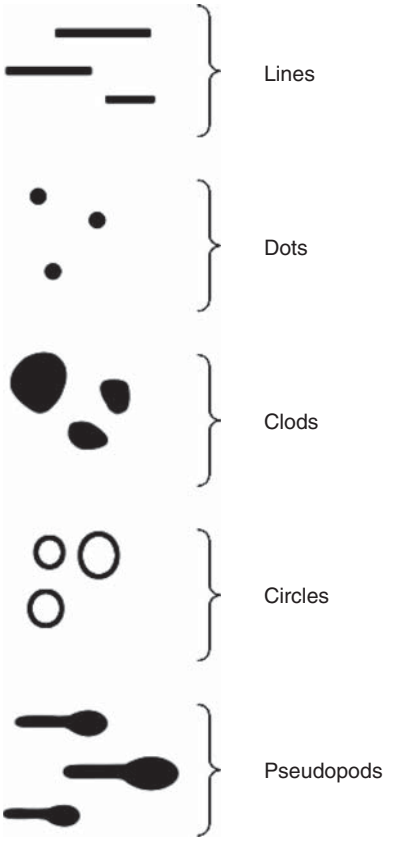


Figure 6h.1 Basic elements.

Colors

Colors seen in dermoscopy are created by various combinations of keratin, melanin, blood (including serum in crusts), collagen, and foreign material. The color of melanin as discerned by dermoscopy, varies greatly depending on localization in the epidermis or dermis (Fig. 6h.7), other materials show less variation. Variation in color description between dermoscopists is minimized by (*i*) not describing shades of brown, gray, and other colors, (*ii*) classifying number of colors only as either one or more than one color, (*iii*) when relevant, classifying colors only as being predominantly those of melanin or predominantly not those of melanin.

AN ALGORITHMIC APPROACH USING PATTERNS, COLORS, AND CLUES

By combining patterns and colors the dermoscopic appearance of every pigmented lesion of the skin can be described in a simple, precise, logical, and repeatable fashion. Revised pattern analysis offers a flexible framework for constructing a personal algorithm to derive as specific a diagnosis as possible for all lesions, benign or malignant, melanocytic or nonmelanocytic. It is based on interpretation of patterns, colors, and clues. It is a procedure that uses a defined series of simple steps in logical sequence. This sequence remains unchanged regardless of the nature of the lesion being analyzed. At each step, options are listed from those with the most diagnostic specificity to those with the least. Particular attention has been paid to making the decisions required of the dermoscopist as simple and unambiguous as possible. This reduces errors due to inevitable variations in perception between dermoscopists. Diagnosis should start with description of the lesion's patterns and colors. Although description and analysis often proceed simultaneously in practice, in a logical sense description should always precede analysis. This precedence of description over analysis becomes critically important in the assessment of difficult lesions. The clarity gained from a full formal description may lead to a diagnosis; if not, it ensures all relevant differential diagnoses are considered.

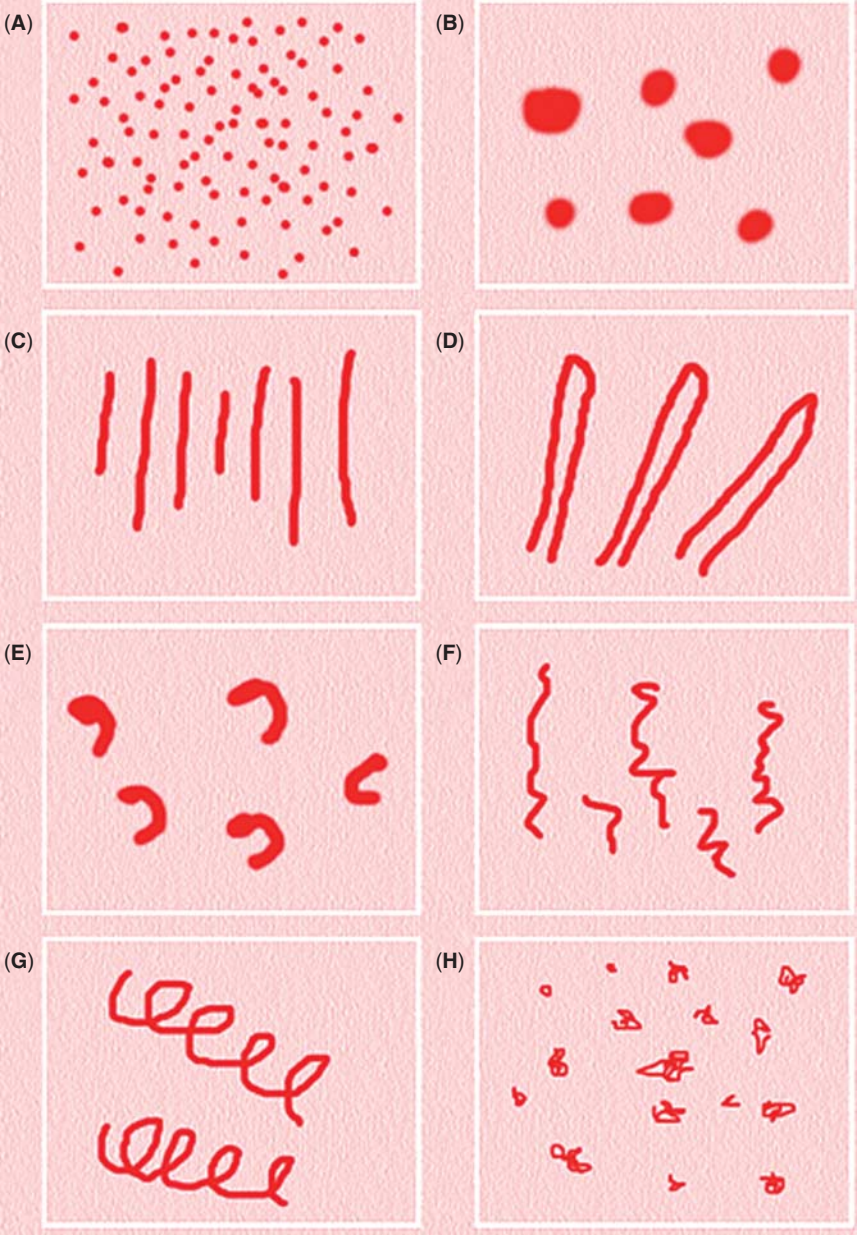


Figure 6h.2 Morphology of vessels described by simple geometric terms (**A**), dots (vessels as dots), (**B**) clods (vessels as clods), **C–H** lines (vessels as lines), Vessels as lines can be (**C**) straight (no bend), (**D**) looped (one sharp bend), (**E**): curved (one gentle bend), (**F**) serpentine (multiple bends), (**G**) helical (multiple bends along a central axis, or (**H**) coiled (multiple, tight bends).

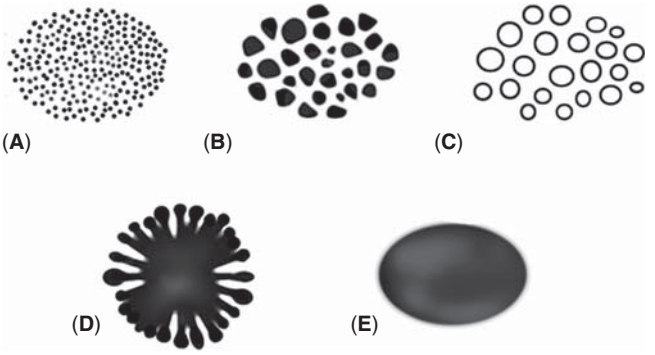


Figure 6h.3 Patterns formed by basic elements (**A**), dots, (**B**), clods, (**C**), circles, (**D**), pseudopods, and (**E**), absence of basic element, that is, structureless.

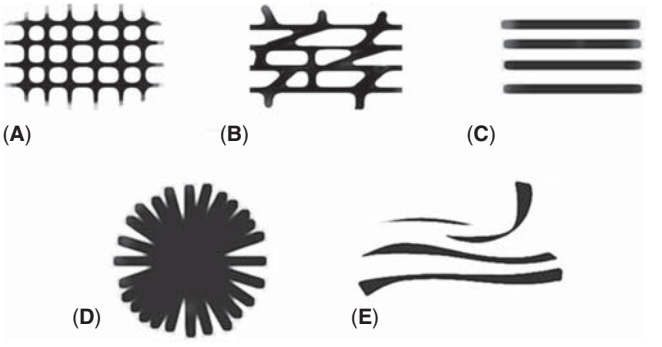


Figure 6h.4 Patterns formed by lines (**A**), reticular, (**B**), branched, (**C**), parallel, (**D**), radial, (**E**), curved.

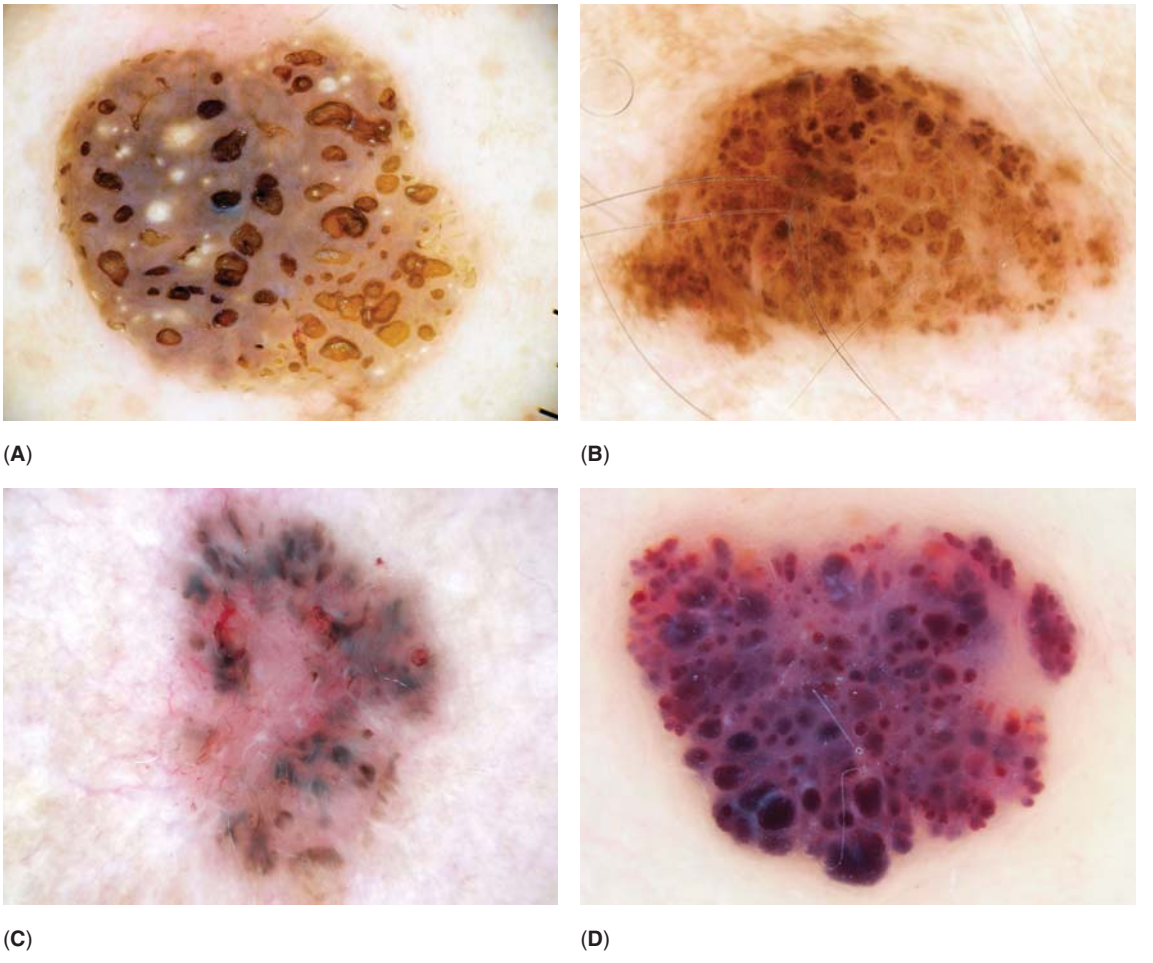


Figure 6h.5 Applied pattern analysis (one pattern: clods). Description of pattern should be independent of color and diagnosis. All four lesions have one pattern, clods (well circumscribed, solid objects larger than a dot). (**A**) Yellow and white clods, seborrheic keratosis; (**B**) polygonal brown clods, nevus. (**C**) brown and gray clods, basal cell carcinoma; (**D**) red and purple clods, hemangioma. This terminology replaces descriptive language such as comedo-like openings, crypts, milia-like cysts, red-blue lacunae, blue-gray ovoid nests, leaf-like areas, globules, and cobblestones.

Table 6h.1 Translation of Metaphoric or Opaque Language into Simple Terminology Based on Simple Geometric Terms (Five Basic Elements)

Metaphoric and opaque language	Language using only simple geometric terms
Pseudonetwork	Circles, brown, and confluent
Strawberry pattern	Circles, red
Grapes	Circles, small
Blue-gray ovoid nests	Clods, blue
Comedo-like openings	Clods, brown, or orange (rarely black), and circles
Cobblestone pattern	Clods, large, brown or skin colored, polygonal
Milky red globules	Clods, pink, and small
Red lacunes	Clods, red
Globules	Clods, small, round, or oval
Milia-like cysts	Dots or clods, white
Peppering	Dots, gray
Annular–granular pattern	Dots, gray and circles, gray
Stars in the sky	Dots, white
Streaks	Lines
Branched streaks	Lines, branched
Brain-like appearance	Lines, curved, and thick
Fat fingers	Lines, curved, and thick
Fissures and ridges	Lines, curved, and thick
Fingerprinting	Lines, curved, and thin (plus circles occasionally)
Fibrillar pattern	Lines, parallel, crossing fissures, and ridges
Peripheral streaks	Lines, radial
Radial streaming	Lines, radial, and segmental
Starburst pattern	Lines, radial or pseudopods, peripheral
Leaf-like areas	Lines, radial, connect to a common base
Spoke-wheel-like area	Lines, radial, converging to a central dot or clod
Pigment network	Lines, reticular
Atypical pigment network	Lines, reticular, and thick
Broadened pigment network	Lines, reticular, and thick
Delicate pigment network	Lines, reticular, and thin
Inverse pigment network	Lines, reticular, white or gray
Reticular depigmentation	Lines, reticular, and white
Negative pigment network	Lines, reticular, white or gray
Crypts	Lines, thick, and curved in combination with clods
Chrysalis/crystalline	Lines, white
Moth-eaten border	Sharply demarcated, scalloped border
Blotch	Structureless zone
Blue hue	Structureless zone, blue
Blue-white veil	Structureless zone, blue
Milky red areas	Structureless zone, pink
Scar-like depigmentation	Structureless zone, white
Central white patch	Structureless zone, white, central

In this context, description is not to be interpreted as an attempt to convey a realistic "photographic" impression of the lesion's appearance. Rather, description is to be seen as the extraction of features relevant to the diagnosis of skin lesions, in the simplest possible terms. It is important to note that there is no single true algorithm. The algorithm is not the method; the extraction of relevant dermoscopic features and formulation

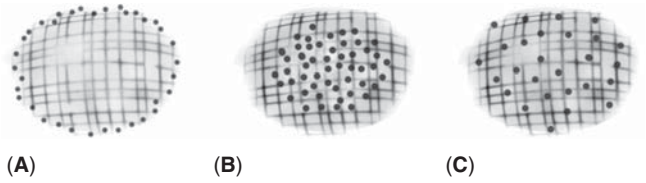


Figure 6h.6 Symmetry and asymmetry of pattern. Two patterns can be combined symmetrically in three ways, here illustrated by combinations of lines reticular and dots. (**A**) Dots at the periphery, lines reticular in the center; (**B**) dots in the center, lines reticular at the periphery; and (**C**) dots scattered evenly on lines reticular. All other combinations of two patterns will result in an asymmetric patterna.

of a structured description in a form that permits logical analysis is the method of revised pattern analysis.

First, pattern(s) of pigmentation are described. The first decision is to determine the number of patterns. For analytic purposes only two options are considered, is there one pattern, or more than one. Rarely is this decision at all ambiguous. Lesions with one pattern are further characterized by their color(s). By definition, lesions with one pattern and one color are symmetrical. If a lesion has more than one color, assessment of symmetry is the next step. A differential diagnosis is then formulated based on pattern and color(s) (Figure 6h.16).

A lesion with more than one pattern is analyzed similarly. The combination of patterns is assessed for symmetry or asymmetry. The higher the number of patterns the more unlikely it is for the lesion to display symmetry. For lesions with more than one pattern, analysis proceeds on the basis of the most specific pattern in a lesion, not the most prominent (Fig. 6h.8). As patterns are listed in order from most specific to least specific, proceeding stepwise through the algorithm achieves this automatically. Therefore, lesions with the pattern lines will be assessed by the differential diagnosis of this pattern. Only a lesion lacking the pattern lines is analyzed by the differential diagnosis of the pattern pseudopods. This process continues sequentially through circles, clods, and dots. A lesion that combines structureless with any other pattern is analyzed according to the other pattern, as structureless is the least specific pattern.

Assessment of patterns and colors may lead to a single diagnosis, but also may lead to a narrow differential diagnosis. In this case, the lesion is then examined for clues to resolve the differential diagnosis. Sometimes a pattern may also constitute a clue, for example, a structureless eccentric zone is both a pattern and a clue to the diagnosis of melanoma. Usually, however, clues are features too localized to constitute a pattern, but nonetheless favoring one diagnosis over another.

For example, the pattern radial lines may equally be seen in melanoma, Reed nevus, and basal cell carcinoma (BCC). If these lines are centrally located or originate from a common base, this would be a clue to the diagnosis of BCC (Fig. 6h.9). Often, however, clues are weak, or even contradictory. For these cases, judgment is required in deciding how much weight to assign to each clue, and hence which final diagnosis should be favored (Fig. 6h.10). As a general principle, more weight should be given to the pattern overall than to any single clue. The most difficult part of dermoscopy is to correctly assign weight to clues, and particularly to avoid overvaluing an unreliable or misleading clue. This is the role of experience in dermoscopy. As each dermoscopist's experience is different, reflecting different temperaments, teachers, practice styles and locations, and almost certainly different interpretations of the same perceptual data, each dermoscopist will over time develop their own algorithm. Revised pattern analysis encourages this process; indeed we consider this an essential step in truly learning dermoscopy. Revised pattern analysis offers a logical framework to make experience more than a series of anecdotes.

A SHORT ALGORITHM BASED ON PATTERN ANALYSIS: "CHAOS AND CLUES"

The authors also recognize a need for a simple diagnostic system based on pattern analysis. This has been achieved by simplifying the goal to that of

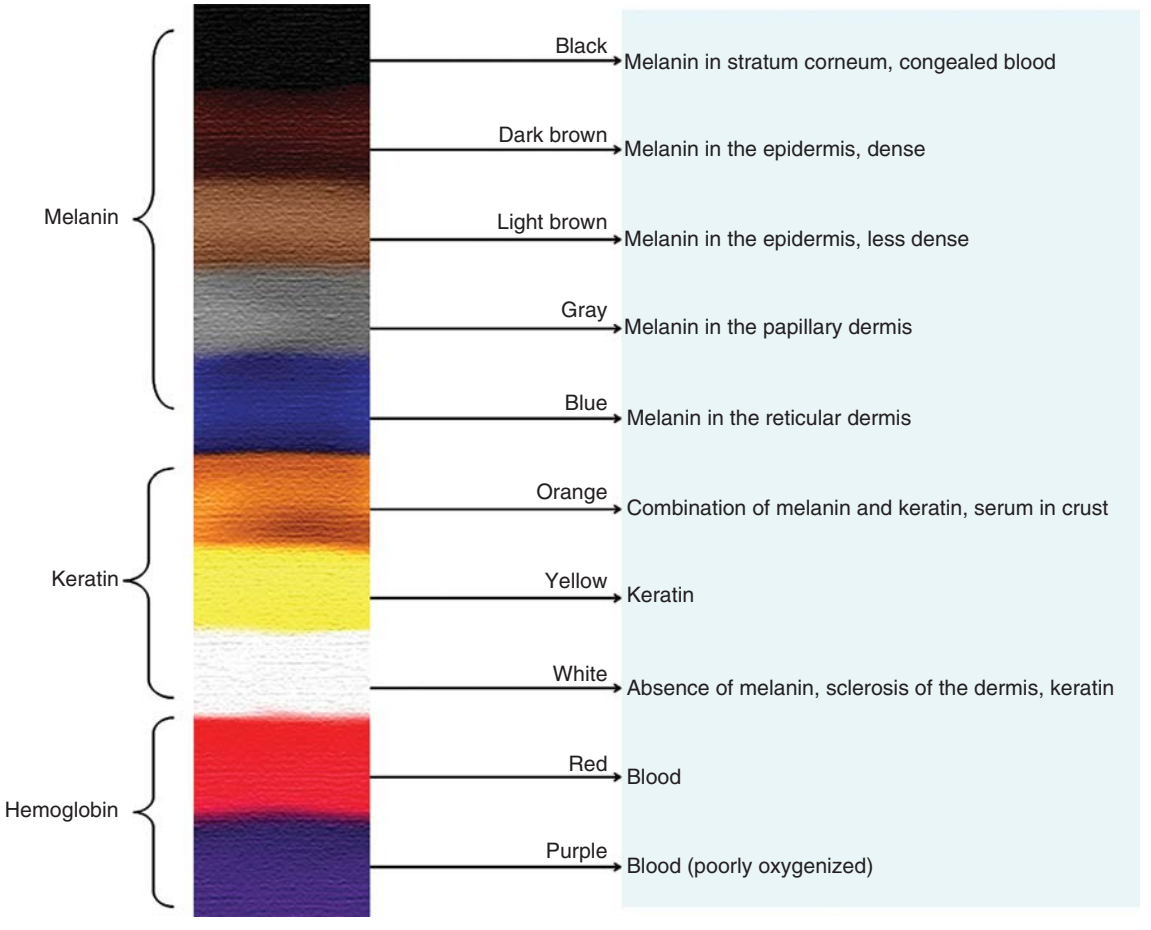


Figure 6h.7 Colors seen by dermoscopy.

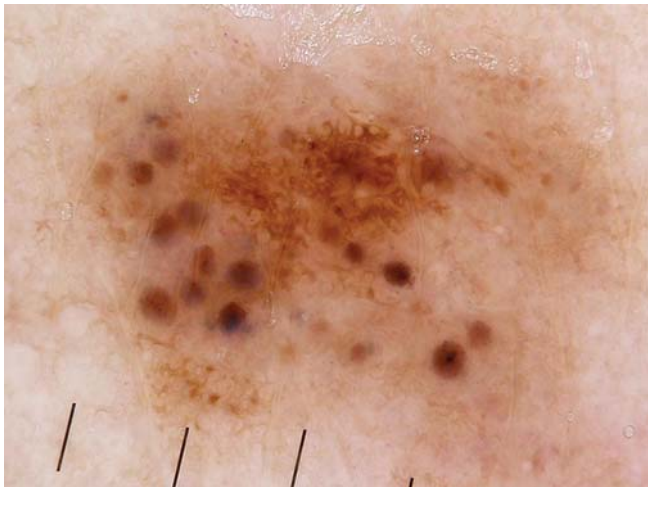


Figure 6h.8 Applied pattern analysis (more than one pattern) Although the pattern clods is the more prominent, lines reticular is the more specific pattern, so analysis is performed according to lines reticular. Clark nevus.

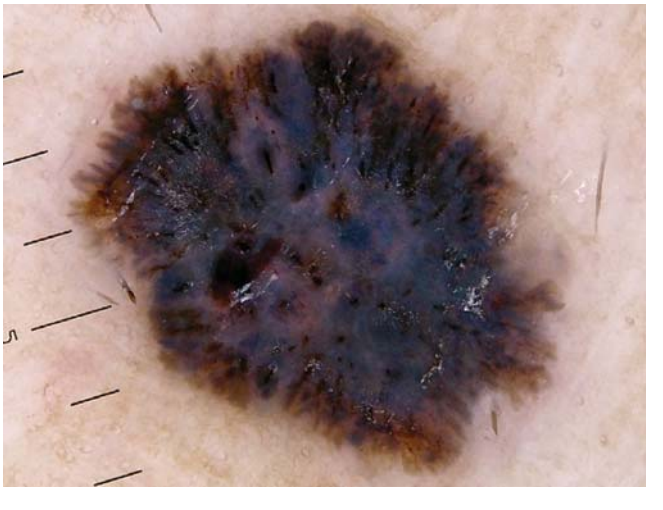


Figure 6h.9 Applied pattern analysis (more than one pattern). Using a two-step algorithm, the description of the peripheral structures determines the final diagnosis. Many would choose "radial streaming" (or "streaks") and not even consider the possibility of "leaf-like structures." Even if both possibilities are considered, simple observation of these peripheral structures will not assist make this distinction. Objectively described, this lesion's patterns are peripheral radial lines distributed segmentally, and are structureless. This description immediately leads to the differential diagnosis of basal cell carcinoma and melanoma, to be resolved by clues. *Source*: Pigmented basal cell carcinoma, image courtesy Dr Jean-Yves Gourhant.

identifying lesions requiring biopsy, rather than reaching a specific diagnosis. "Chaos and Clues" is a system which can be applied to every pigmented lesion. It does not require a decision as to whether a lesion is melanocytic and it will detect pigmented malignancy with accuracy comparable to the earlier systems. The system has been tested on a set of consecutive, pigmented lesions, including a significant proportion of benign and malignant nonmelanocytic lesions.

How the System is Applied

As suggested by the name, "Chaos and Clues" has two steps. First, each pigmented lesion is assessed for "chaos," defined as asymmetry of structure or color. If there is no such asymmetry the lesion is considered to be benign. Lesions with asymmetry are classified as having chaos and then they are further examined to determine if the lesion has at least one of eight defined clues to malignancy. If one or more of these clues are present then a biopsy is indicated. The more experienced dermoscopist then has the option of using revised pattern analysis to reach a specific diagnosis. The specificity of this simple method can be increased if lesions with chaos that can be unambiguously diagnosed as seborrheic keratoses are excluded.

Chaos

Chaos is defined as asymmetry produced by the pattern of structures or colors within a lesion, and is assessed by the same process as used in revised pattern analysis. The shape of a lesion is not relevant but any color other than skin color at the edge of a lesion (such as white) should be regarded as part of the lesion. Lesions without chaos are not analyzed any further. There are three exceptions, where biopsy is indicated in lesions lacking chaos: (*i*) facial lesions with gray or blue structures, (*ii*) acral lesions with parallel lines on the ridges, and (*iii*) any elevated, firm, and continuously growing lesion (Chamberlain et al., 2003).

Clues

In pattern analysis, a clue is a feature that favors one diagnosis over another if analysis of patterns and colors has not lead to a specific diagnosis. In chaos and clues, a clue is simply a feature which, when present, indicates that a lesion requires biopsy. One clue is sufficient. Both chaos and clue can be produced by the same feature. Lesion descriptions in chaos and clues use the same method and language as revised pattern analysis (Fig. 6h.11). There are eight clues to pigmented malignancy (melanoma, pigmented basal cell carcinoma (pBCC), and pigmented Bowen's disease (pBD).

1. Eccentric structureless area: any color except skin color.
2. Gray or blue structures: Gray dots may be seen in pBCC and pBD as well as melanoma (Altamura et al., 2010; Cameron et al., 2010; Braun et al., 2007). They are a very common finding even in noninvasive melanomas due to free melanin or melanin in macrophages in the dermis. Gray circles occur in noninvasive facial melanomas (Fig. 6h.12). Dense deposition of melanin in the dermis causes blue clods or blue structureless areas in pBCC and invasive melanomas.
3. Black dots or clods, peripheral: Peripheral black dots and clods are generally produced by melanoma cells or nests, respectively, close to or at the level of the stratum corneum due to pagetoid spread. Black structures are rarely seen in pigmented BCC or pBD.
4. Lines radial or pseudopods, segmental: Lines radial may be seen at any location in BCC. Pseudopods or lines radial when circumferential are a feature of Reed nevus, but if segmental they are highly specific for melanoma (Menzies et al., 1995).
5. Polymorphous vessels: Vessels are called polymorphous when more than one pattern of vessel is seen. Polymorphous vessels reflect disordered malignant growth pattern and possibly increased metabolic demand of actively growing tumor tissue. If vessels as dots are present, melanoma is more likely than BCC.
6. White lines: To qualify as a clue, white lines must be clearly lighter than perilesional skin.
7. Lines reticular or branched, thick: To be called thick, the lines must be thicker than the spaces they surround. This pattern is produced by melanoma cells proliferating in the rete ridges and is not seen in pBCC or pBD.
8. Lines parallel, ridges (acral skin): This is a clue to malignancy even in the absence of chaos. Subcorneal hemorrhage also produces this pattern. Whether pigment lies on ridges or furrows is often easier to assess at the edges of a lesion.

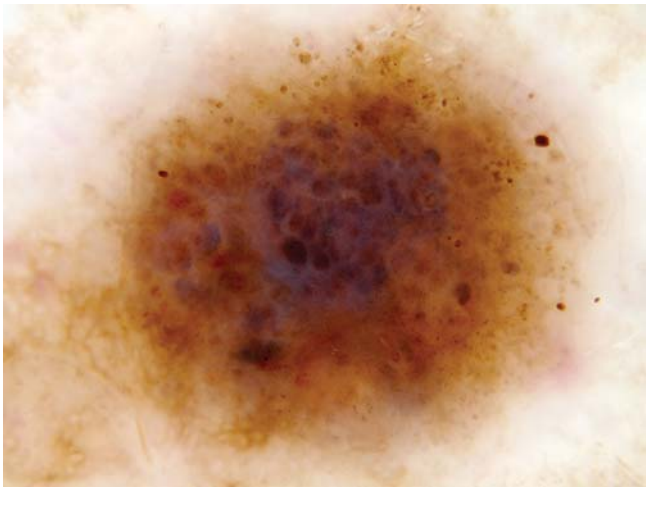


Figure 6h.10 Applied pattern analysis of more than one pattern. Pattern analysis is robust and minimizes errors of description. This lesion is most correctly analyzed as lines reticular plus clods (any lines reticular constitute a pattern, and is a more specific pattern than clods) combined asymmetrically, with more than one color, leading to a differential diagnosis of melanoma and nevus. If the area of reticular lines is either not noted or not called a pattern, assessment then proceeds as for one pattern clods. This leads to a differential diagnosis of BCC and melanoma. The same BCC/melanoma differential diagnosis is reached if the few dots are mistakenly accorded the status of a pattern. In all cases, the correct diagnosis of melanoma lies in the differential diagnosis. Breslow thickness 0.55 mm. *Abbreviation*: BCC, basal cell carcinoma.

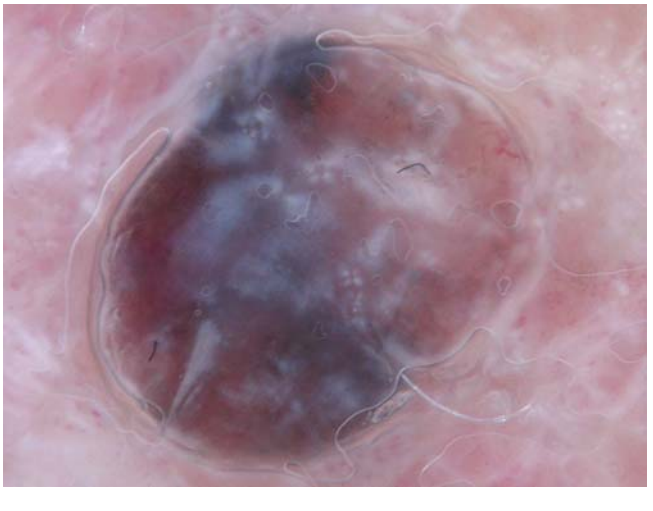


Figure 6h.11 Application of chaos and clues. Melanoma, invasive (Breslow thickness >1 mm) on the back. There is only one pattern (structureless), but chaos is produced by asymmetry of color. This combined with the clue of "gray lines" mandates biopsy.

Figures 6h.11–6h.15 show examples of how "Chaos and Clues" is applied in practice. Examining for "chaos" is a screening procedure and with practice requires minimal cognition and time. If "chaos" is encountered clues are searched for. This part of the process requires more cognition and a slightly greater investment of time but as there are no "calculations" required the process can be done with ease in a busy practice setting. The experienced dermoscopist may then choose to apply revised pattern analysis to resolve the differential diagnosis, but the prior application of "Chaos and Clues" will have reduced this workload.

This flow diagram provides an overview of the revised pattern analysis approach in the evaluation of both melanoctyic and nonmelanocytic tumors (Fig. 6h.16).

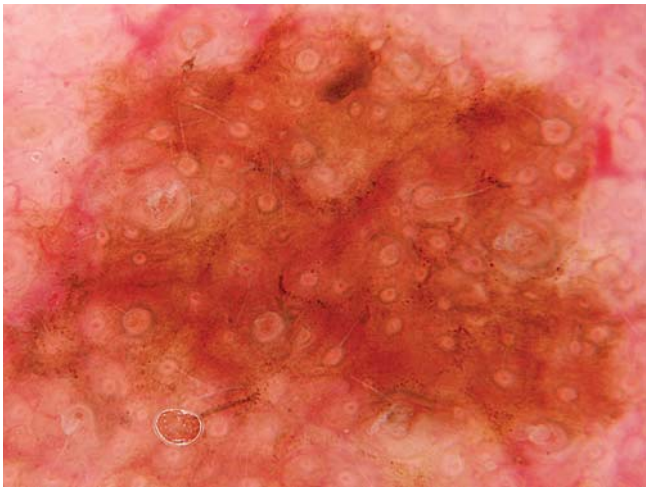


Figure 6h.12 Application of chaos and clues. Melanoma in situ (lentigo maligna) on the face. This lesion is arguably symmetrical by color and structure. However, on the face melanomas may not exhibit chaos and the presence of the clue of gray circles is suffi cient to require biopsy.f chaos and clues.

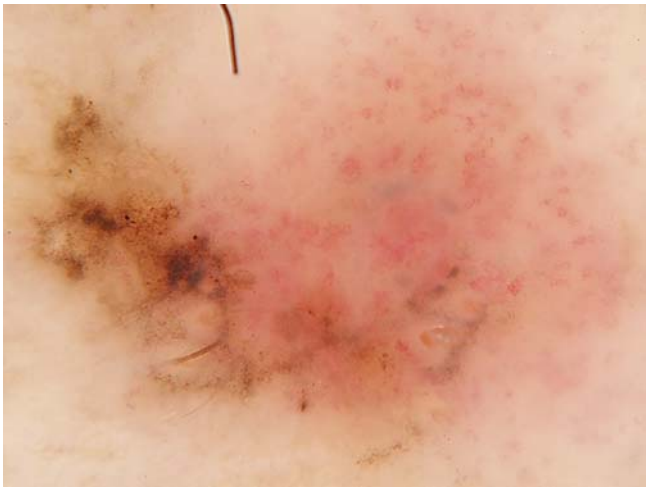


Figure 6h.14 Application of chaos and clues. Basal cell carcinoma: There is chaos and the clue of gray dots, therefore the lesion requires biopsy. In this case it is not possible to differentiate between the three types of pigmented malignancy (BCC, SCC and melanoma) with pattern analysis. Even the distinction between melanocytic and nonmelanocytic cannot be made dermoscopically and must be left to the pathologist.

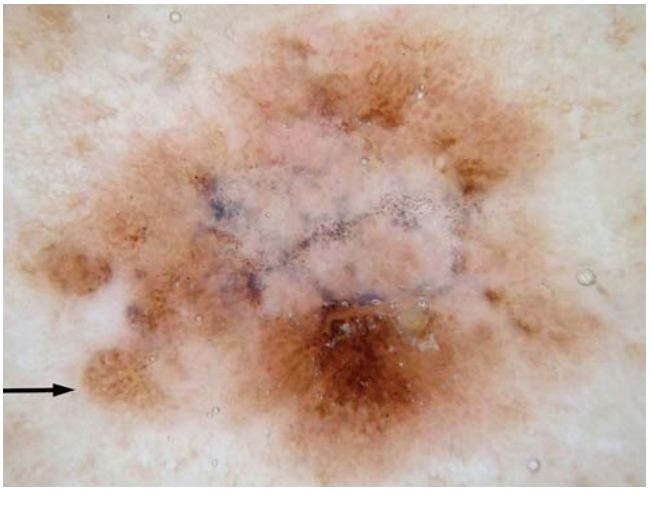


Figure 6h.13 Application of chaos and clues. pBD: There is chaos and the clue of gray dots and therefore a biopsy is required. Optionally, a specific diagnosis can be reached by applying pattern analysis to differentiate between melanoma, BCC, pBD, and lichen planus-like keratosis. Dots arranged in lines (*arrow*) are a clue to the diagnosis of pBD. *Abbreviations*: BCC, basal cell carcinoma; pBD, pigmented Bowen's disease.

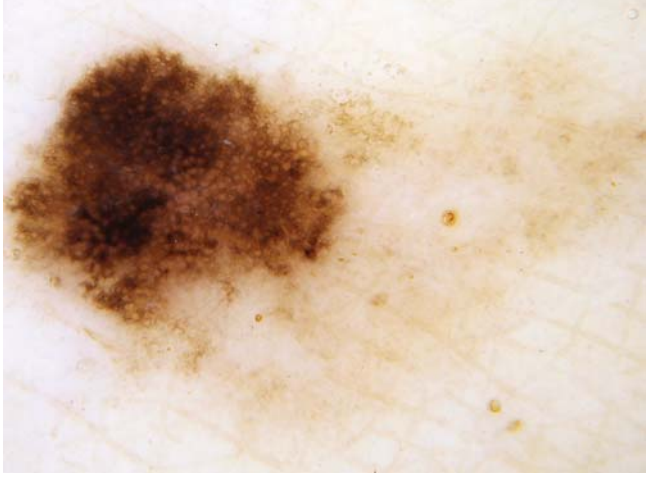


Figure 6h.15 Application of chaos and clues. Melanoma in situ. This lesion exhibits chaos and the clue of thick lines reticular, and so requires biopsy. In this case, the lesion can be classified as melanocytic by the dermoscopist with reasonable certainty, but this is not a part of the decision to biopsy. Reticular lines should not be depended upon to diagnose a lesion as melanocytic; they are also seen in nonmelanocytic lesions, such as seborrheic keratoses and dermatofibromas.

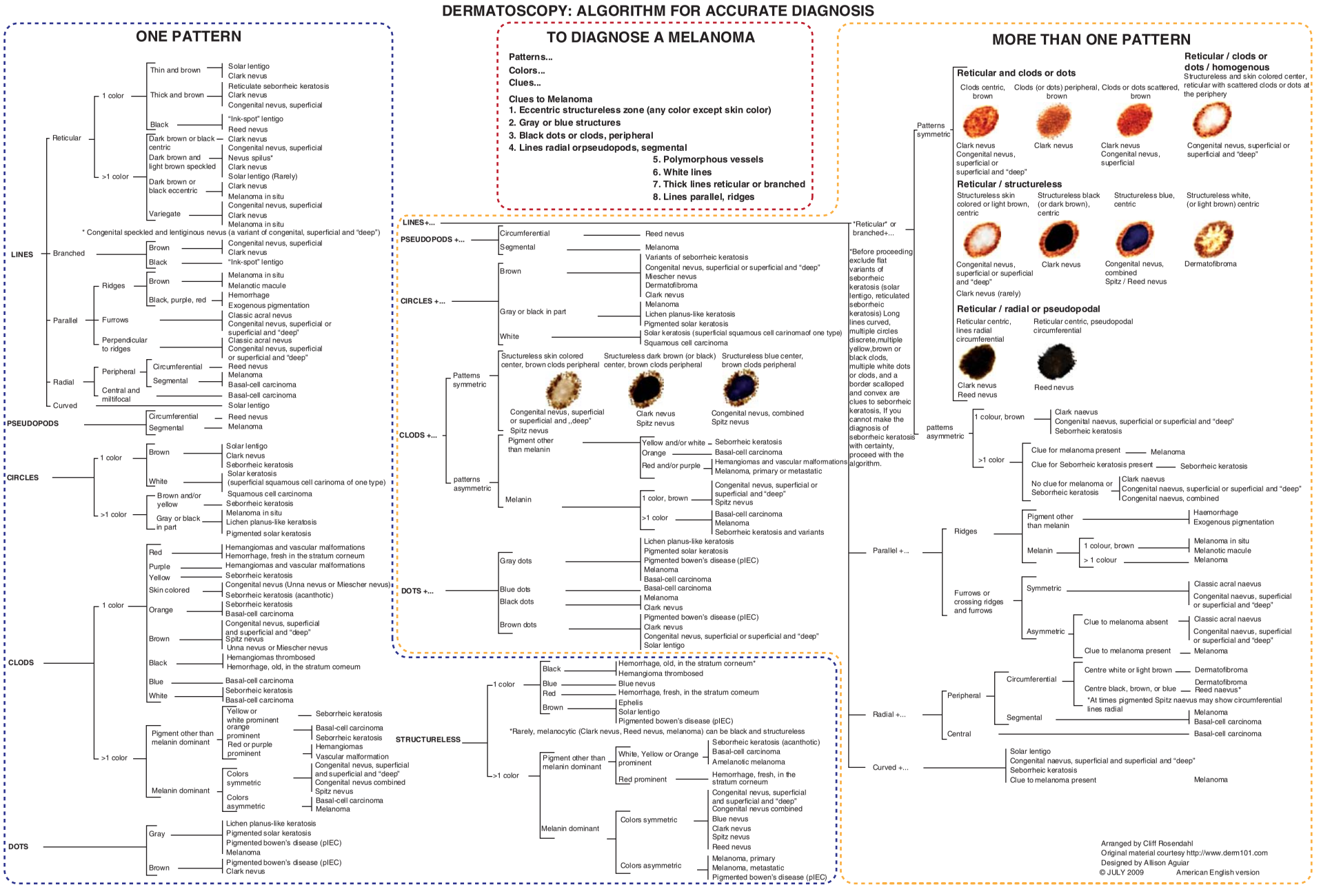


Figure 6h.16 Revised pattern analysis can also be applied in the evaluation of nonmelanocytic tumors. This flow diagram provides an overview of the revised pattern analysis approach in the evaluation of both melanoctyic and nonmelanocytic tumors. *Source*: Original material courtesy of www.derm101.com; designed by Allison Aguiar.

REFERENCES

Altamura, D., Menzies, S.W., Argenziano, G., et al., 2010, Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *J Am Acad Dermatol*, 62, 67–75.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Binder, M., Kittler, H., Steiner, A., et al., 1999, Reevaluation of the ABCD rule for epiluminescence microscopy. *J Am Acad Dermatol*, 40(2 Pt 1), 171–6.

Binder, M., Schwarz, M., Winkler, A., et al., 1995, Epiluminescence microscopy. A useful tool for the diagnosis of pigmented skin lesions for formally trained dermatologists. *Arch Dermatol*, 131, 286–91.

Braun, R.P., Gaide, O., Oliviero, M., et al., 2007, The significance of multiple blue-grey dots (granularity) for the dermoscopic diagnosis of melanoma. *Br J Dermatol*, 157, 907–13.

Cameron, A., Rosendahl, C., Tschandl, P., Riedl, E. & Kittler, H., 2010, Dermatoscopy of pigmented Bowen's disease. *J Am Acad Dermatol*, 62, 597–604.

Chamberlain, A.J., Fritschi, L. & Kelly, J.W., 2003, Nodular melanoma: patients' perceptions of presenting features and implications for earlier detection. *J Am Acad Dermatol*, 48, 694–701.

Kittler, H., 2007, Dermatoscopy: introduction of a new algorithmic method based on pattern analysis for diagnosis of pigmented skin lesions. *Dermatopathol Pract Conc*, 13, 1.

Kittler, H., Riedl, E., Rosendahl, C. & Cameron, A., 2010, Dermatoscopy of unpigmented lesions of the skin: a new classification of vessel morphology based on pattern analysis. *Dermatopathol Pract Conc*, 14, 3.

Menzies, S.W., Crotty, K.A. & McCarthy, W.H., 1995, The morphologic criteria of the pseudopod in surface microscopy. *Arch Dermatol*, 131, 436–40.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

7 Benign melanocytic lesions

7a Congenital melanocytic nevi

Ashfaq A. Marghoob

INTRODUCTION

Congenital melanocytic nevi (CMN) are melanocytic nevi whose presence is determined in utero. In contrast, acquired melanocytic nevi form after birth and their development appears to be dependent on environmental factors. However, the distinction between congenital and acquired nevi has become more nebulous in recent years. Although most CMN are present at birth, some may not become clinically apparent for months or even years after birth. These tardive CMN are not visible at birth due to either the lack of visible pigment or because the growing nidus of the nevus is imperceptible due to its small size. As the tardive CMN grows and/or develops pigment, it eventually becomes apparent on the skin. Although the appearance of nevi after birth are often deemed to be acquired nevi (Changchien et al., 2007), tardive CMN are actually congenitally derived. Melanocytic nevi possessing clinical features consistent with CMN, but in which clinical history is lacking to conclusively verify their presence since early life, are termed congenital nevus-like nevi (CNLN). Although it is possible that some CNLN are acquired nevi, most are probably tardive CMN. Between 1% and 6% of the population have a CMN or a CNLN (Happle, 2009).

The most widely used classification of CMN divides lesions into categories based on size: small (<1.5 cm); medium (1.5–19.9 cm); large (≥20 cm); and giant (≥50 cm) (Kovalyshyn et al., 2009). While melanoma may develop in association with any CMN, irrespective of size, the risk of developing melanoma appears proportional to the size of the CMN. Patients with CMN can develop cutaneous or extracutaneous melanoma (Kovalyshyn et al., 2009). The location and age at onset of melanoma differs between small to medium and large CMN. Melanomas developing in smaller CMN tend to appear after puberty and are more likely to originate at the dermoepidermal junction (DEJ) and at the peripheral edge of the CMN. Thus, dermoscopy is an ideal instrument to evaluate smaller CMN for melanoma since it can easily help the clinician observe morphologic changes at the DEJ that may be indicative of melanoma. In contrast, melanomas occurring in large CMN develop earlier in life and frequently have their origin below the DEJ. Thus, dermoscopy has a limited role in evaluating large CMN, especially those that are thick and rugous, since it cannot adequately visualize morphologic changes that may be indicative of melanoma developing below the papillary dermis. One type of CMN requires special mention here. A nevus spilus or speckled lentiginous nevus is a CMN that consists of a lentiginous patch of skin that is studded with nevi. There are two variants of a nevus spilus. Nevus spilus maculosus consists of dark macular speckles on a light brown background (Marghoob, 2002). The speckles, all of approximately the same size, have a reticular or homogenous appearance under dermoscopy. In contrast, nevus spilus papulosis consists of variously sized dark macules and papules unevenly distributed on a light brown background (Marghoob, 2002). With dermoscopy these macules and papules can be reticular, homogenous, globular, or can manifest a combined pattern. Although melanoma can develop in any nevus spilus, the risk is highest in larger speckled lentiginous nevi of the maculosa variant.

The current management options for CMN include close clinical followup with or without baseline photographs and/or prophylactic surgical excision, when feasible (Marghoob et al., 2007). Most physicians, however, are electing to follow CMN, especially those that have a homogenous clinical appearance and are small to medium in size, by periodic followup examinations. Dermoscopy has improved our ability to clinically monitor CMN, especially the smaller ones. Knowledge of the dermoscopic features and patterns common to CMN can aid physicians in following these lesions and recognizing aberrancy that may be suggestive of melanoma. In other words, if a significant change occurs or the dermoscopic pattern does not conform to the known CMN patterns, then a biopsy or an excision may be warranted. Needless to say, many physicians find baseline photographs and dermoscopy to be very helpful in the followup monitoring of CMN (Nehal et al., 2002a; Nehal et al., 2002b). Ideally, the photographs of CMN should include overview clinical images and dermoscopic images (Nehal et al., 2002b). The dermoscopic images should capture the representative architecture and border of the CMN (Braun et al., 2001). In addition, supplemental dermoscopic images should be obtained of any areas within the CMN that are of "special interest" (Braun et al., 2001).

DERMOSCOPIC EVALUATION OF CMN

Most small and medium CMN are fairly homogenous, both clinically and dermoscopically. Large CMN, on the other hand, are often heterogenous, displaying multiple islands of color and irregular topography. Under dermoscopy, multiple patterns can be seen within the same lesion, but each "island" within the large CMN tends to be fairly homogenous in its appearance.

Previously, authors have documented dermoscopic features and patterns common to CMN of all sizes, including the presence of reticular network, globules that may form a cobblestone pattern, and diffuse homogenous pigmentation (Seidenari & Pellacani, 2002; Seidenari et al., 2003; Braun et al., 2001; Wang et al., 2000a; Wang et al., 2000b; Soyer et al., 2001b). Other features associated with CMN include terminal hairs, perifollicular hypo- or hyperpigmentation, and milia-like cysts. This chapter reviews the dermoscopic features of CMN. For a lesion to be categorized as a CMN, it must meet the following criteria:

1. Any melanocytic nevus that was documented to be present since birth, or;
2. Any CNLN in which the history is reliable that it was present since early life and the clinical examination or histology is consistent with a CMN (Kenet et al., 1993).

DERMOSCOPIC FEATURES OF CMN

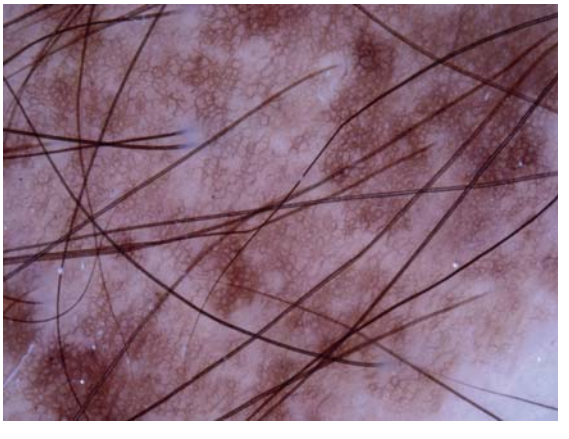
Dermoscopic evaluation of a CMN begins by observing dermoscopic structures (Table 7a.1). A reticular network consists of a honeycomb-like grid of brown-black pigment in which the pigmented lines correspond to rete ridges, and the open holes or spaces correspond to the suprapapillary plate overlying the dermal papillae (Soyer et al., 1989; Kenet et al., 1993; Soyer et al., 2001a). The reticular network, as seen in CMN, is characterized by its:

1. Quality, which can be fine (Fig. 7a.1) and/or thick (Fig. 7a.2);
2. Distribution, in which the network can be present homogenously throughout the lesion (Fig. 7a.3), or present focally (patchy) (Fig. 7a.4), or may be present only at the periphery (Fig. 7a.5);
3. Specific type, thick linear network fragments that resemble hyphal elements (i.e., resemblance to the tubular branching of fungal hyphae) (Figs. 7a.6 and 7a.7).

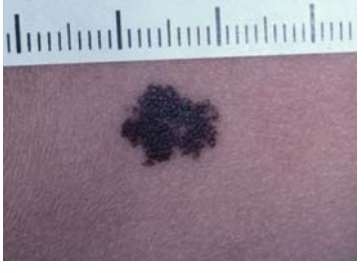
Table 7a.1 Dermoscopic Structures and Features Observed in Congenital Melanocytic Nevi

Pattern (Frequency)	Definition	Characteristics (Frequency)
Reticular network (71%)	Honeycomb-like network	Quality Fine (48%) Thick (27%) Distribution Homogeneously throughout (39%) Patchy throughout (27%) Peripheral (34%) Specific type Linear fragments (Hyphal-like) (23%)
Globules (82%)	Sharply circumscribed, round to oval aggregates of brown pigment. Sometimes the globules can be black or blue in color	Quality Small and/or large (46%) Distribution Diffusely throughout (sparse or dense concentration) (73%) Central (23%) Specific type Cobblestone (17%) Target (35%)
Diffuse background pigmentation (4%)	Diffuse distribution of brown background pigment	Structureless with or without the presence of small focal areas with network fragments or a few scattered globules

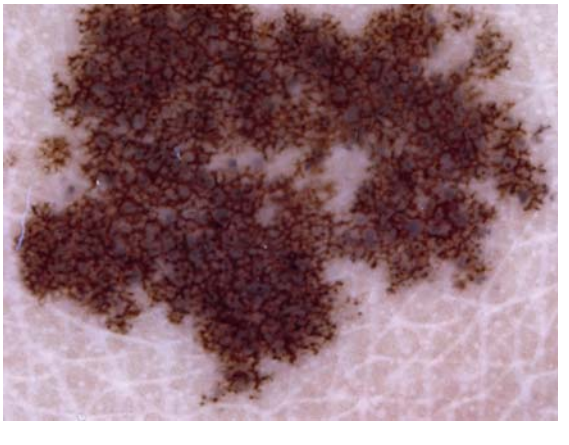
▲ **Figure 7a.1a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.1b** CMN with a fine reticular network throughout. Note the hypertrichosis, which is frequently seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.



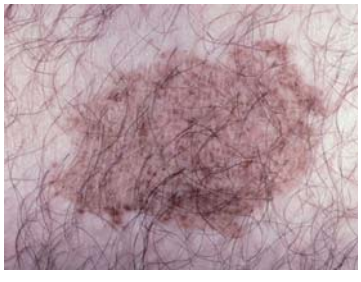
▲ **Figure 7a.2a** Clinical image of a small CMN.



◀ **Figure 7a.2b** CMN with a thick reticular network throughout. Note the presence of a few small bluish globules within this CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

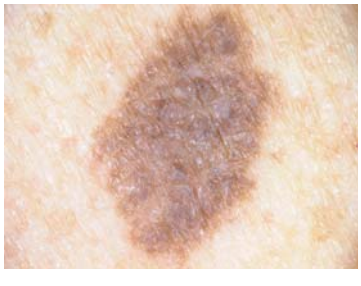
▲ **Figure 7a.3a** Clinical image of a medium-sized CMN.

◀ **Figure 7a.3b** CMN with homogenous reticulation throughout the lesion. Other features that are often seen in CMN include hypertrichosis, as can be seen in this nevus. *Abbreviation*: CMN, congenital melanocytic nevus.

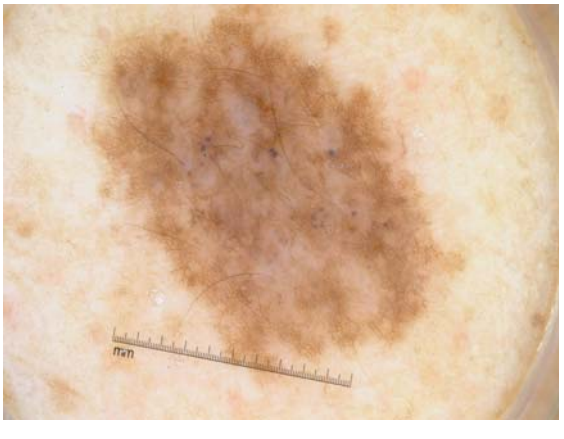


▲ **Figure 7a.4a** Clinical image of a medium-sized CMN.

◀ **Figure 7a.4b** CMN with patchy reticulation throughout the lesion. Other features that are common to CMN include hypertrichosis and perifollicular hypopigmentation, as seen in this CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

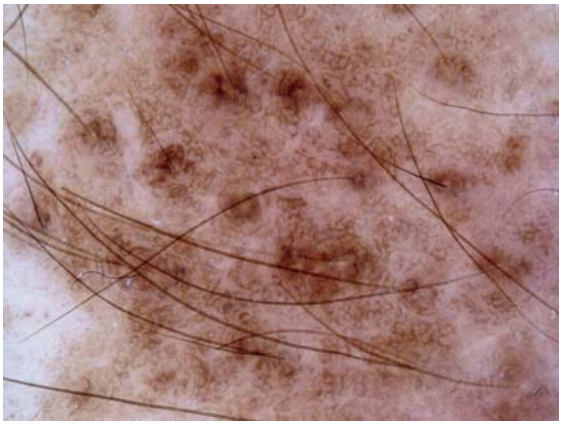


▲ **Figure 7a.5a** Clinical image of a small CMN.



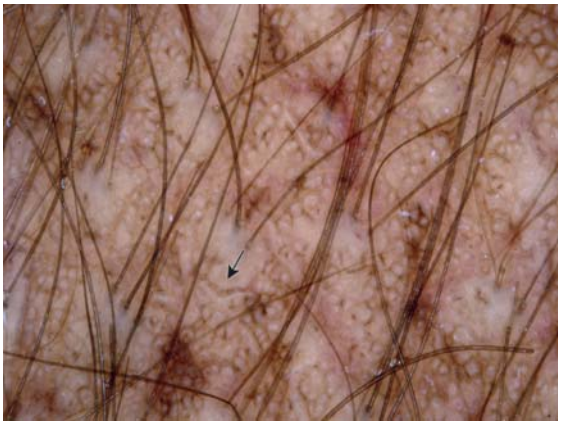
◀ **Figure 7a.5b** This CMN has a reticular pattern with hypopigmented structureless areas in the center. It also has hypertrichosis. Although globules in CMN tend to be aggregated and brown in color, on rare occasions one can find nonaggregated globules with a blue color, as is evident in this CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.6a** Clinical image of a medium-sized CMN.



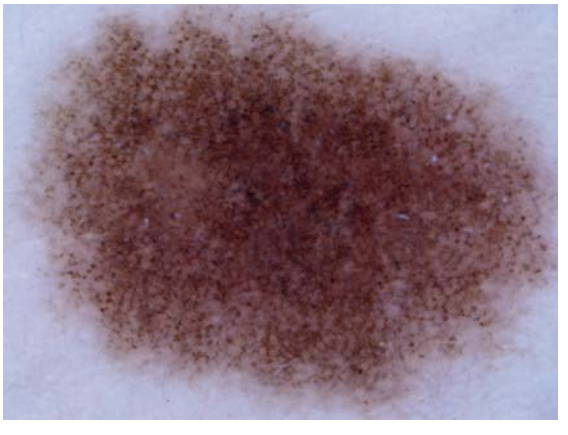
◀ **Figure 7a.6b** CMN can have network fragments that resemble hyphal-like structures. Other features seen in this nevus that are common to CMN include hypertrichosis and perifollicular hyperpigmentation. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.7a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.7b** CMN can have network fragments that resemble hyphal-like structures (*arrow*). *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.8a** Clinical image of a small CMN.



◀ **Figure 7a.8b** CMN with small globules. The homogenous brown background color as seen in this nevus is a feature commonly seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

Globules consist of sharply circumscribed, round-to-oval aggregates that are usually brown in color; however, they can also appear with a black or blue color. Globules correspond to nests of melanin-containing nevomelanocytes within the dermis. Globules in CMN are characterized by their:

1. Quality, which can be small (Fig. 7a.8) and/or large (Figs. 7a.9 and 7a.10);
2. Distribution, in which the globules can be present diffusely throughout the lesion in a sparse or dense distribution (Figs. 7a.11 and 7a.12), or clustered centrally and surrounded by reticulation (Fig. 7a.13);
3. Specific type, in which the globules form a cobblestone-like arrangement (Fig. 7a.14) or form target-like structures (Figs. 7a.15 and 7a.16). Target-like structures consist of the presence of globules within the "holes" of the network as depicted in Figs. 7a.15 and 7a.16. Target network with globules corresponds to the presence of nevomelanocytic nests in the dermal papillae (Changchien et al., 2007).

Diffuse homogenous background pigmentation is due to the diffuse distribution of melanin in the epidermis and dermis (Kenet et al., 1993). Often these CMN appear structureless, in that one cannot see any discernible dermoscopic structures (i.e., network or globules) (Fig. 7a.17), but on occasion a few scattered reticular network fragments and/or globules (Fig. 7a.18) may be visible focally within the lesion.

OTHER DERMOSCOPIC FEATURES SEEN IN CMN

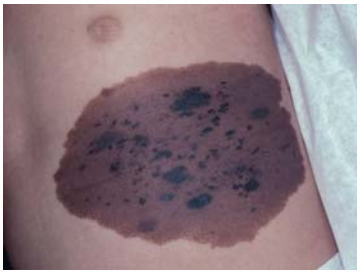
Other structures frequently observed in CMN viewed with dermoscopy include the following (Table 7a.2):

1. Milia-like cysts
2. Hypertrichosis
3. Blood vessels
4. Perifollicular pigment changes.

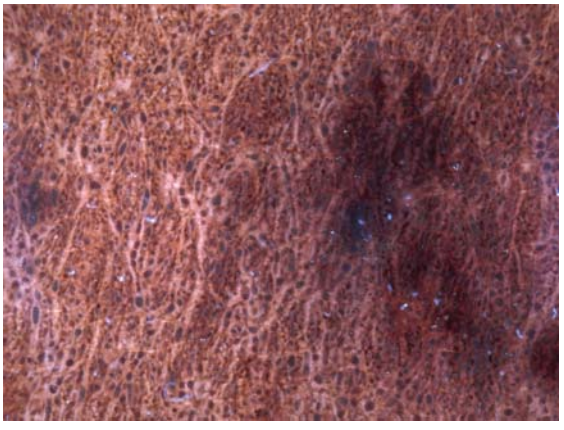
Milia-like cysts (Figs. 7a.19 and 7a.20) are white to yellow, rounded, often hazy structures that correlate histologically with intraepidermal keratin cysts/pseudocysts (Soyer et al., 1989). They derive their name from their resemblance to the small seeds or millets of various grain grasses. They may be observed scattered throughout a CMN (Changchien et al., 2007). It is important to stress that although the presence of milia-like cysts is one of the dermoscopic hallmarks of seborrheic keratosis, they can also be seen in melanocytic neoplasms, including CMN, papillomatous dermal nevi and, rarely, in melanomas (Braun et al., 2002; Argenziano et al., 2003). Thus, if the lesion is deemed to be a nonmelanocytic growth then the presence of multiple milia-like cysts favors the diagnosis of seborrheic keratosis; however, if the lesion is a melanocytic tumor then the presence of multiple milia-like cysts favors a diagnosis of CMN. With that being said, it is important to remember that in a melanocytic tumor the presence of milia-like cysts, in and of themselves, are not diagnostic of a CMN since they can also be seen in melanoma. Hypertrichosis is characteristic of CMN and is often accompanied by perifollicular hyperpigmentation (Figs. 7a.6 and 7a.21) or hypopigmentation (Fig. 7a.22). In addition, the presence of blood vessels of varying morphologies is commonly observed in CMN. Occasionally, the blood vessels can be seen within the hole of the network and correspond to vessels in the dermal papillae. When a network surrounds these vessels they create a target structure called "target network with blood vessels."

DERMOSCOPIC PATTERNS

After identifying the local dermoscopic features commonly seen in CMN, it becomes apparent that these nevi often exhibit specific dermoscopic patterns (Table 7a.3). In CMN, these global patterns are generally

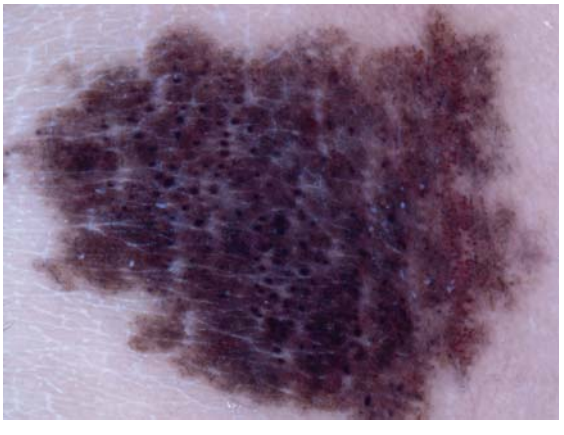


▲ **Figure 7a.9a** Clinical image of a large CMN.



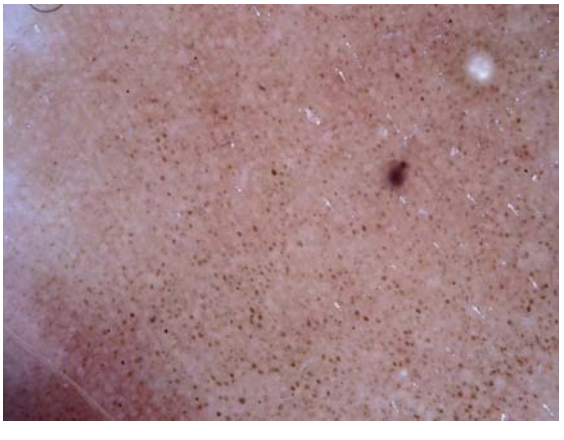
◀ **Figure 7a.9b** CMN with large globules. Note the homogenous brown background pigment, which is often seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.10a** Clinical image of a small CMN.



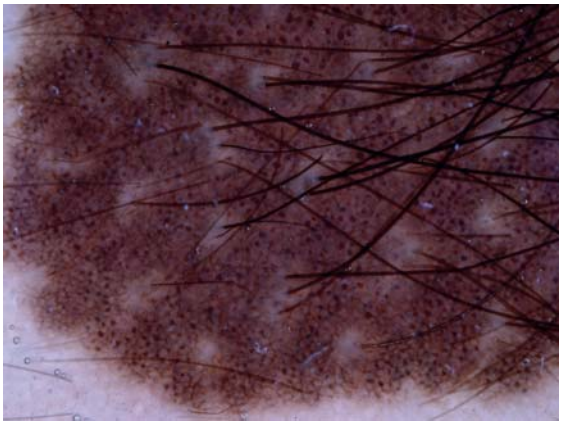
◀ **Figure 7a.10b** CMN with large and small globules. Note the diffuse brown background color, which is a common occurrence in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.11a** Clinical image of a medium-sized CMN.

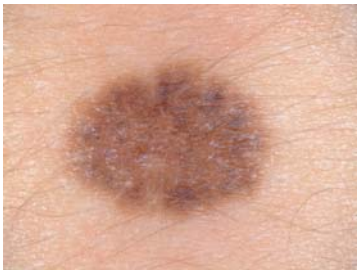


◀ **Figure 7a.11b** CMN with globules present throughout the lesion and distributed in a sparse concentration. Other features seen in this nevus, common to CMN, include diffuse background pigment and the presence of a milia-like cyst. *Abbreviation*: CMN, congenital melanocytic nevus.

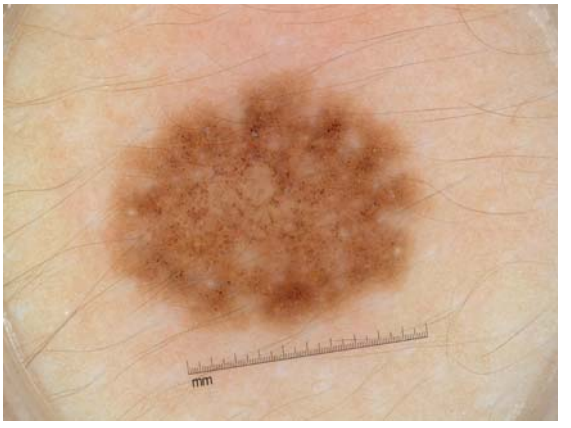
▲ **Figure 7a.12a** Clinical image of a medium-sized CMN.



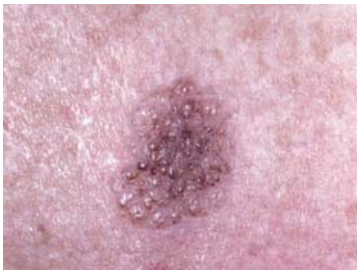
◀ **Figure 7a.12b** CMN with globules throughout the lesion and distributed in dense concentration. Other features seen in this nevus are hypertrichosis, perifollicular hypopigmentation, and diffuse brown background color, all of which are commonly found in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.



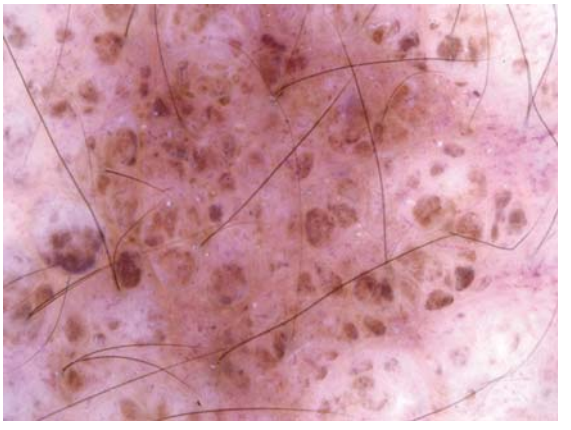
▲ **Figure 7a.13a** Clinical image of a CMN.



◀ **Figure 7a.13b** CMN with globules present centrally and surrounded by a reticular network. Note the presence of milia-like cysts, which can often be seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

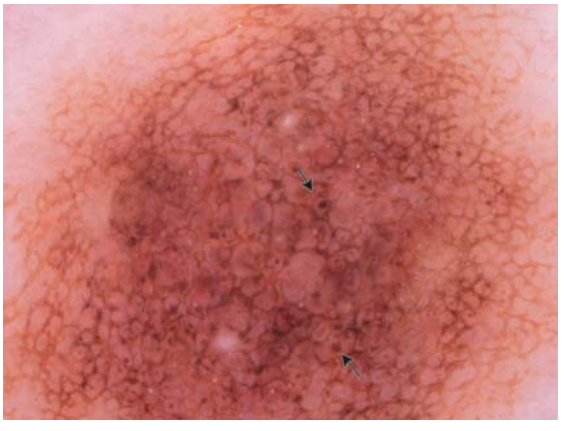


▲ **Figure 7a.14a** Clinical image of a small CMN.

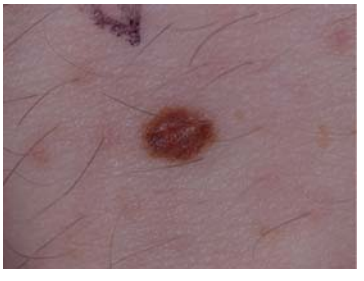


◀ **Figure 7a.14b** CMN with cobblestone-like globules. Note the hypertrichosis, which is frequently seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.15a** Clinical image of a medium-sized CMN.



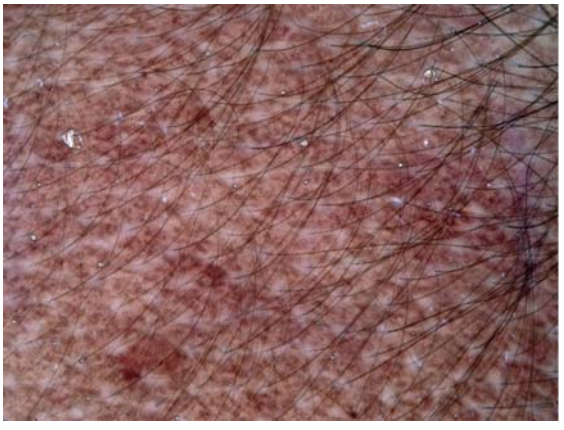
◀ **Figure 7a.15b** CMN with target network with globules (*arrows*). *Abbreviation*: CMN, congenital melanocytic nevus.



▲ **Figure 7a.16a** Clinical image of a small CMN.

◀ **Figure 7a.16b** CMN with target globules. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.17a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.17b** CMN with a diffuse brown background pigment without any discernible structures. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.18a** Clinical image of a medium-sized CMN.

◀ **Figure 7a.18b** CMN with a diffuse brown background and with a few globules and network fragments. *Abbreviation*: CMN, congenital melanocytic nevus.

Table 7a.2 Other Dermoscopic Features Seen in Congenital Melanocytic Nevi

Feature (Frequency)	Definition
Milia-like cysts (52%)	White to yellow, rounded, often hazy structures resembling the small seeds or millets of various grain grasses
Target network with vessels (33%)	Blood vessels situated within the holes of the network
Target network with globules (target globules) (27%)	Globules present within the holes of the network
Blood vessels of varying morphologies (68%)	Blood vessel morphology can include any or all of the morphologies described for nevi (i.e., comma vessels) and melanoma (i.e., dotted, linear serpentine, coiled, and hairpin.)
Hypertrichosis (79%)	Increased number of terminal hairs
Perifollicular pigment changes (42%)	Hypopigmentation or hyperpigmentation occurring around the hair follicles

appearing symmetric and organized. The four primary global patterns that emerge are

1. Reticular (reticular throughout or patchy reticular throughout);
2. Globular;
3. Reticuloglobular with globules in the center and network at the periphery;
4. Diffuse brown pigmentation (with or without network fragments and/or presence of a few sparse globules).

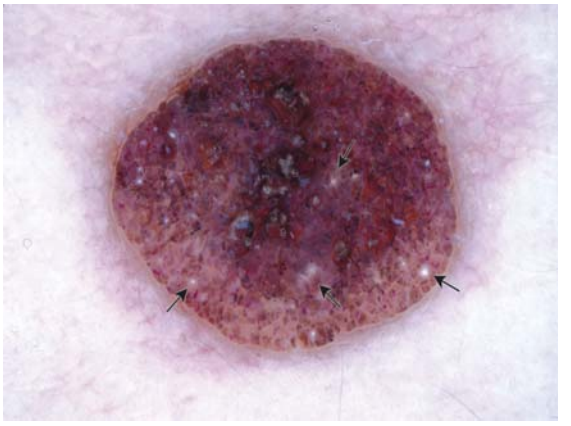
Some CMNs are either primarily reticular (Figs. 7a.23 and 7a.24) or primarily globular (Figs. 7a.25 and 7a.26). Others exhibit peripheral reticulation in conjunction with central globules, and are designated reticuloglobular (Figs. 7a.13 and 7a.27). As noted earlier, CMN that primarily have diffuse brown pigmentation are often structureless, but some may contain fragments of reticulation and/or globules (Figs. 7a.28 and 7a.29). Approximately 7% of CMN will manifest a multicomponent pattern. If the structures in a multicomponent nevus are distributed asymmetrically then differentiating these CMN from melanoma may be challenging (Figs. 7a.30 and 7a.31). In addition, thick mamillated CMN are often difficult to evaluate using dermoscopy (Fig. 7a.32). These lesions often have ridges, comedo-like openings, and many blood vessels as can be seen in Figure 7a.32. This pattern can sometimes mimic a seborrheic keratosis.

Although any of the above-mentioned dermoscopic patterns could be present in CMN at any anatomical location, CMN on the torso are more frequently globular and CMN on the lower extremities are more frequently reticular (Changchien et al., 2007).

CONCLUSION

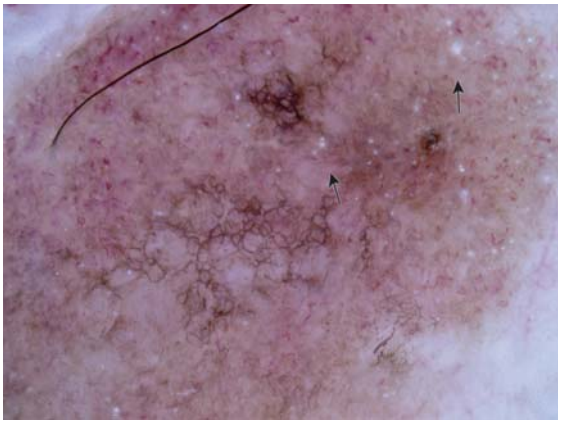
Dermoscopy can be enormously valuable in the diagnosis and followup of CMN (Braun et al., 2005; Lodha et al., 2003). This noninvasive in vivo technique allows the clinician to examine morphologic structures within the epidermis, DEJ, and superficial dermis. Since most melanomas arising in association with smaller CMN develop along the DEJ, dermoscopy is an ideal instrument to help in the evaluation, screening, and monitoring of these nevi. Dermoscopy may also assist in evaluating, screening, and monitoring of flat large CMN. However, due to the limitation of how deep into the skin dermoscopy allows the observer to see, this tool is not ideal for evaluating large rougouse CMN, because melanomas developing in such lesions are often located below the papillary dermis. Although dermoscopy can assist in evaluating the superficial component of these thicker CMN, other techniques, such as palpation, ultrasound, or other

▲ **Figure 7a.19a** Clinical image of a small CMN.



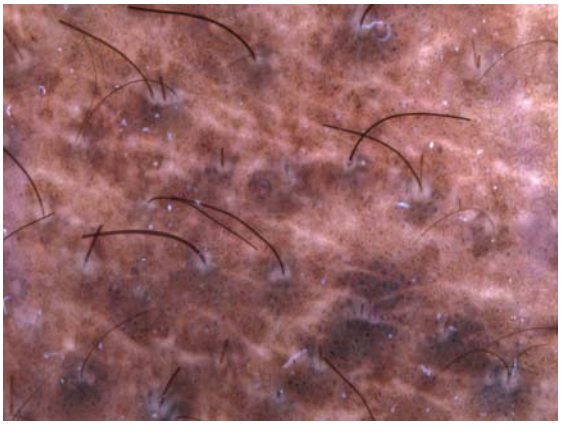
◀ **Figure 7a.19b** CMN with milia-like cysts (*arrows*). This lesion also has globules and vessels. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.20a** Clinical image of a medium-sized CMN.

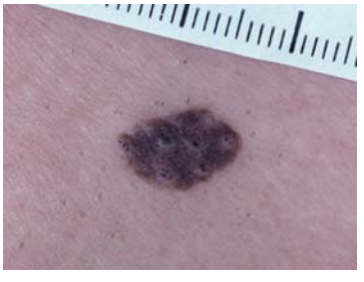


◀ **Figure 7a.20b** CMN with milia-like cysts (*arrows*). This lesion also has a patchy network, vessels, and diffuse background pigmentation. *Abbreviation*: CMN, congenital melanocytic nevus.

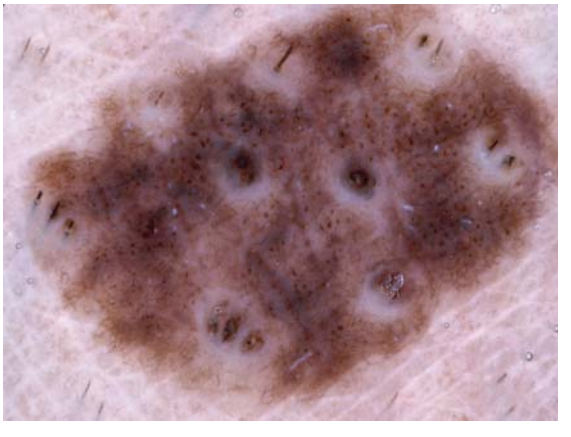
▲ **Figure 7a.21a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.21b** CMN with perifollicular hyperpigmentation. Note the target globules in the right upper corner of the image and the diffuse brown background pigment—both features commonly seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.



▲ **Figure 7a.22a** Clinical image of a small CMN.

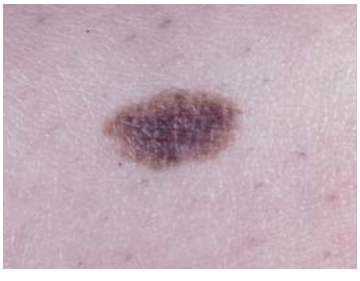


◀ **Figure 7a.22b** CMN with perifollicular hypopigmentation. This lesion also has a few target globules and peripherally placed network, both of which are common features seen in CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

Table 7a.3 Congenital Melanocytic Nevi Dermoscopic Patterns

Global pattern (Frequency)	Definition
Reticular (23%)	Primarily reticular in pattern
Globular (18%)	Primarily globular in pattern
Reticuloglobular (16%)	Peripheral reticulation in conjunction with central globules
Diffuse brown pigmentation (4%)	Primarily diffuse structureless pattern with or without reticular networks fragments and/or a few sparse globules
Multicomponent (7%)	Three or more melanocytic dermoscopic structures present in the same lesion. The melanocytic structures include network, streaks, negative network, globules, crystalline, blotch, and blue-white veil

imaging modalities, may need to be used to evaluate the deeper nevus component. The classification system proposed in this chapter should provide the foundation for the recognition of CMN. Those CMN that do not conform to the known patterns described above should be viewed with caution. One such example is provided in Figure 7a.30. Within one section of this asymmetric melanocytic lesion one can see the classic cobblestone globular pattern of a CMN. This part of the lesion also reveals milia-like cysts, hypertrichosis, and multiple blood vessels—all structures commonly seen in CMN. However, another portion of the same lesion has features that are not seen in CMN and are, in fact, features commonly seen in melanoma. This lesion was excised and revealed a melanoma arising in association with a CMN.

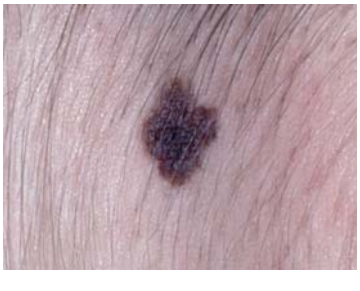


▲ **Figure 7a.23a** Clinical image of a small CMN.

◀ **Figure 7a.23b** CMN with a reticular network pattern. *Abbreviation*: CMN, congenital melanocytic nevus.

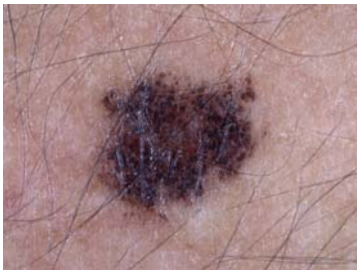
▲ **Figure 7a.24a** Clinical image of a medium-sized CMN.

◀ **Figure 7a.24b** CMN with a patchy reticular network pattern. *Abbreviation*: CMN, congenital melanocytic nevus.

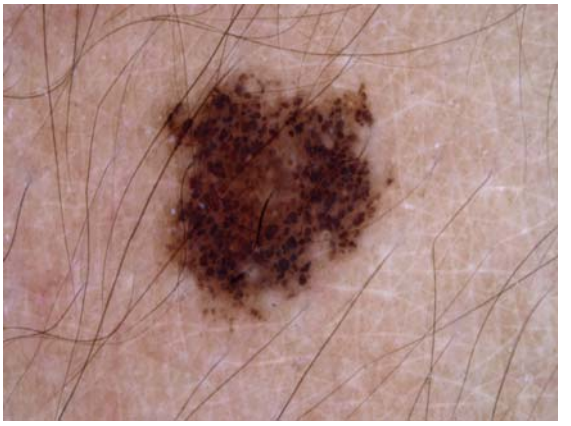


▲ **Figure 7a.25a** Clinical image of a small CMN.

◀ **Figure 7a.25b** CMN with a globular pattern. *Abbreviation*: CMN, congenital melanocytic nevus.

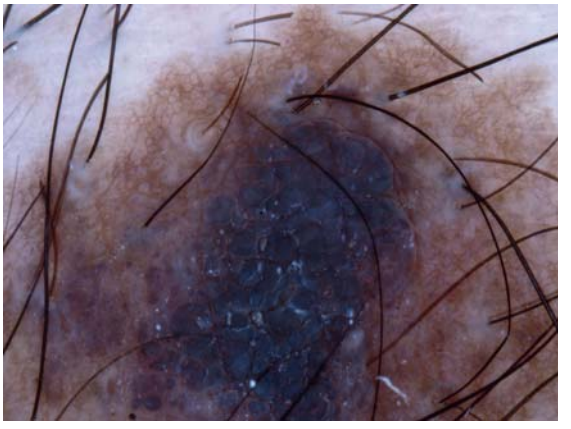


▲ **Figure 7a.26a** Clinical image of a small CMN.



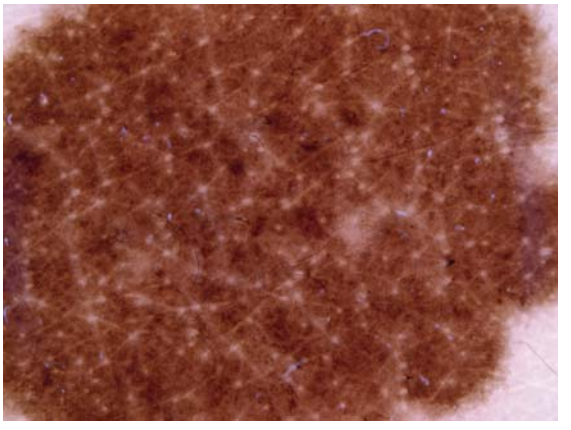
◀ **Figure 7a.26b** CMN with a globular pattern. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.27a** Clinical image of a medium-sized CMN.

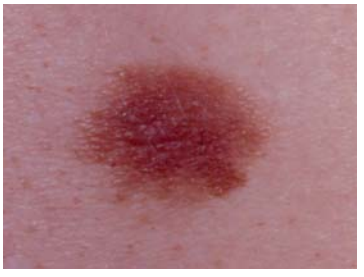


◀ **Figure 7a.27b** CMN with a reticuloglobular pattern. Notice the fine network around the periphery of the lesion and the large globules clustered in the center. This same pattern can be seen in Figure 7a.13. *Abbreviation*: CMN, congenital melanocytic nevus.

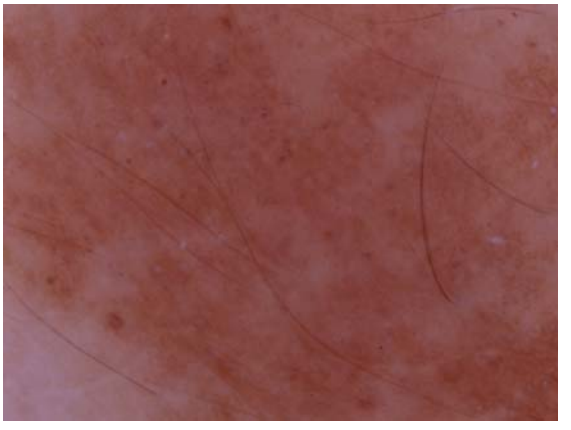
▲ **Figure 7a.28a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.28b** CMN with a diffuse brown background pigment pattern. There are no discernible structures. *Abbreviation*: CMN, congenital melanocytic nevus.

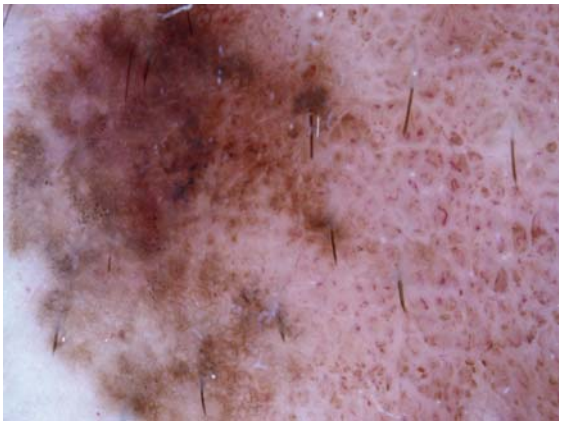


▲ **Figure 7a.29a** Clinical image of a medium-sized CMN.



◀ **Figure 7a.29b** CMN with a diffuse brown background pigment pattern. There are a few globules and network fragments discernible. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.30a** Clinical image of a CMN in which a melanoma has developed.

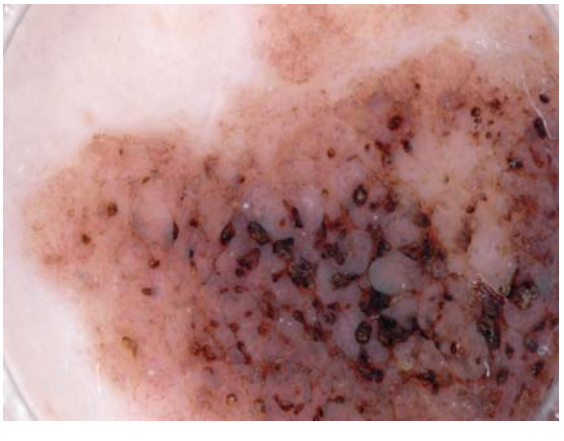


◀ **Figure 7a.30b** This CMN developed a focal pigment change. Under dermoscopy, one can see the classic CMN cobblestone pattern on the right. This area also reveals hypertrichosis, milia-like cysts, and comma-shaped blood vessels, which are all features common to CMN. The left side of the lesion reveals irregular dots, atypical network, and blue-gray areas, which are features commonly associated with melanoma. This lesion manifests an asymmetric multicomponent pattern. This lesion was excised and revealed a melanoma arising in association with a CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.31a** Clinical image of a small CMN.

◀ **Figure 7a.31b** This CMN has a multicomponent pattern with network, blotch, dots, and globules. The lesion also has milia-like cysts. Due to the asymmetric pattern this lesion was excised and step sectioned. The pathology confirmed the diagnosis of a CMN. *Abbreviation*: CMN, congenital melanocytic nevus.

▲ **Figure 7a.32a** Clinical image of a mamillated medium-sized CMN.



◀ **Figure 7a.32b** The undulating surface of this CMN creates invaginations that resemble crypts and comedo-like openings commonly seen in seborrheic keratosis. This CMN also reveals numerous blood vessels of varying morphologies. *Abbreviation*: CMN, congenital melanocytic nevus.

Key Points

1. Structures commonly seen in CMN include network, globules, diffuse brown structureless areas, milia cysts, target network, vessels, hypertrichosis, perifollicular pigment changes.
2. The most common dermoscopic patterns seen in CMN include reticular, globular, peripheral reticular with central globules, homogeneous brown, and multicomponent pattern.
3. CMN on the lower extremity predominantly have a reticular pattern. CMN on the torso and head and neck predominantly have a globular pattern.
4. Knowledge of the structures and patterns commonly seen in CMN can help in their evaluation. Lesions that deviate from the known patterns or reveal structures not commonly associated with CMN should be monitored closely or biopsied.

REFERENCES

Argenziano, G., Rossiello, L., Scalvenzi, M., et al., 2003, Melanoma simulating seborrheic keratosis: a major dermoscopy pitfall. *Arch Dermatol*, 139, 389–91.

Braun, R.P., Calza, A.M., Krischer, J. & Saurat, J.H., 2001, The use of digital dermoscopy for the follow-up of congenital nevi: a pilot study. *Pediatr Dermatol*, 18, 277–81.

Braun, R.P., Rabinovitz, H.S., Krischer, J., et al., 2002, Dermoscopy of pigmented seborrheic keratosis: a morphological study. *Arch Dermatol*, 138, 1556–60.

Braun, R.P., Rabinovitz, H.S., Oliviero, M., Kopf, A.W. & Saurat, J.H., 2005, Dermoscopy of pigmented skin lesions. *J Am Acad Dermatol*, 52, 109–21.

Changchien, L., Dusza, S.W., Agero, A.L., et al., 2007, Age- and site-specific variation in the dermoscopic patterns of congenital melanocytic nevi: an aid to accurate classification and assessment of melanocytic nevi. *Arch Dermatol*, 143, 1007–14.

Happle, R., 2009, Speckled lentiginous naevus: which of the two disorders do you mean? *Clin Exp Dermatol*, 34, 133–5.

Kenet, R., Kang, S., Kenet, B., et al., 1993, Clinical diagnosis of pigmented lesions using digital epiluminescence microscopy. Grading protocol and atlas. *Arch Dermatol*, 129, 157–74.

Kovalyshyn, I., Braun, R. & Marghoob, A., 2009, Congenital melanocytic naevi, *Australas J Dermatol*, 50, 231–40; quiz 241–2.

Lodha, R., McDonald, W.S., Elgart, G.W. & Thaller, S., 2003, Dermoscopy for congenital melanocytic nevi. *J Craniofac Surg*, 14, 661–5.

Marghoob, A.A., 2002, Congenital melanocytic nevi. Evaluation and management. *Dermatol Clin*, 20, 607–16, viii.

Marghoob, A.A., Borrego, J.P. & Halpern, A.C., 2007, Congenital melanocytic nevi: treatment modalities and management options. *Semin Cutan Med Surg*, 26, 231–40.

Nehal, K.S., Oliveria, S.A., Marghoob, A.A., et al., 2002a, Use of and beliefs about baseline photography in the management of patients with pigmented lesions: a survey of dermatology residency programmes in the United States. *Melanoma Res*, 12, 161–7.

Nehal, K.S., Oliveria, S.A., Marghoob, A.A., et al., 2002b, Use of and beliefs about dermoscopy in the management of patients with pigmented lesions: a survey of dermatology residency programmes in the United States. *Melanoma Res*, 12, 601–5.

Seidenari, S. & Pellacani, G., 2002, Surface microscopy features of congenital nevi. *Clin Dermatol*, 20, 263–7.

Seidenari, S., Martella, A. & Pellacani, G., 2003, Polarized light-surface microscopy for description and classification of small and medium-sized congenital melanocytic naevi. *Acta Dermato-Venereologica*, 83, 271–6.

Soyer, H., Smolle, J., H"dl, S., Pachernegg, H. & Kerl, H., 1989, Surface microscopy: a new approach to the diagnosis of cutaneous pigmented tumors. *Am J Dermatopathology*, 11, 1–10.

Soyer, H.P., Argenziano, G., Chimenti, S. & Ruocco, V., 2001a, Dermoscopy of pigmented skin lesions. *Eur J Dermatol*, 11, 270–6; quiz 277.

Soyer, H.P., Argenziano, G., Ruocco, V. & Chimenti, S., 2001b, Dermoscopy of pigmented skin lesions (Part II). *Eur J Dermatol*, 11, 483–98.

Wang, S., Katz, B., Rabinovitz, H.S., Kopf, A. & Oliviero, M., 2000a, Lessons on dermoscopy. Compound congenital melanocytic nevus. *Dermatol Surg*, 26, 397–8.

Wang, S., Katz, B., Rabinovitz, H.S., Kopf, A. & Oliviero, M., 2000b, Lessons on dermoscopy: case #9. Congenital melanocytic nevus. *Dermatol Surg*, 26, 977–8.

7b Dysplastic (atypical) nevi

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THE CONCEPT OF DYSPLASTIC NEVI

Dysplastic (atypical) nevi (DN) (Tucker et al., 1997) are benign acquired melanocytic neoplasms that clinically resemble melanoma since they frequently share some or all of the clinical ABCDE (A, asymmetry; B, border irregularity; C, color variability; D, diameter >6 mm; E, evolving) morphologic features of melanoma. The significance of DN is that individuals with such atypical moles are at significant increased risk of developing melanoma (Tucker et al., 1997) independent of the total number of nevi present (Bevona et al., 2003; Roesch et al., 2006). Although most melanomas developing in individuals with DN arise de novo, between 25 and 40% develop in contiguity with a DN, leading to the hypothesis that certain DN may be nonobligate precursors to a subset of melanomas (Fig. 7b.1) (Bevona et al., 2003). The goal of the clinical evaluation and management of patients who present with DN is to excise those DN that have given rise to melanoma and to determine which newly developing lesions and/or changing melanocytic neoplasms should be biopsied and which can be safely monitored. In this clinical decision-making process, dermoscopy has proved to be extremely valuable (Roesch et al., 2006).

Since DN far outnumber melanomas and since patients with the DN phenotype often have many nevi and intermittently develop new nevi, the continuous prophylactic excision of all DN is an impractical management strategy. Experience has shown that the combined use of patient history, total cutaneous examination, dermoscopy, utilizing the comparative approach (Argenziano et al., 2011) sequential imaging of suspicious (but lacking definitive criteria for melanoma) lesions, and lifelong followup is an effective approach at detecting early curable melanomas, while limiting the number of unnecessary biopsies of biologically stable lesions. For select patients total cutaneous photographs coupled with short-term (three months) dermoscopic mole monitoring can greatly assist the clinician in detecting biologically relevant lesions, such as curable de novo melanomas and melanomas arising from pre-existing melanocytic nevi and perhaps even lesions that may be destined to become melanoma (i.e., severely atypical nevi that are changing) (Altamura et al., 2008; Menzies et al., 2001; Kittler et al., 2006).

It is currently assumed that all DN are acquired melanocytic neoplasms and as such all DN will appear as new lesions. These lesions will progressively change until they enter senescence. These senescent DN are in fact stable lesions (Tucker et al., 2002). With that being said, it should come as no surprise that the vast majority of new or changing melanocytic lesions are DN and not melanoma (Fuller et al., 2007; Kittler et al., 2000; Banky et al., 2005). Since change is a sensitive indicator of melanoma, two important questions need to be addressed when confronted with a new or changing lesion: "Is the atypical melanocytic lesion a melanoma or is it the much more common dysplastic nevus?" and "Can the lesion be monitored or should it be biopsied?". To this end, better appreciation of primary morphology of the lesion in question may help determine which lesion requires biopsy. The clinical ABCD acronym cannot be expected to distinguish melanoma from DN because both lesions, by definition, share the same features clinically. However, dermoscopy often, but not always, can distinguish malignant from benign melanocytic lesions that are clinically indeterminate by the naked eye. Specific dermoscopic structures and patterns can aid in the decision as to which lesions can be followed and which lesions require biopsy.

THE ROLE OF DERMOSCOPY IN ASSESSING ATYPICAL MELANOCYTIC NEOPLASMS

It is important to emphasize that most DN are rather stable lesions, whereas melanomas are generally changing (e.g., biologically dynamic) lesions. Furthermore, despite their ABCD clinical features, the vast majority of DN can be diagnosed dermoscopically as benign melanocytic neoplasms by experienced dermoscopists. Such lesions do not have to be biopsied but can be followed, thus avoiding unnecessary surgery and reducing the cost of medical care. On the other hand, a significantly changing lesion could be biologically relevant since it may be a melanoma or a true melanoma precursor. Such lesions are generally best biopsied (Fig. 7b.2).

Different score-based dermoscopy algorithms (e.g., ABCD, Menzies, seven-point checklist, CASH) have been developed to assist clinicians in distinguishing DN from melanoma (Stolz et al., 1994; Menzies, 2009; Argenziano et al., 1998). Many DN that are clinically suspicious for melanoma can be correctly identified as benign using such dermoscopy algorithms. Yet, there still remains a significant portion of DN that score in the "suspicious" range implying the algorithm cannot distinguish these DN from melanoma with assurance. This is due to the considerable overlap in the primary morphology between DN and melanoma not only clinically but also dermoscopically. Pattern analysis, the most frequent method used by experienced dermoscopists, has been shown to better discriminate between many DN and melanomas as compared with other scoring algorithms (Argenziano et al., 2003). Pattern analysis involves determining the overall (global) dermoscopic pattern (Table 7b.1, Fig. 7b.3) based on the presence or absence of network, globules, homogenous (structureless) areas, and identifying the presence or absence of specific local features (Table 7b.2). In evaluating patterns, the observer must consider not only the overall dermoscopic pattern, but also the number and distribution of colors and structures, whether the dermoscopic structures are "regular" or "irregular" (see chap. 6a for further details), and whether the colors and structures are distributed symmetrically or asymmetrically and in an organized or disorganized manner.

DERMOSCOPIC PATTERNS OF DYSPLASTIC NEVI

The global patterns of melanocytic nevi used for classification are reticular, globular, homogenous, reticular–globular, reticular–homogenous, globular–homogenous, and two components (Hofmann-Wellenhof et al., 2001; Blum et al., 2003). Benign melanocytic nevi often present with one of the well-recognized symmetric and organized patterns listed in Table 7b.1 and depicted schematically in Figure 7b.3. In addition, it is not uncommon to encounter dysplastic with a multicomponent pattern (Fig. 7b.3). By definition, lesions with a multicomponent pattern must possess three or more of the following structures: globules, reticulation, blotches, dots, veil, regression structures, and/or structureless areas. Melanoma usually enters the differential diagnosis of lesions manifesting a multicomponent pattern.

The reticular type dysplastic nevus presents with a pigmented network. The "lines" of the network represent pigmented melanocytes/nevus cells and melanized keratinocytes in or along the epidermal rete ridges. The "holes" are created by the relative paucity of pigment overlying the suprapapillary epidermal plate overlying the dermal papilla. Benign patterns include network diffusely distributed throughout the lesion (Figs. 7b.4–7b.6) and network scattered in patches throughout the lesion (Figs. 7b.7 and 7b.8). Within the benign spectrum of reticular DN, pigmentation may also vary depending on the patient's phenotype. In fair skin there will often be a central area of hypopigmentation (often structureless) and in darker skin there will be a central area of hyperpigmentation or blotch (obscuring the network) (Figs. 7b.9–7b.12). These are considered reticular–homogenous DN.

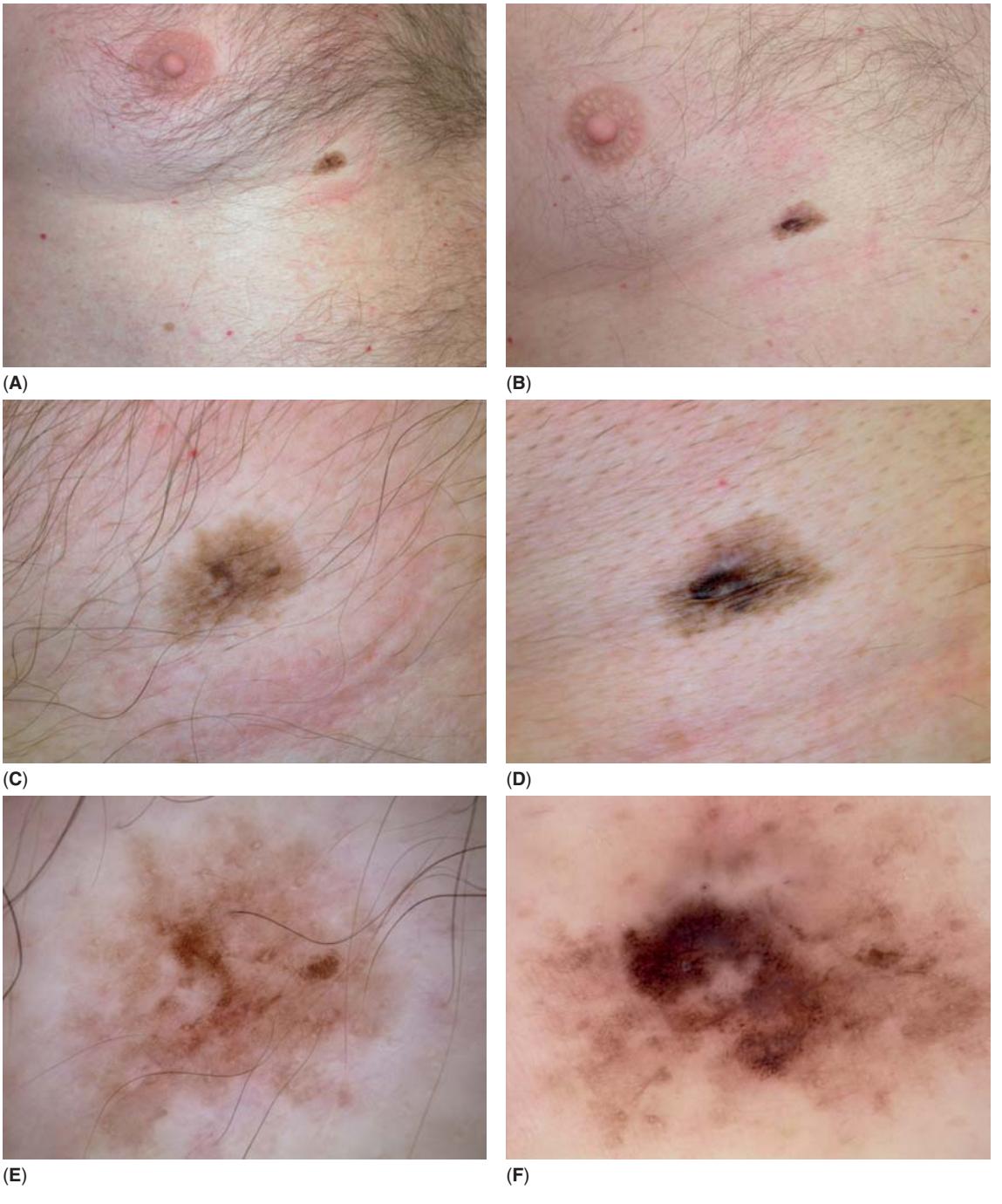


Figure 7b.1 This patient had a patchy reticular pattern dysplastic nevus on his chest (**A, C, E**). After remaining unchanged during eight years of followup, it eventually developed focal darkening and enlargement (**B, D, F**). Excisional biopsy revealed a 1.8 mm melanoma arising in association with a dysplastic nevus.

The globular type DN prominently features globules, which represent nevocytic nests of melanocytes. Benign patterns include globules distributed evenly throughout the lesion and the globular–homogenous pattern, which has structureless areas distributions within the lesion (Figs. 7b.13 and 7b.14).

The homogenous type DN is distinguished by its predominant lack of structures. Although a few globules and/or network fragments may be found focally, the overall pattern and pigmentation is homogenous (Figs. 7b.15 and 7b.16). We have observed through confocal microscopy and histology that homogenous DN morphologically may be junctional, compound, or intradermal nevi.

Reticular–globular DN display a combination of aforementioned features seen in reticular and globular DN. Common benign patterns include central globules with peripheral network (Figs. 7b.17 and 7b.18) and central network or homogenous areas with brown globules located at the periphery (Fig. 7b.2). The peripheral globules, usually corresponding to junctional nevomelanocytic nests at the tips of rete ridges, are frequently encountered in nevi undergoing enlargement (i.e., growing nevi) (Figs. 7b.2 and 7b.19).

Starburst pattern is a specific pattern commonly seen in Spitz nevi. The starburst pattern can manifest with peripheral globules tiered one on top of the other (Fig. 7b.20) or with steaks around the entire perimeter (Fig. 7b.21). The starburst pattern with peripheral streaks is quite specific for the diagnosis of Spitz nevus. Although the starburst pattern with peripheral tiered globules is commonly seen in Spitz nevi, it can also be seen in dysplastic nevi with spitzoid features (Fig 7b.20).

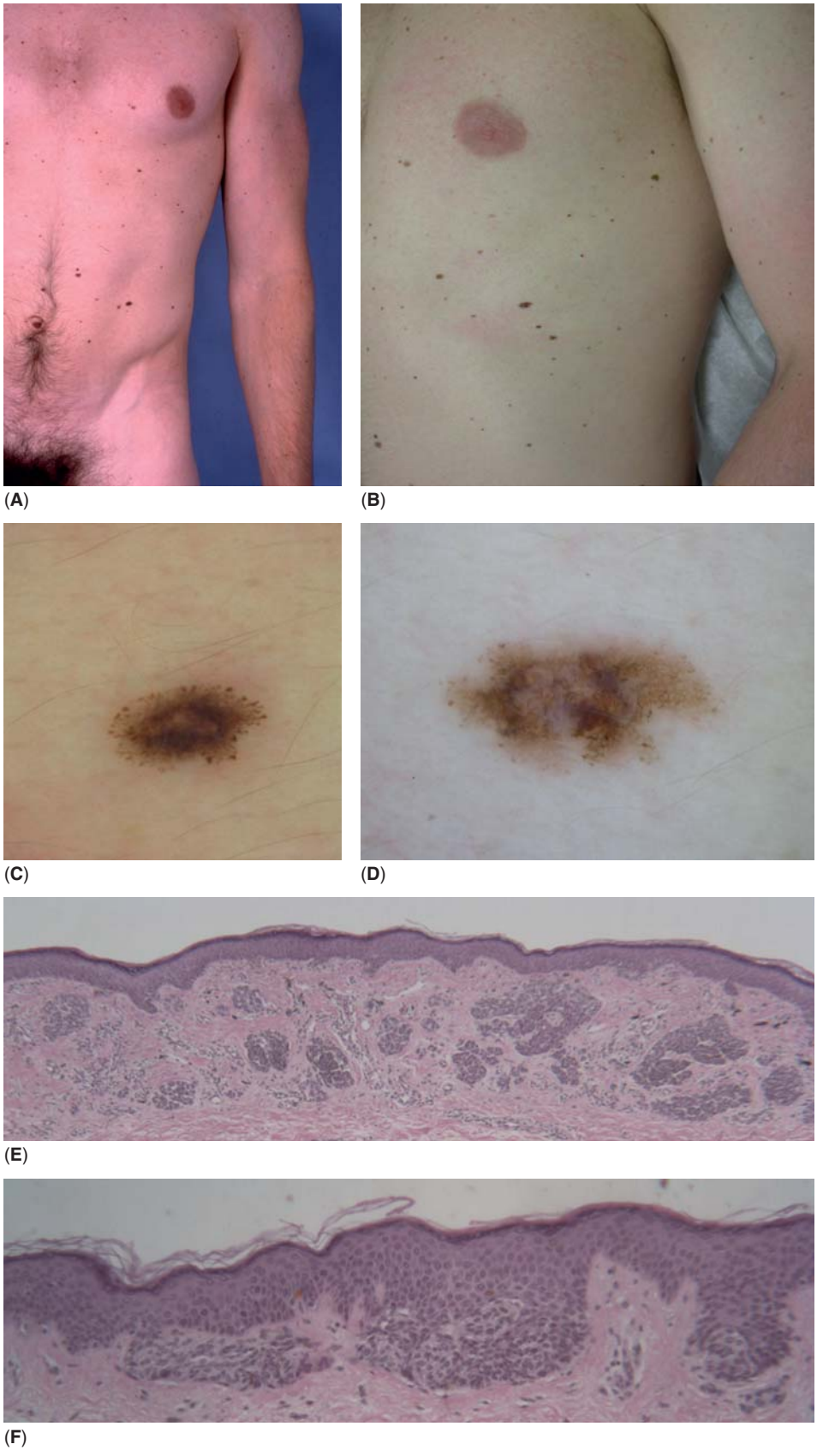


Figure 7b.2 A 26-year-old man with the classic atypical mole syndrome was followedup with baseline total body photographs (**A**). He developed a new mole on the left abdomen (**B**). This lesion was evaluated and it was determined that the lesion had a benign pattern with a peripheral rim of globules (**C**). The lesion was followed and over the course of one year it changed (**D**) revealing features concerning for melanoma (asymmetric growth and blue-white veil). The lesion was excised and the pathology report was that of a dysplastic nevus (**E** and **F**). Dysplastic nevi can at times be impossible to differentiate from melanoma clinically, dermoscopically, and occasionally even histologically. Such indeterminate lesions require biopsy.

Table 7b.1 Benign Dermoscopic Patterns Encountered in Nevi

Global pattern	Definition
Reticular diffuse	Diffuse network with uniform thickness and color of lines. The holes of the network are of relatively uniform size. The network tends to fade at the periphery. This pattern can be seen in congenital nevi, especially those located on the lower extremity, and in acquired nevi
Reticular patchy	Network with uniform thickness and color of lines. However, the network is not contiguous due to the presence of intervening homogenous structureless areas. This pattern can be seen in congenital nevi, especially those located on the lower extremity, and in acquired nevi
Peripheral reticular with central hypopigmentation	A relatively uniform network at the periphery of the lesion with a central homogenous and hypopigmented, but not depigmented, structureless area. This type of acquired nevus is more common in fair skin phenotypes
Peripheral reticular with central hyperpigmentation	A relatively uniform network at the periphery of the lesion with a central homogenous and hyperpigmented blotch. This type of acquired nevus is more common in darker skin phenotypes. The blotch can often be removed or lightened by tape stripping
Globular	Globules of similar shape, size, and color distributed symmetrically throughout the lesion. This pattern is seen most commonly in congenital nevi
Peripheral reticular with central globules	A relatively uniform network at the periphery of the lesion with multiple globules in the center. Nevi with this pattern often have histopathology features suggestive that the nevus has a congenital origin
Peripheral globules with central network or homogeneous area	The central component of this type of nevus is either reticular or homogenous. Relatively uniform globules surround the entire perimeter of the lesion. This pattern is suggestive of an acquired growing nevus that has not yet undergone senescence
Starburst	Streaks (radial streaming or pseudopods) present around the perimeter of the lesion giving the appearance of an exploding star. The starburst pattern can also manifest with peripheral globules that are tiered one on top of the other
Homogenous tan, brown, or blue pigmentation	Primarily diffuse structureless pattern with or without the presence of small foci of reticular network, network fragments, and/or globules. When tan in color they usually represent acquired nevi in fair skin phenotypes. When darker brown in color they usually represent congenital nevi. When blue in color they represent blue nevi
Two component	These lesions reveal two different patterns (reticular–globular, reticular–homogenous, or globular–homogenous). A half of the lesion manifests one pattern, whereas the other half of the lesion manifests a different pattern

Two component nevi reveal two different patterns (reticular–globular, reticular–homogenous, or globular–homogenous). One half of the lesion manifests one pattern while the other half of the lesion manifests a different pattern (Fig. 7b.22).

Multicomponent DN have three or more patterns, including reticular, globular, and homogenous areas. The homogenous areas include blotches, which by definition are hyperpigmented, and structureless areas, which by definition are hypopigmented areas (NB: depigmented scar-like areas are not classified as structureless hypopigmented areas but rather as areas with regression). An alternative definition of a "multicomponent pattern" is a lesion that has three or more of the following structures: network, streaks, negative pigment network, chrysalis, dots, globules, blotches, structureless areas, and blue-white structures. If these structures are distributed symmetrically (at least in one axis) and in an organized manner, the lesion will usually prove to be a dysplastic nevus on biopsy (Fig. 7b.23). However, if distributed asymmetrically, or in a disorganized manner then the diagnosis of melanoma must be considered understanding dysplastic nevi can share the same dermoscopic features of melanoma and, therein lies the knotty problem of their differentiation (Fig. 7b.24).

INDETERMINATE DYSPLASTIC NEVI DERMOSCOPIC PATTERNS

Familiarity with the dermoscopic patterns exhibited by melanocytic nevi, which typically demonstrate symmetry of pattern, structures, and colors, assists in distinguishing benign from malignant melanocytic lesions. Identification of these benign dermoscopic patterns in a lesion that appears suspicious to the naked eye usually will alleviate concerns for melanoma and directs the management toward conservative clinical followup. Although dermoscopy allows many DN to be correctly identified as benign, even dermoscopy experts are challenged by a subset of indeterminate DN (i.e., multicomponent pattern) that are difficult, if not impossible, to differentiate from melanoma (Figs. 7b.23–7b.26). Excisional biopsy or short-term mole monitoring (i.e., short-term mole monitoring criteria include melanocytic lesions without evidence of melanoma, moderately atypical, flat or slightly raised lesions without a history of change, or mildly atypical lesions with a history of change) is recommended for most of such melanoma mimicking lesions. Although short-term mole monitoring can greatly increase specificity, this technique should never be employed in monitoring indeterminate nodular lesions. Such lesions should be biopsied without delay since even modest delays in the diagnosis of nodular melanoma can have deleterious consequences. With that said, with experience, the vast majority of DN can be recognized as benign lesions that do not have to be biopsied, but even such nevi should be followed by periodic patient self-examination and periodic physician-based examination remembering that these patients are at increased risk for developing melanoma and melanomas may on occasion arise in association with atypical nevi.

As stated above, recognition of the commonly encountered benign dermoscopic patterns of melanocytic neoplasms can help in the evaluation of clinically suspected lesions. However, some benign nevi may deviate from these well-defined dermoscopic patterns (Figs. 7b.24–7b.26) or reveal melanoma-specific structures as listed in Table 7b.2. Lesions with atypical structures or any variation from the symmetry and even distribution of colors and structures associated with benign patterns should be viewed with caution. An important approach to the differentiation of melanoma from DN is the degree of architectural order *versus* disorder present in the lesion (see chapter 6f, "The CASH algorithm"). Another

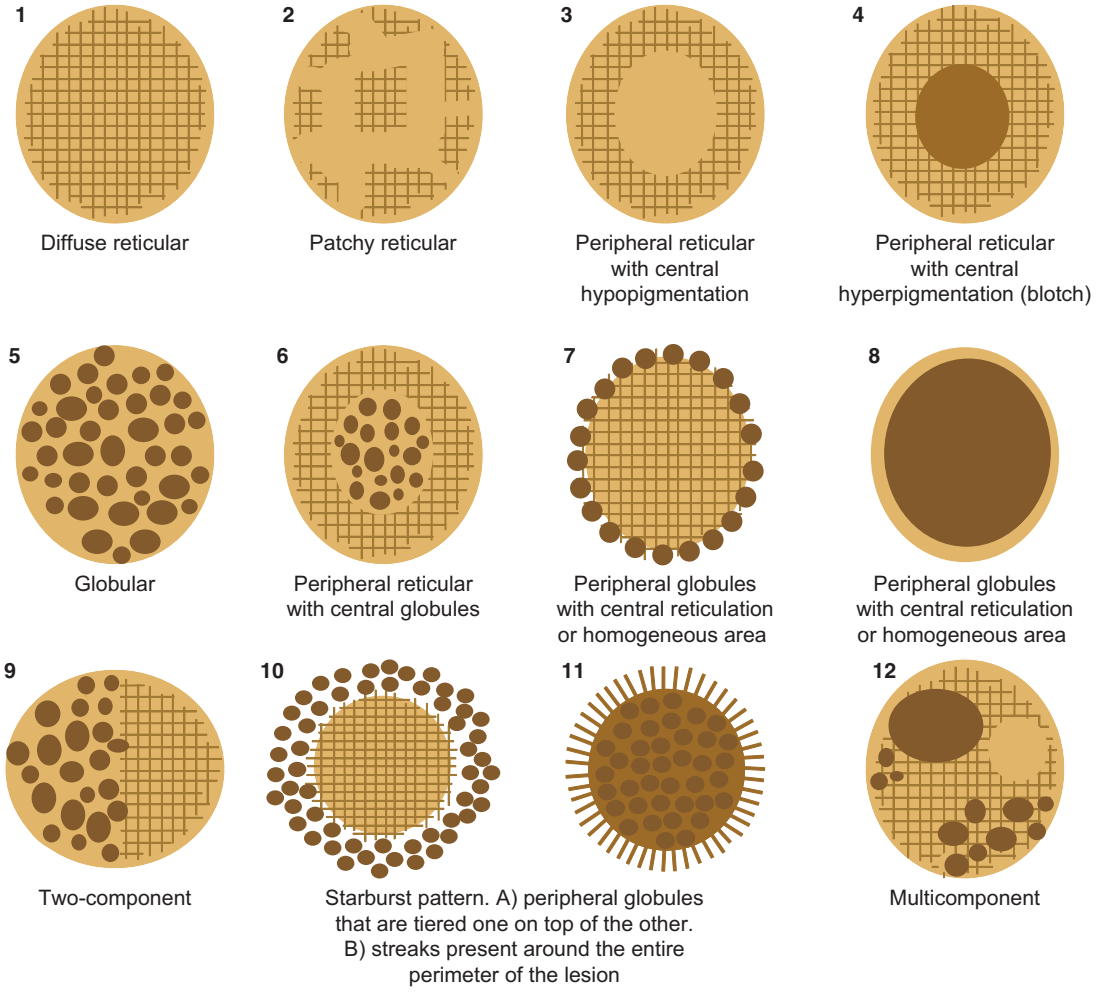


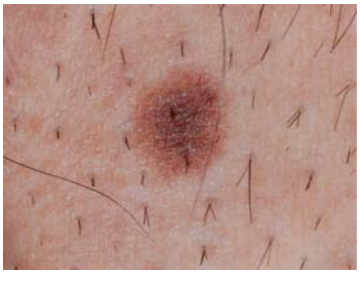
Figure 7b.3 A schematic of the most frequently encountered patterns in CMN, Spitz, and acquired nevi. The first nine patterns are commonly seen in acquired nevi, including dysplastic nevi. Dysplastic nevi can also manifest pattern #10 and #12 but such lesions should be viewed with suspicion since melanoma can also present with a similar pattern. Patterns 1, 2, 5, 6, and 8 are commonly seen in CMN. CMN can also manifest pattern #12, making it difficult to differentiate them from melanoma. Spitz nevi often manifest a starburst pattern as shown in pattern #10 and #11.

important component of the analysis is the findings revealed by careful medical history, especially including the evolution (change) and symptomatology (especially pruritus, pain, formication, spontaneous crusting, or bleeding) of the lesion. In general, if the lesion manifests one of the benign patterns (Table 7b.1) depicted in Figure 7b.3 and have none of the melanoma-specific structures listed in Table 7b.2 then the lesion can be considered benign. If the lesion manifests an overall benign pattern, but also has one of the melanoma-specific structures listed in Table 7b.2 then the lesion should be biopsied or subjected to short-term mole monitoring. The decision to biopsy or monitor will be greatly influenced by whether or not the lesion is a dermoscopic outlier lesion, whether or not it manifests a pattern similar to neighboring nevi and whether or not it is palpable (nodular). For lesions that do not manifest one of the benign nevus patterns while at the same time revealing at least one of the melanoma-specific structures listed in Table 7b.2, a biopsy should be strongly considered to rule out melanoma. Lastly, if the lesion does not adhere to one of the benign nevus patterns and has no melanoma-specific structures then the lesion can be monitored or biopsied. The decision to biopsy or monitor will be greatly influenced by whether or not the lesion is a dermoscopic outlier lesion (appears different compared with surrounding nevi), whether or not it manifests a pattern similar to neighboring nevi and whether or not it is palpable (nodular). Based on the aforementioned management outline it should be clear that the principal management decision with indeterminate lesions is excisional biopsy *versus* short-term monitoring. Although the decision to biopsy or monitor will be influenced greatly by whether or not the lesion is a dermoscopic outlier lesion, whether or not it manifests a pattern similar to neighboring nevi and whether or not it is palpable (nodular), the decision will also be influenced by the physician's experience; the patient's history with regard to the lesion (i.e., the physician should not dismiss a patient that insists the lesion should be removed); the patient's total mole count (i.e., the threshold for excision is lower in a patient with a single atypical lesion than in a patient floridly expressing DN); the availability of the total-cutaneous photographs and/or sequential digital monitoring; and the anticipated patient compliance with followup (Argenziano et al., 2008).

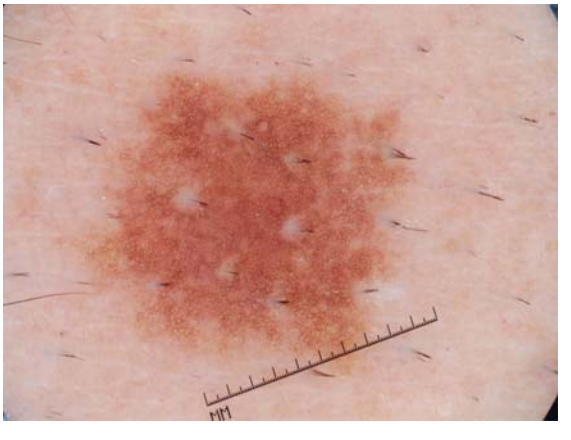
Although distinguishing between some DN and melanoma can be difficult, there is reason for optimism. The development of new criteria may improve the differentiation of indeterminate lesions, which in turn may shrink the subset of lesions subjected to biopsy. Current studies are also considering the use of polarized *versus* nonpolarized light dermoscopy; confocal microscopy; automated (classification by "computer vision" analysis); and other new emerging technologies to help in this endeavor. Also, the advent of teledermoscopy is upon us by which high-quality dermoscopic images can be instantly sent worldwide by Internet to expert dermoscopists who are able to render their interpretations of difficult lesions and assist in the therapeutic management decisions.

Table 7b.2 Melanoma-specific Structures

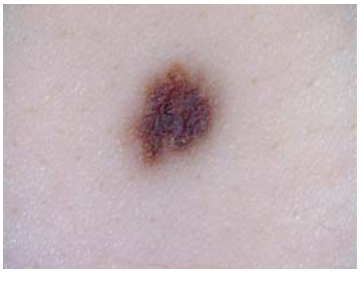
Dermoscopic structure	Description	Histopathologic correlate
Atypical pigment network	Reticulated grid of heterogenous brown lines with focal broadened, thickened, or darkened areas that may end abruptly at the periphery	Atypical lentiginous or nested melanocytic proliferation along the dermoepidermal junction
Streaks (radial streaming or pseudopods)	Linear, radially oriented pigmented projections at the perimeter of a lesion that radiate from the tumor towards normal skin	Confluent junctional nests of melanocytes at the periphery (radial growth phase)
Negative pigment network	Serpiginous interconnecting hypopigmented lines, which surround irregularly shaped pigmented structures that resemble elongated curvilinear globules	Thin elongated rete ridges that are relatively hypopigmented compared with the large irregular melanocytic nests that are located within a widened papillary dermis. Alternatively, bridging of adjacent rete ridges may also contribute to the appearance of a negative network
Crystalline	Fine, white, shiny streaks within a lesion, visible only under polarized light dermoscopy	Remodeled or new dermal collagen
Atypical dots and globules	Dark, punctate, or round to oval structures of varying shape, size, color, distribution within a lesion	Junctional or dermal nests of melanocytes; dots can also represent pagetoid nests
Irregular blotches	Dark areas of diffuse pigmentation with irregular shapes, multiple hues, sharp margins, or eccentric locations	Melanin pigmentation throughout the epidermis or dermis or both
Blue-white veil over raised areas	Confluent blue pigmentation with an overlying white "ground glass" haze	Compact orthokeratosis overlying melanophages, melanocytes, or free melanin in the papillary dermis
Regression structures, including blue-white veil over flat areas, peppering or granularity, and scar-like depigmentation	White areas, blue areas, or both, overlying nonpalpable portions of a lesion. The peppering consists of fine gray-blue granules	Fibrosis within the papillary dermis and melanosis (melanophages and free melanin "dust" within the dermis)
Atypical vascular structures	Milky red areas, dotted, linear, serpentine, or twisted red structures	Tumor-induced neoangiogenesis
Peripheral brown structureless areas	Peripherally arranged light brown or tan areas of variable shape lacking perceptible structures	Flattening of the rete ridges with pagetoid spread of atypical melanocytes



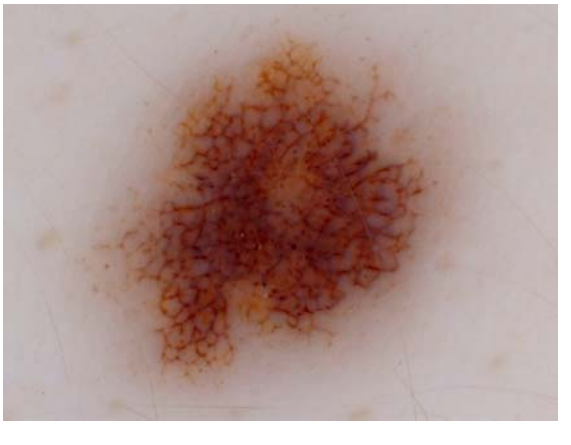
▲ **Figure 7b.4a** Clinical image.



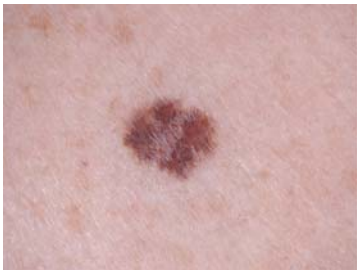
◀ **Figure 7b.4b** Dermoscopy reveals a typical reticular pattern nevus.



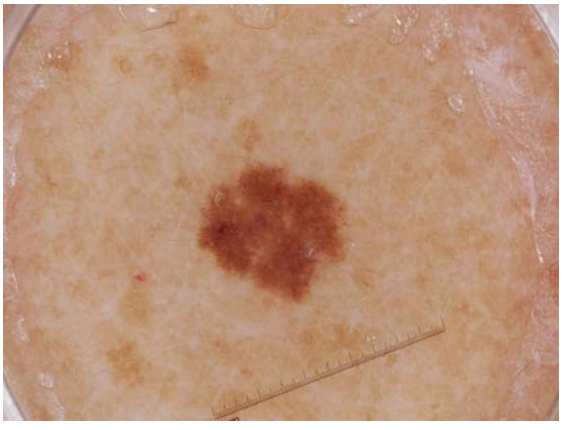
▲ **Figure 7b.5a** Clinical image.



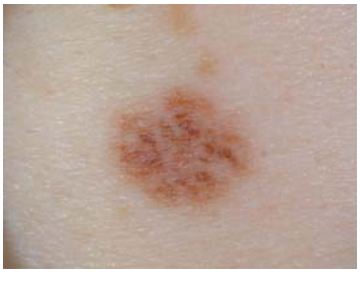
◀ **Figure 7b.5b** Dermoscopy reveals a diffuse reticular pattern nevus. Dots overlying the network lines can be ignored. They represent small junctional nests located at the tips of rete ridges—a feature that speaks in favor of a benign nevus.



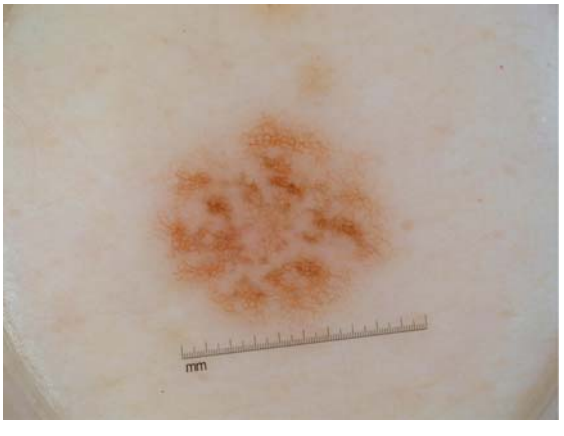
▲ **Figure 7b.6a** Clinical image.



◀ **Figure 7b.6b** Dermoscopy reveals a nevus with a diffuse reticular pattern. Dots overlying the network lines represent small junctional nevus nests located at the tips of the rete ridges. This is a common finding in benign nevi and can thus be ignored.

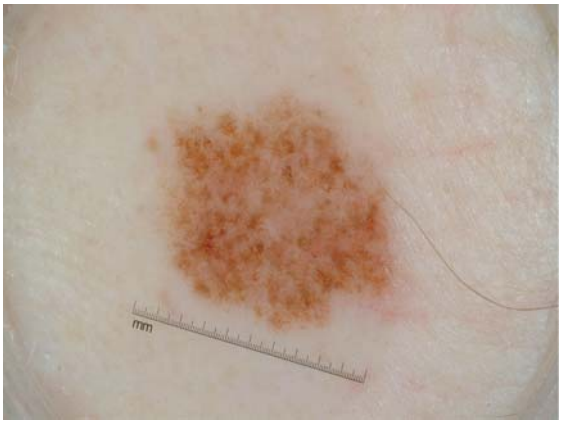


▲ **Figure 7b.7a** Clinical image.



◀ **Figure 7b.7b** Dermoscopy reveals a patchy network pattern nevus.

▲ **Figure 7b.8a** Clinical image.

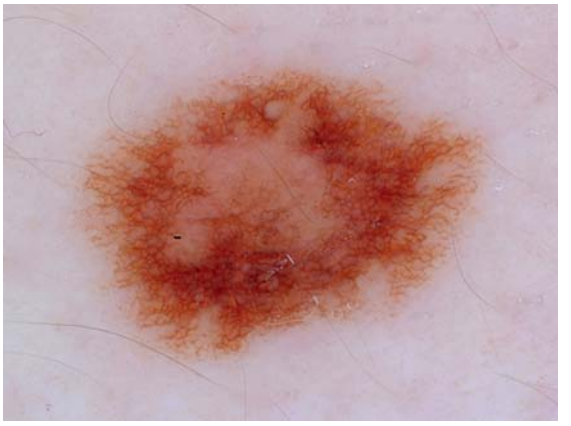


◀ **Figure 7b.8b** This nevus has a patchy network pattern as seen with dermoscopy.

▲ **Figure 7b.9a** Clinical image.

◀ **Figure 7b.9b** This nevus has a pattern with peripheral network with central hypopigmentation. This pattern is commonly seen in fair skin individuals.

▲ **Figure 7b.10a** Clinical image.

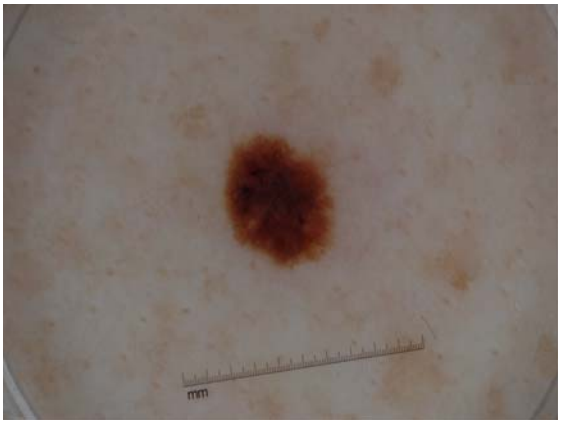


◀ **Figure 7b.10b** Dermoscopy reveals a nevus with peripheral reticulation (network) and central hypopigmentation.

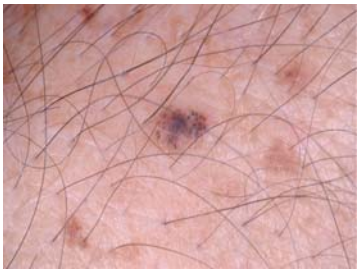
▲ **Figure 7b.11a** Clinical image.

◀ **Figure 7b.11b** Dermoscopy of this nevus shows a nevus with a peripheral network and central hyperpigmentation (blotch). The blotch in such nevi can often be removed by tape stripping. Nevi with this pattern are commonly seen in darker skin individuals.

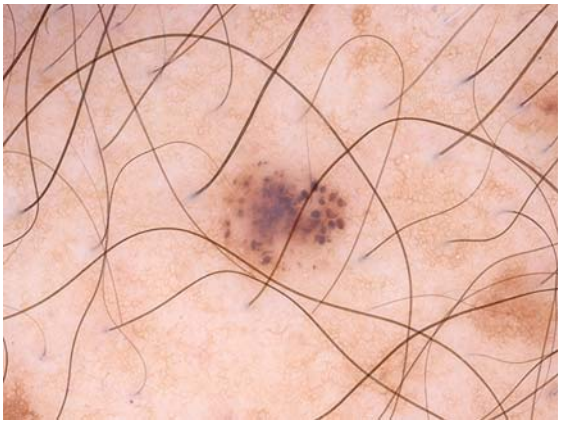
▲ **Figure 7b.12a** Clinical image.



◀ **Figure 7b.12b** Dermoscopy of this nevus shows a pattern with peripheral network and central hyperpigmentation.

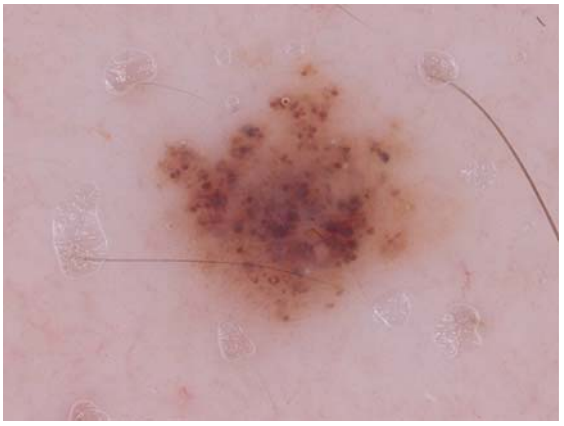


▲ **Figure 7b.13a** Clinical image.



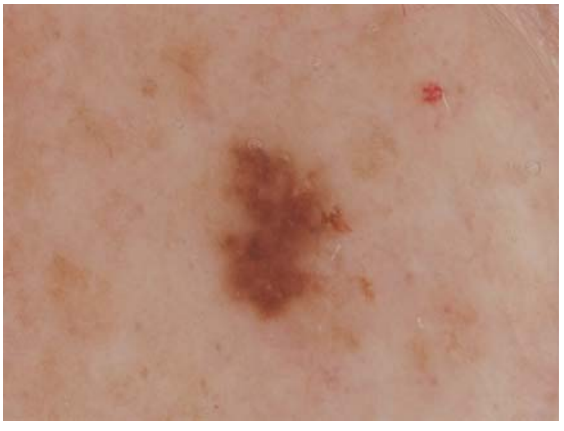
◀ **Figure 7b.13b** Dermoscopy reveals a nevus with a globular pattern.

▲ **Figure 7b.14a** Clinical image.

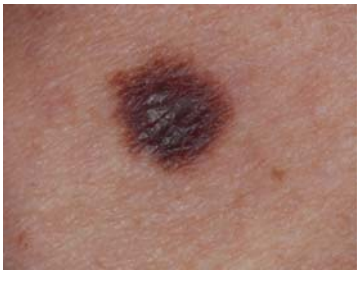


◀ **Figure 7b.14b** Dermoscopy of this biopsy-proven dysplastic nevus reveals a globular pattern.

▲ **Figure 7b.15a** Clinical image.

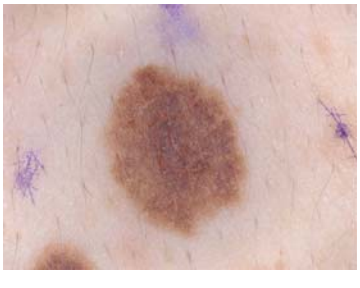


◀ **Figure 7b.15b** This nevus has a homogenous pattern.

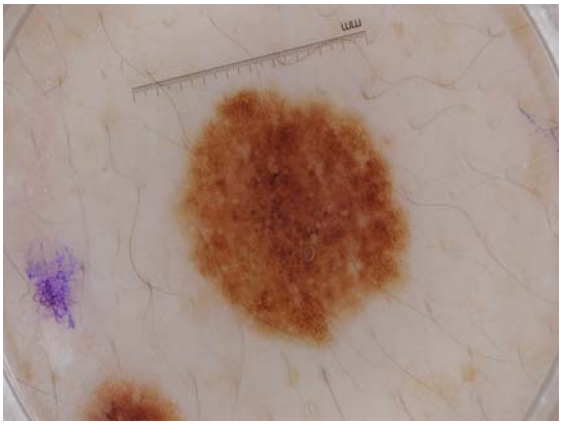


▲ **Figure 7b.16a** Clinical image.

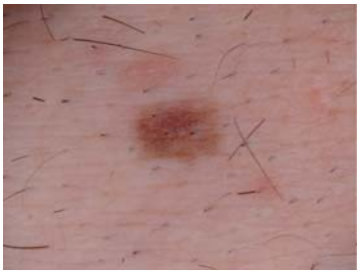
◀ **Figure 7b.16b** This nevus has a homogenous pattern.



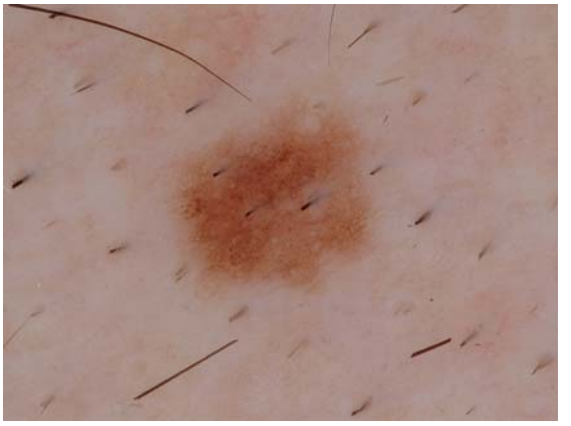
▲ **Figure 7b.17a** Clinical image.



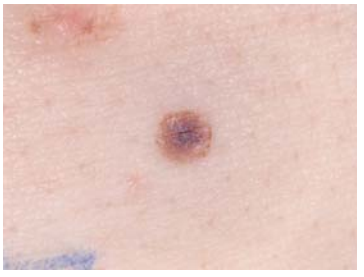
◀ **Figure 7b.17b** Dermoscopy of this nevus reveals a pattern consisting of peripheral network with central globules. This is a pattern often seen in small congenital nevi located on the torso.



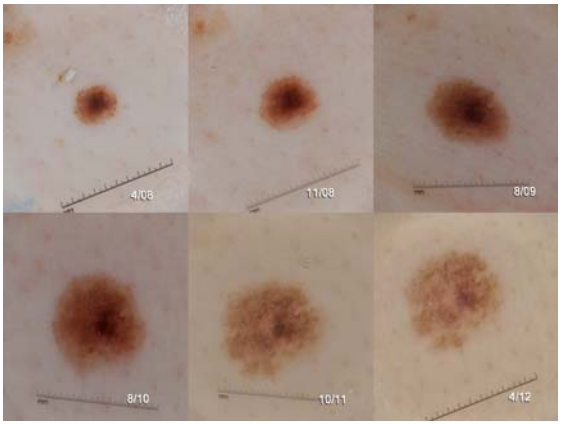
▲ **Figure 7b.18a** Clinical image.



◀ **Figure 7b.18b** This nevus has a peripheral network pattern with central globules.



▲ **Figure 7b.19a** Clinical image.



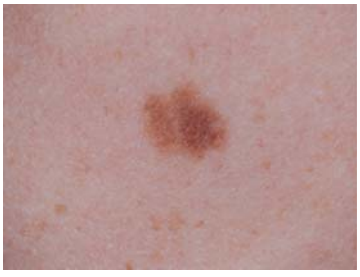
◀ **Figure 7b.19b** Dermoscopy of this nevus reveals a peripheral globular pattern. This pattern is often seen in nevi that are enlarging as is evident in the sequence of images of this nevus taken over time. Once the nevus enters senescence the globules are no longer visible and the lesion stops growing as can be seen in this lesion.

▲ **Figure 7b.20a** Clinical image.

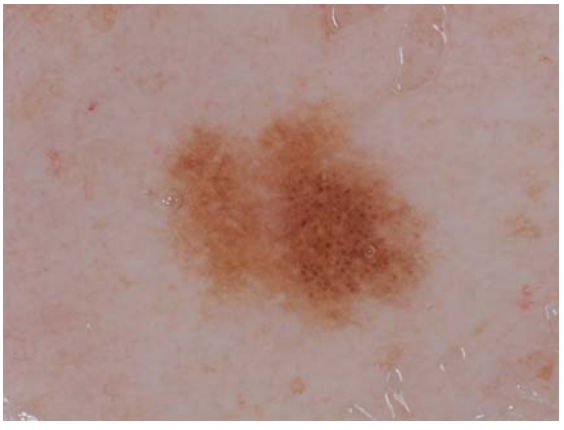
◀ **Figure 7b.20b** Dermoscopy reveals a starburst pattern consisting of peripheral globules that are tiered, one on top of the other. Notice how this differs from the peripheral globular pattern shown in Figure 7b.19 where only one rim of globules are present. This tiered globular patter can be seen in Spitz nevi and in DN with spitzoid features. This lesion was biopsied and the pathology was consistent with a dysplastic nevus with spitzoid features.

▲ **Figure 7b.21a** Clinical image.

◀ **Figure 7b.21b** This is a Spitz nevus displaying a classic starburst pattern. The streaks at the periphery can consist of radial streaming or pseudopods.

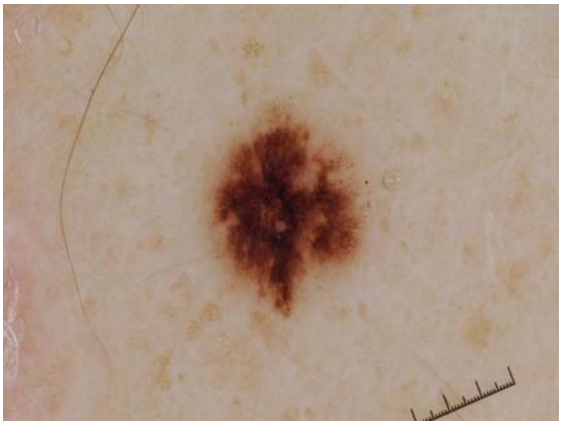


▲ **Figure 7b.22a** Clinical image.



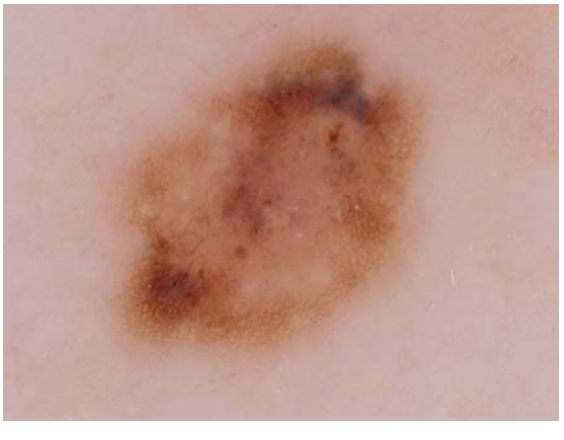
◀ **Figure 7b.22b** Dermoscopy reveals a two-component pattern nevus.

▲ **Figure 7b.23a** Clinical image.



◀ **Figure 7b.23b** This nevus has a relatively symmetric multicomponent pattern. It has network, blotches, and a few globules. It is clinically often difficult to rule out melanoma in lesions with this pattern. If this is a clinical or dermoscopic outlier lesion then a biopsy would be the prudent management decision. However, if the pattern in this nevus is similar to the patient's other nevi then monitoring would be an acceptable alternative to biopsy.

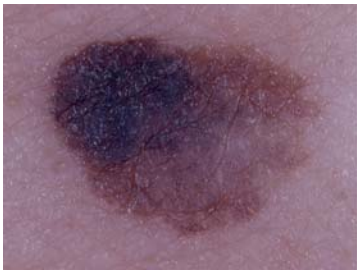
▲ **Figure 7b.24a** Clinical image.



◀ **Figure 7b.24b** Dermoscopy reveals a symmetric multicomponent pattern. This acquired lesion has network, globules, homogenous areas, and blue-white veil. The differential diagnosis for this lesion is between dysplastic nevus and melanoma. Excisional biopsy and pathology proved that this was a dysplastic nevus.

▲ **Figure 7b.25a** Clinical image.

◀ **Figure 7b.25b** Dermoscopy of this lesion reveals a multicomponent pattern with network, dots, blue-white veil, and peppering. Excisional biopsy and pathology of this lesion was consistent with a dysplastic nevus.



▲ **Figure 7b.26a** Clinical image.

◀ **Figure 7b.26b** Dermoscopy of this lesion reveals a multicomponent pattern with atypical network, dots, blotch, blue-white to pink veil, and peppering. Excisional biopsy and pathology of this lesion revealed that this was a dysplastic nevus.

Key Points

- Dysplastic (a.k.a. atypical) nevi (DN) are benign melanocytic neoplasms that clinically share some or all of the ABCDE (A, asymmetry; B, border irregularity; C, color variability; D, diameter >6 mm; E, evolving) features of melanoma. Currently, the clinical differentiation of DN from MM is one of the most difficult and trying challenges in cutaneous oncology.
- Dermoscopically, DN can also share some or all of the features of melanoma. However, in the vast majority of DN their benign nature is readily recognized by expert dermoscopists.
- The principal method used in the dermoscopic differentiation of DN from melanoma is the recognition of global patterns and local features. In addition, architectural order *versus* disorder provides useful information.
- Despite the marked improvement in diagnostic accuracy afforded by dermoscopy (compared with clinical "naked-eye" assessment alone) there remains a substantial proportion of DN that fall into the "indeterminate" range that require further investigation such as biopsy, short-term mole monitoring or confocal microscopy.
- For those melanocytic neoplasms that have some dermoscopic atypicalities (but not to the degree usually seen in melanoma), short-term (three-month) monitoring can be employed if the patient is reliable in keeping appointments and the lesion is not nodular.
- Newer technologies are on the horizon that may add further information on differentiation of DN from melanoma.

REFERENCES

Altamura, D., Avramidis, M. & Menzies, S.W., 2008, Assessment of the optimal interval for and sensitivity of short-term sequential digital dermoscopy monitoring for the diagnosis of melanoma. *Arch Dermatol*, 144, 502–6.

Argenziano, G., Catricalà, C., Ardigo, M., et al., 2011, Dermoscopy of patients with multiple nevi: improved management recommendations using a comparative diagnostic approach. *Arch Dermatol*, 147, 46–49.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Mordente, I., Ferrara, G., et al., 2008, Dermoscopic monitoring of melanocytic skin lesions: clinical outcome and patient compliance vary according to follow-up protocols. *Br J Dermatol*, 159, 331–6.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Banky, J.P., Kelly, J.W., English, D.R., Yeatman, J.M. & Dowling, J.P., 2005, Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. *Arch Dermatol*, 141, 998–1006.

Bevona, C., Goggins, W., Quinn, T., Fullerton, J. & Tsao, H., 2003, Cutaneous melanomas associated with nevi. *Arch Dermatol*, 139, 1620–4; discussion 1624.

Blum, A., Soyer, H.P., Garbe, C., et al., 2003, The dermoscopic classification of atypical melanocytic naevi (Clark naevi) is useful to discriminate benign from malignant melanocytic lesions. *Br J Dermatol*, 149, 1159–64.

Fuller, S.R., Bowen, G.M., Tanner, B., Florell, S.R. & Grossman, D., 2007, Digital dermoscopic monitoring of atypical nevi in patients at risk for melanoma. *Dermatol Surg*, 33, 1198–206; discussion 1205–6.

Henning, J.S., Stein, J.A., Yeung, J., et al., 2008, CASH algorithm for dermoscopy revisited. *Arch Dermatol*, 144, 554–5.

Hofmann-Wellenhof, R., Blum, A., Wolf, I.H., et al., 2001, Dermoscopic classification of atypical melanocytic nevi (Clark nevi). *Arch Dermatol*, 137, 1575–80.

Kittler, H., Guitera, P., Riedl, E., et al., 2006, Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. *Arch Dermatol*, 142, 1113–19.

Kittler, H., Seltenheim, M., Dawid, M., et al., 2000, Frequency and characteristics of enlarging common melanocytic nevi. *Arch Dermatol*, 136, 316–20.

Menzies, S.W., 2009, Dermoscopy: An Atlas, Sydney: McGraw-Hill.

Menzies, S.W., Gutenev, A., Avramidis, M., Batrac, A. & McCarthy, W.H., 2001, Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. *Arch Dermatol*, 137, 1583–9.

Roesch, A., Burgdorf, W., Stolz, W., Landthaler, M. & Vogt, T., 2006, Dermatoscopy of "dysplastic nevi": a beacon in diagnostic darkness. *Eur J Dermatol*, 16, 479–93.

Stolz, W., Riemann, A., Cognetta, A., et al., 1994, ABCD rule of dermatoscopy: a new practical method for early recognition of malignant melanoma. *Eur J Dermatol*, 4, 521–7.

Tucker, M.A., Fraser, M.C., Goldstein, A.M., et al., 2002, A natural history of melanomas and dysplastic nevi: an atlas of lesions in melanoma-prone families. *Cancer*, 94, 3192–209.

Tucker, M.A., Halpern, A., Holly, E.A., et al., 1997, Clinically recognized dysplastic nevi. A central risk factor for cutaneous melanoma. *JAMA*, 277, 1439–44.

7c Banal nevi and growing nevi

Iris Zalaudek

INTRODUCTION

Before reading this chapter, it is imperative to acknowledge the lack of consensus regarding the clinical criteria to define a banal nevus. In fact, the term "banal" is quite subjective and is influenced by one's experience, confidence, and the overall clinical scenario. Although dermoscopy has been shown to improve the ability to recognize banal nevi and differentiate them from atypical lesions, it still remains a matter of "subjective" judgment whether a nevus will be classified as banal or not. With that being said, in this chapter simple criteria are described that allow the clinician, in most situations, to diagnose a banal nevus and to differentiate it from an atypical melanocytic lesion.

CLINICAL DEFINITION

A clinically banal nevus can be defined as a lesion lacking the clinical ABCD (asymmetry, border irregularity, color variegations, diameter >5 mm) criteria, which have been established for the identification of atypical nevi (also called dysplastic nevi or Clark nevi) and melanoma. In other words, a clinically banal nevus is a symmetric (usually with a round or oval shape), uniform pigmented (usually brown) lesion with regular borders, and a size that is usually less than 5 mm in greatest diameter. Furthermore, banal nevi can be flat, slightly elevated, or raised with a smooth or papillomatous surface.

DERMOSCOPIC DEFINITION

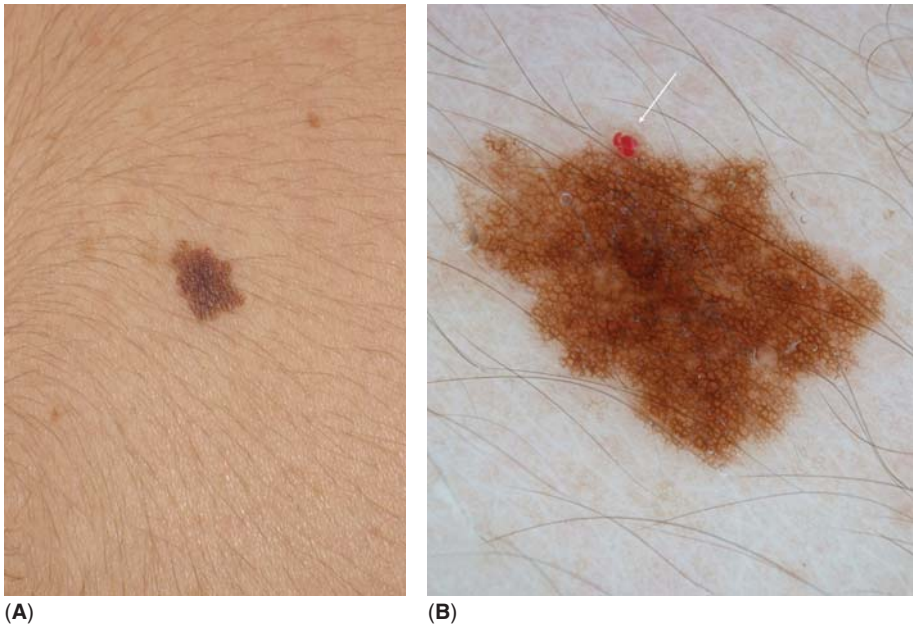
Dermoscopically, a banal nevus can be defined as a lesion revealing a striking symmetry of colors and structures. Importantly, symmetry in dermoscopy refers to a regular distribution of colors and structures resulting in a symmetric pattern. The shape, contour, and size of the nevus do not factor into whether the lesion is dermoscopically symmetric or asymmetric. Accordingly, a clinically large and asymmetric nevus (Fig. 7c.1) can be dermoscopically symmetric, whereas a clinically regular-shaped and small nevus may reveal dermoscopic asymmetry (Fig. 7c.2).

THE CONCEPT OF THE PREDOMINANT NEVUS TYPE

In addition to the recognition of dermoscopic patterns associated with a single individual nevus, the knowledge that most individuals harbor a predominant nevus pattern among all their nevi (repetitive patterns that are seen in more than 30% of all nevi) is an important concept to understand. The fact that most individuals have nevi that resemble each other like siblings (i.e., moles breed true or signature nevus concept) permits identification of atypical lesions that deviate from the predominant nevus pattern (*concept of the ugly duckling sign*) (Grob et al., 1998; Gachon et al., 2005; Hofmann-Wellenhof et al., 2001; Scope et al., 2008). The recognition of the predominant nevus pattern requires the examination of all nevi in a given individual, which has been shown to take on average less than 3 minutes (Zalaudek et al., 2008).

DERMOSCOPIC PATTERNS OF NEVI AND HISTOPATHOLOGIC CORRELATES

Generally, banal nevi reveal either a single or at most a combination of two colors and morphologic structures. The most common colors seen in banal nevi are different shades of brown and the most common patterns are the reticular, reticular–globular, globular, or cobblestone pattern. These dermoscopic criteria correspond to specific histopathologic correlates (Zalaudek et al., 2006). The knowledge of the dermoscopic–histopathologic correlates aids in the better understanding of features associated with banal nevi.



(**A**) (**B**)

Figure 7c.1 Clinically this nevus reveals border irregularity and an asymmetric shape (**A**), while dermoscopy (**B**) shows a striking symmetry of colors (brown) and structures (reticular pattern). The red globule-like structure (*arrow*) is a small angioma in close vicinity to the nevus.

Colors

Colors in dermoscopy are important because they allow estimations about the location of pigmented cells in the different compartments of the skin. Black and brown color is due to pigmentation in the superficial and basal layers of the epidermis, respectively. Gray is due to pigmentation in the upper dermis and can be related to pigmented melanocytes or pigment-laden melanophages in areas of regression. Blue color signifies a dense infiltrate of pigmented cells in the upper and deeper parts of the dermis. Other colors such as white or red correspond to dermal fibrosis or neovascularization. Among these colors, black, brown, and to a lesser extent gray (due to pigmented melanocytes and NOT due to regression) are the most common colors seen in banal nevi.

Pigment Distribution

Six common types of pigment distributions were originally described for atypical nevi (synonyms: Clark nevi or dysplastic nevi); however, these six pigment distributions also apply to banal nevi (Hofmann-Wellenhof et al., 2001). The original six types are the uniform pigmentation (Fig. 7c.3), the multifocal hyper-/hypopigmentation (Fig. 7c.4), the central hyperpigmentation (Fig. 7c.5), the central hypopigmentation (Fig. 7c.6), the eccentric hyperpigmentation (Fig. 7c.7), and the eccentric hypopigmentation (Fig. 7c.8).

Banal nevi most commonly reveal a uniform or central hyperpigmentation or central hypopigmentation, while the multifocal hyper-/hypopigmentation occurs more commonly in reticular nevi with a size larger than 5 mm. The remaining types of pigmentation are rather infrequent, but for completeness are mentioned here.

Nevi with eccentric hyperpigmentation are often referred to as melanoma simulators, since this pigmentation type may also occur in melanoma. However, in nevi the focus of hyperpigmentation typically reveals the same pattern as seen in the rest of the nevus, whereas melanoma often exhibits either an overall asymmetry of patterns or different features within the area of hyperpigmentation (Arevalo et al., 2008).

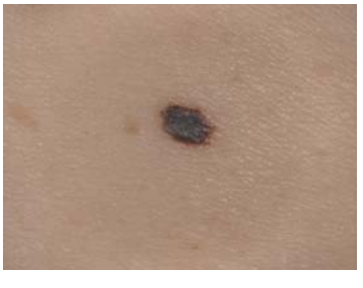
Nevi with eccentric hypopigmentation are even less frequent than nevi with eccentric hyperpigmentation, but should be differentiated from an eccentric focus of regression in an atypical melanocytic lesion. This can be facilitated by examining the surrounding skin, since areas of hypopigmentation reveal the same color or slightly darker color as compared with the background color of surrounding normal skin (Fig. 7c.9), whereas regression appears whiter than the surrounding skin and is often associated with gray dots (peppering or granularity) (Fig. 7c.10) (Zalaudek et al., 2004; Braun et al., 2007).

Nevus Patterns

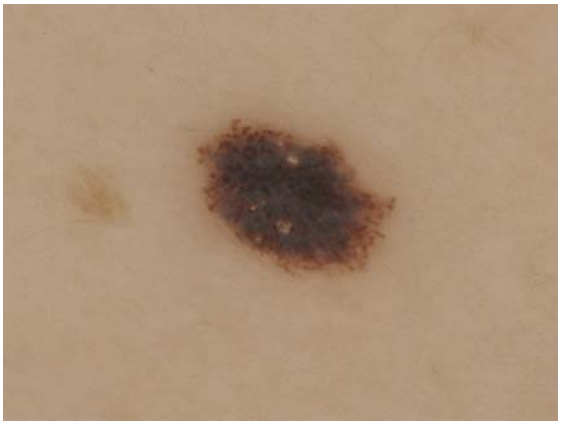
The most common patterns seen in nevi are depicted schematically in Figure 7c.11.

Reticular Pattern

The reticular or network pattern consists of regularly distributed and shaped brownish interconnected lines over a background of tan diffuse pigmentation that typically fade out towards the periphery (Fig. 7c.12) (Argenziano et al., 2003). Histopathologically this pattern corresponds to pigmented melanocytes arranged in small nests or in single units at the dermoepidermal junction (DEJ) of the tips of elongated rete ridges.



▲ **Figure 7c.2a** Clinically this nevus is a symmetric lesion.



◀ **Figure 7c.2b** However, dermoscopy reveals an asymmetric pattern.

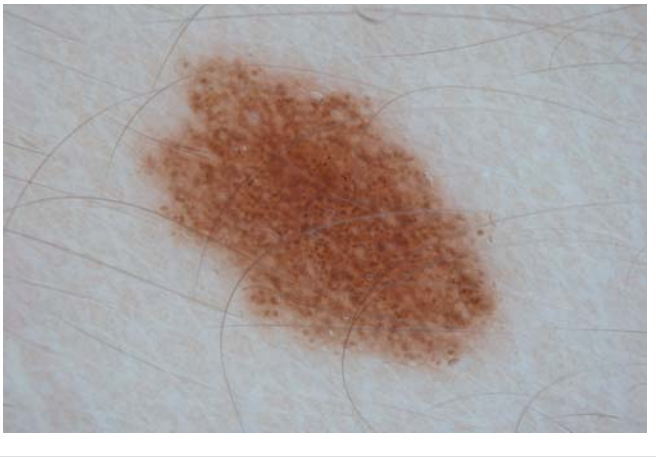


Figure 7c.3 Dermoscopy of a nevus with uniform pigment distribution.

Figure 7c.4 Dermoscopy of a nevus showing a multifocal pigment distribution characterized by small areas revealing dark and light brown color.

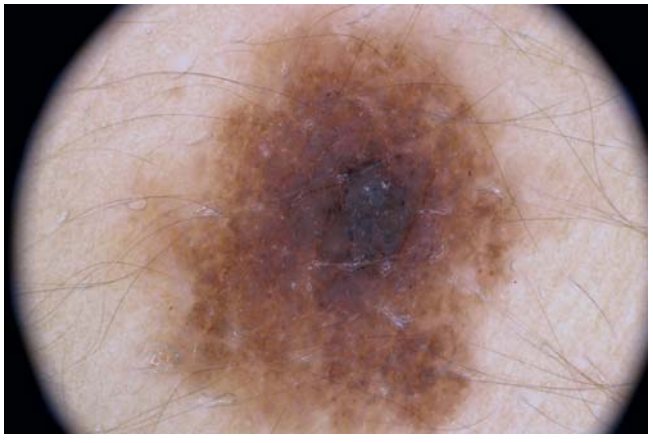


Figure 7c.5 Dermoscopy of a nevus showing central hyperpigmentation.

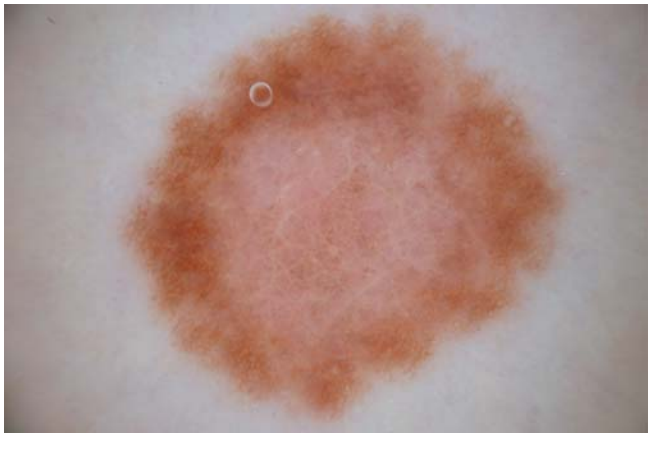


Figure 7c.6 Dermoscopy of a nevus showing central hypopigmentation.

Figure 7c.7 Dermoscopy of a nevus revealing eccentric hyperpigmentation. Note that the pattern (in this case a reticular pattern) corresponding to the area of hyperpigmentation is the same as in the rest of the nevus.

Figure 7c.8 Nevus showing dermoscopically eccentric hypopigmentation. This pigmentation type is quite infrequent, but it is important to differentiate it from an eccentric focus of regression. This can be facilitated by examining the surrounding normal skin. The structureless hypopigmented area will have the same or slightly darker hue as compared with the normal uninvolved skin.

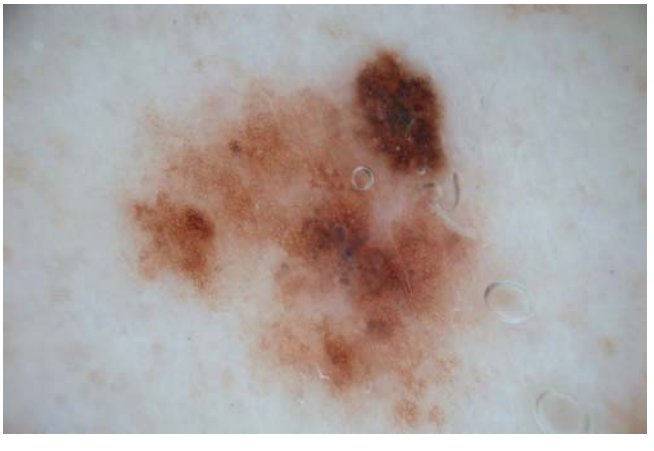


Figure 7c.9 Melanoma showing an eccentric focus of hyperpigmentation. This lesion has a striking asymmetry of colors and structures, the eccentric hyperpigmented focus reveals features different to the ones seen in the other areas within this lesion.

Figure 7c.10 Dermoscopy of melanoma showing an eccentric area of regression. Note that the area of regression appears whiter than the surrounding skin and is associated with gray peppering.

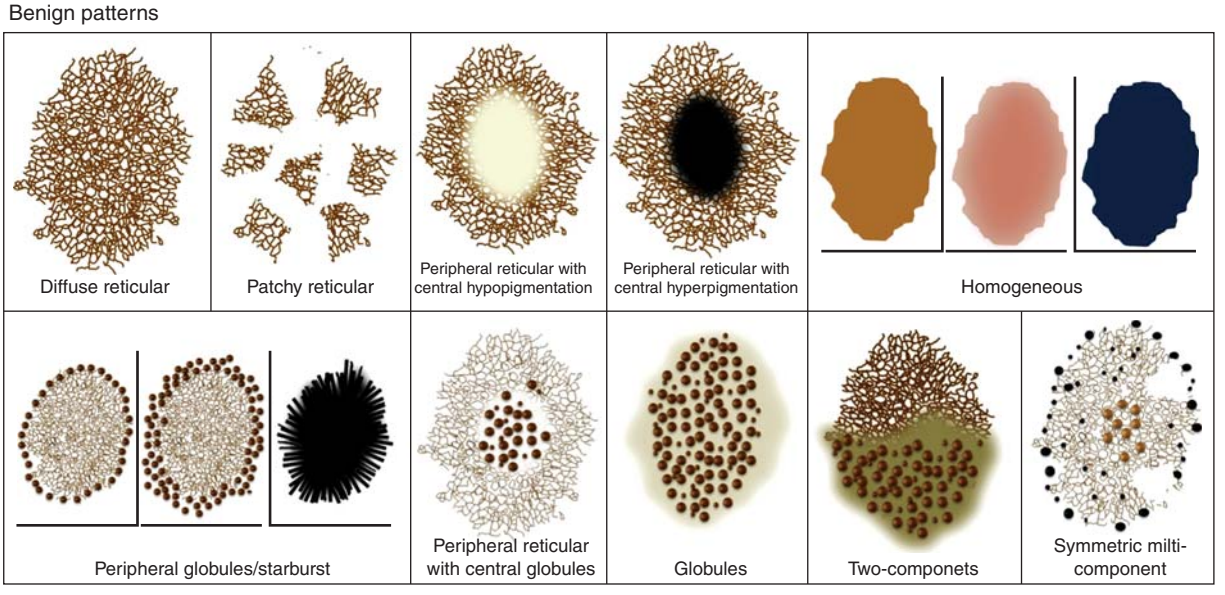


Figure 7c.11 Schematic representation of the most common patterns seen in nevi.

Figure 7c.12 Dermoscopy of a reticular nevus reveals a regular network with regular network meshes and holes. The pigmented lines typically fade out at the periphery.

Figure 7c.13 Nevi of individuals with a fair skin type are dermoscopically characterized by a light brown color, reticular pattern, and central hypopigmentation.

Accordingly, the reticular pattern is the dermoscopic hallmark of clinically flat nevi that reveal on histopathology a prominent junctional or lentiginous component (Zalaudek et al., 2006).

The knowledge that brown or black color in dermoscopy correlates with pigmentation in the epidermis explains why reticular nevi typically reveal either a brown or brown to black color. Furthermore, this knowledge also helps explain why the presence of other colors, such as gray, white, blue, or red, should be considered atypical in an otherwise reticular nevus.

Epidemiology

Nevi with reticular pattern are variable in number and can occur at any body site, but appear most commonly randomly distributed on the trunk and extremities. Reticular pattern is the most common nevus pattern of nevi in adults (Zalaudek et al., 2006). Their predominant color and pigment distribution is influenced by the skin type of a given individual (Zalaudek et al., 2007). Individuals with a fair skin type (I or II) harbor commonly reticular nevi with a light brown color and central hypopigmentation or uniform pigmentation (Fig. 7c.13). In contrast, dark skin types (IV) typically harbor nevi with a dark brown to black color and central hyperpigmentation, also known as so-called black nevus or hypermelantoic nevus. The central hyperpigmentation is often due to a central black lamella corresponding histopathologically to pigmented parakeratosis (Fig. 7c.14). The dark lamella precludes the ability to visualize structures below the stratum corneum and it can be confused for a blotch, which is a feature commonly associated with melanoma. However, whereas a blotch cannot be removed by tape stripping the stratum corneum, the black lamella can easily be removed by tape stripping the stratum corneum. Once the lamella has been removed the clinician can easily visualize the underlying structures, such as a regular network, and render a diagnosis of a benign nevus with high degree of confidence (Fig. 7c.15).

Hypopigmented Variants

Hypopigmented variants of reticular nevi are infrequent and represent a major diagnostic challenge because they often reveal overlapping features with atypical nevi, Spitz nevi and most importantly hypopigmented or amelanotic melanoma. These nevi often reveal erythema, dotted vessels either alone or in combination with comma or linear vessels, and nonspecific shades of structureless brown pigmentation.

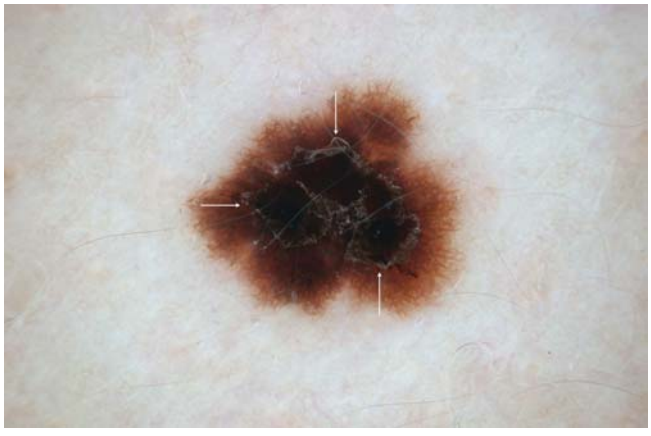
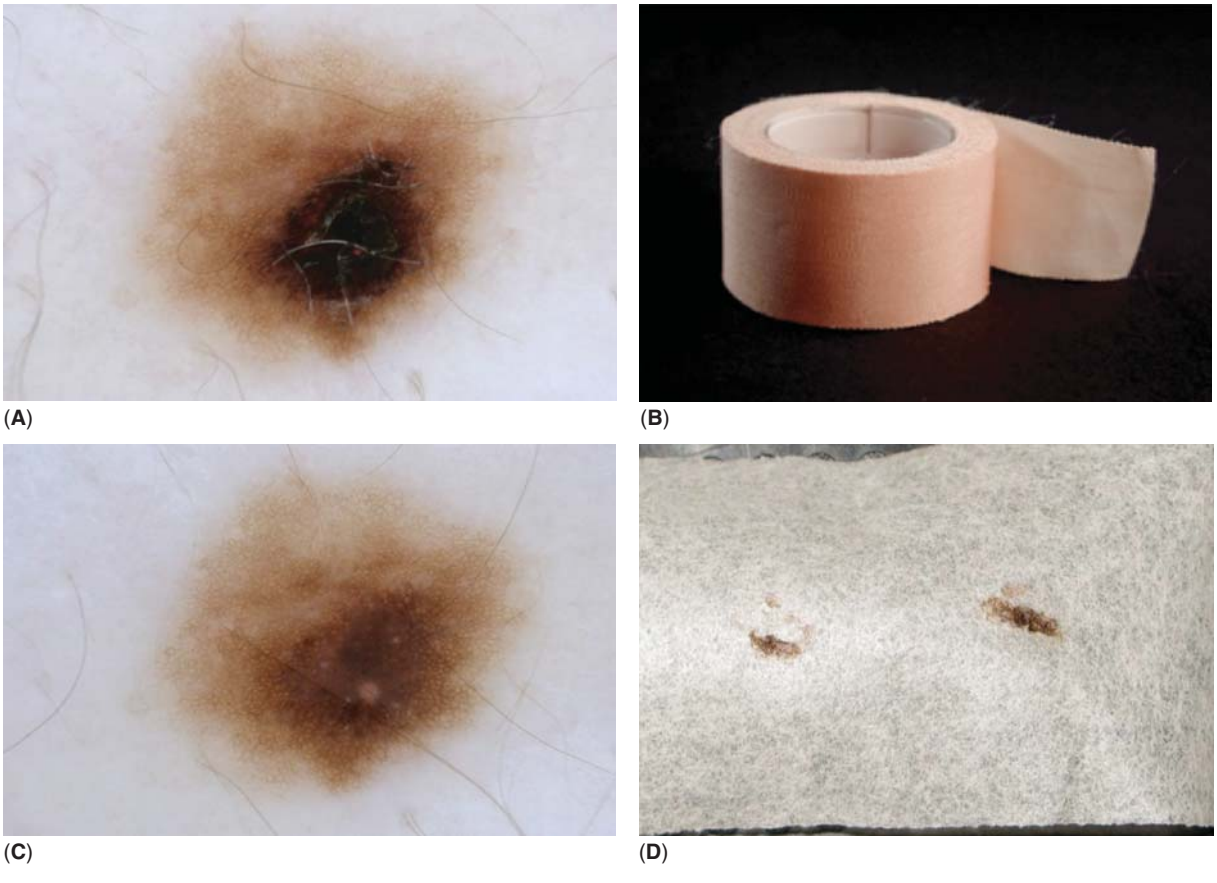


Figure 7c.14 Classic appearance of a nevus of an individual with dark skin type (so-called black nevus) exhibiting dark brown and black color, reticular network, and central hyperpigmentation. The central hyperpigmentation is caused by a black lamella (*arrow*) corresponding histopathologically to pigmented parakeratosis.

Figure 7c.16 Dermoscopically this globular nevus shows densely aggregated, uniformly sized small brown globules and a homogenous brown pigmentation. The globular pattern is the most typical pattern of nevi in childhood.



(**A**) (**B**) (**C**) (**D**)

Figure 7c.15 (**A**) Typical example of a black nevus showing a central black lamella covering an area of the nevus. After removing the superficial black lamella using tape stripping (**B**), the regular network of the nevus becomes clearly visible (**C**). Note the pigmented lamella scale attached to the tape (**D**).

Globular Pattern

The globular pattern is defined by the presence of densely aggregated, small round-to-oval structures revealing shades of brown or gray-black color (Fig. 7c.16) (Argenziano et al., 2003). Histopathologically, the globules correspond to small nests of melanocytes either in the superficial dermis and at the DEJ as often seen in compound nevi or nevi with congenital-like features (Zalaudek et al., 2006).

Epidemiology

Nevi with globular pattern are clinically often slightly elevated, few in numbers, and mostly located on the upper trunk. Although they are one of the most common nevus pattern in children, they can be seen in individuals of any age (Oliveria et al., 2004; Scope et al., 2008; Zalaudek et al., 2006). Some adults with few nevi may even harbor the globular type as the predominant nevus pattern. Similar to reticular nevi, the prevailing color

of globular nevi depends of the individuals' skin type. Fair-skinned individuals tend to manifest globular nevi with a light brown-gray color, whereas individuals with a dark skin type commonly reveal nevi showing dark brown-gray color. With that said, the vast majority of globular nevi reveal a uniform pigmentation.

Cobblestone Pattern

This pattern is considered a variation of the globular pattern, because it is characterized by larger, closely aggregated, and somewhat angulated brown-gray globule-like structures reminiscent of cobblestones. These large globules correspond histopathologically to large nests of nevomelanocytes in the upper and deeper parts of the dermis (i.e., dermal nevi or small congenital nevi) (Fig. 7c.17) (Argenziano et al., 2003; Zalaudek et al., 2008). Additional features that are often seen are terminal hairs, a few comedo-like openings, and/or small milia-like cysts know as starry milia cysts. It is not uncommon to see nevi with both regular globules and cobblestone globules within the same lesion (Fig. 7c.18).

Epidemiology

Similar to globular nevi cobblestone nevi are found few in numbers and are mostly located on the upper trunk and are seen throughout all ages (from infancy to elderly). However, cobblestone nevi are clinically larger and more raised, often with a papillomatous surface, as compared with noncobblestone globular nevi (Argenziano et al., 2007).

Hypopigmented Variants

Hypopigmented variants of both, globular and cobblestone nevi, are clinically easily recognized as dermal nevi Unna or Miescher type (Figs. 7c.19a and 7c.20a). Notably, dermoscopic evaluation of these nevi often causes initial diagnostic difficulties, particularly for beginners in dermoscopy. This can be explained by the fact that these nevi often reveal an asymmetry of colors and structures composed by irregularly distributed pigmented globules or cobblestones or brown gray structureless blotches over a typically brownish to flesh colored background along with comma-like vessels (Fig. 7c.20a). The latter are often variable in size and caliber but quite monomorphous in shape (Fig. 7c.20b). On occasion the vessels in these intradermal nevi can appear arborizing. However, these vessels tend to be out of focus as compared with arborizing vessels seen in basal cell carcinoma, which are usually sharply in focus. In addition to the above-mentioned structures, few comedo-like openings or milia-like cysts, as well as terminal hairs may be present in these intradermal nevi. With some training and experience it is relatively easy to recognize these repetitive patterns and come to the diagnosis of intradermal nevus with confidence (Argenziano et al., 2004).

Globular–Reticular Nevi

Another nevus type, showing both a globular/cobblestone and reticular pattern, is the so-called fried egg nevus type (Argenziano et al., 2007). This nevus type consists of a central elevated portion showing a globular

Figure 7c.17 Nevus showing heavily pigmented cobblestone pattern. In addition, a solitary milia-like cyst (*arrow*) and terminal hair (*asterisk*) are visible.

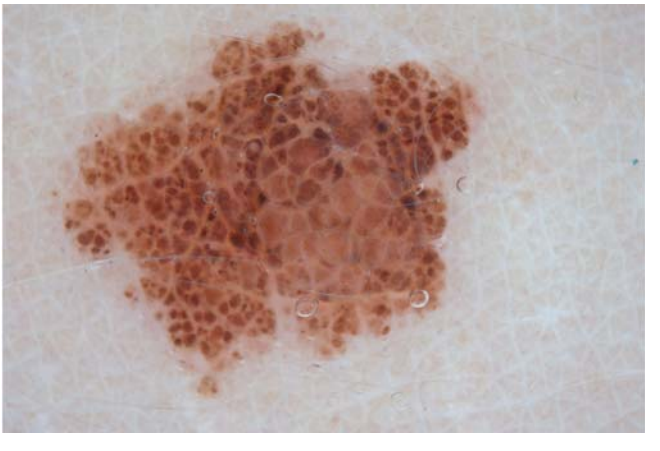
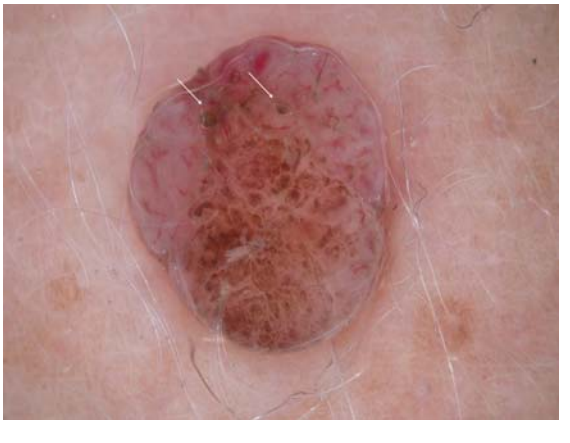


Figure 7c.18 Dermoscopy of a nevus composed of brown to gray globular and cobblestone pattern.

▲ **Figure 7c.19a** Clinical view of a dermal nevus—Unna type.



◀ **Figure 7c.19b** Dermoscopy of the same nevus as shown in Figure 7c.19a exhibiting a striking asymmetry of colors and structures. The nonpigmented area reveals comma-like vessels of different size and diameter, and the pigmented area reveals a mixture of structureless homogenous pattern and residual globules and cobblestones. Terminal hairs or few comedo-like openings (*arrows*) are often present in such nevi.

pattern or a nonpigmented unspecific pattern and a peripheral clinically flat portion showing a reticular pattern (Figs. 7c.21 and 7c.22). Histopathologically, this nevus is composed of a central dermal component and a lateral epidermal component.

Epidemiology

After the reticular pattern the globular-reticular pattern is the most frequent nevus type in adult. They are often larger than 5 mm and are more frequently located on the trunk than in the extremities. In addition, this pattern is a common appearance of nevi located on the scalp.

Nevogenesis

The epidemiologic and morphologic differences between nevi with reticular pattern and globular/cobblestone nevi have recently led to the consideration that these two types of nevi follow different pathways of evolution (Zalaudek et al., 2007). According to this dual concept of nevogenesis hypothesis, nevi with a prevailing globular/cobblestone pattern represent primary dermal melanocytic proliferations that develop due to constitutional pathways during early childhood and generally persist throughout life. This category includes small congenital melanocytic, compound, and dermal nevi (Fig. 7c.23).

In contrast, reticular nevi represent predominantly epidermal proliferations that have a dynamic life cycle, first developing around puberty and increase in number until the 4th to 5th decades of life (Kincannon & Boutzale, 1999). Later in life (after the 6th to 7th decades of life), their numbers decline, which may be explained by their progressive involution or regression (Fig. 7c.24). However, it must be underscored that this dual concept is purely hypothetical and requires further confirmation.

Dermoscopic Pattern of Growing Nevi

Digital dermoscopic followup studies demonstrated that one subset of growing nevi typically reveal a peripheral rim of small, homogenously sized, brown globules, which correspond to small junctional nests of melanocytes at the tips of the rete ridges at the border of junctional or compound nevi (Kittler et al., 2000). This peripheral rim of brown globules is a well-recognized sign of actively growing nevi (Fig. 7c.25).

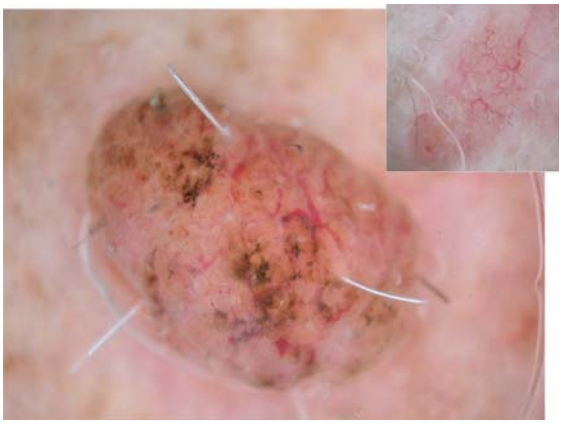
Reticular Nevi with Peripheral Globules

During followup, such nevi usually reveal a symmetric, horizontal enlargement, resulting from the peripheral extension of the small globules together with the progressive appearance of a reticular pattern within the central part of the nevus. Once the nevus enters senescence the peripheral globules disappear and the entire nevus manifests a reticular pattern (Fig. 7c.26). Because reticular nevi tend to develop at puberty it should come as no surprise that the peripheral rim of brown globules pattern is most commonly observed in young adults (age 14–25 years).

Globular and Cobblestone Nevi

In contrast to the striking dermoscopic sign of growth of reticular nevi, the dermoscopic features of growing globular or cobblestone nevi are not

▲ **Figure 7c.20a** Clinical view of a dermal nevus—Miescher type.



◀ **Figure 7c.20b** Dermoscopy of the nevus shown in Figure 7c.20a. Only residual pigmentation appearing as irregularly distributed brown-to-gray blotches are visible. The short but large caliber vascular pattern (comma-like vessels) appears blurred, which is an important criterion to differentiate dermal nevi on the face from nodular basal cell carcinoma. In the latter, the vessels are typically elongated and sharply in focus (*insert*).

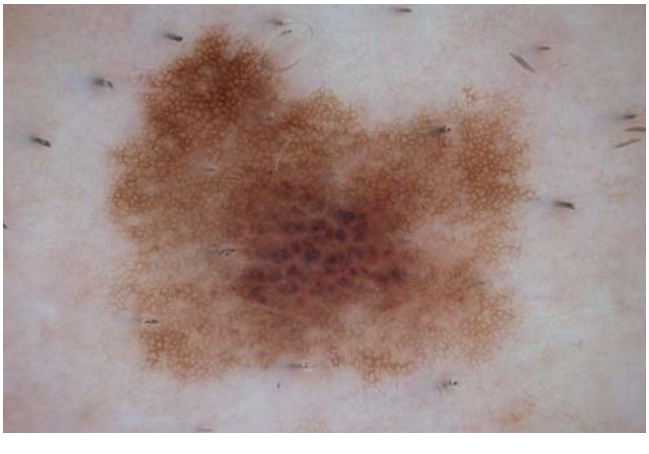
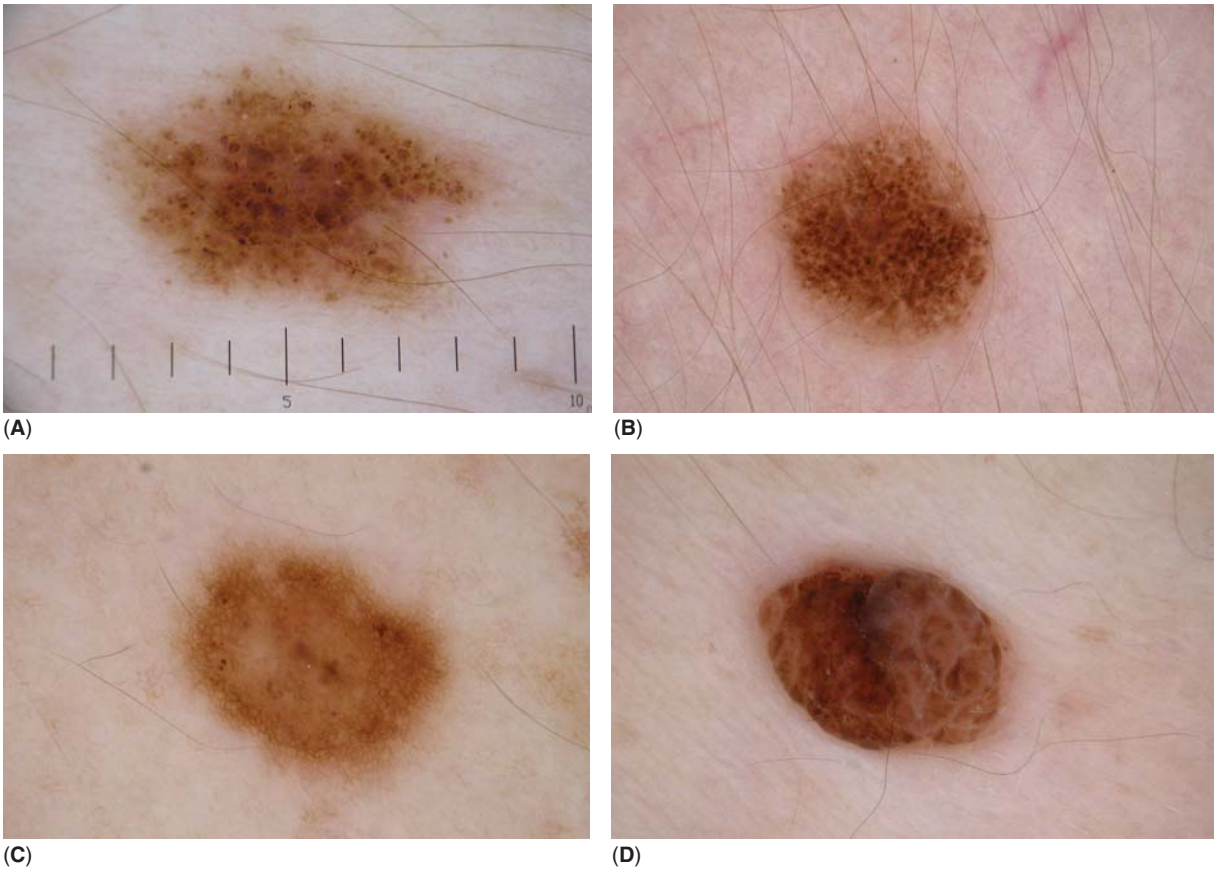


Figure 7c.21 Globular–reticular nevi are composed of a central dermal component with globules surrounded by a regular reticular network.

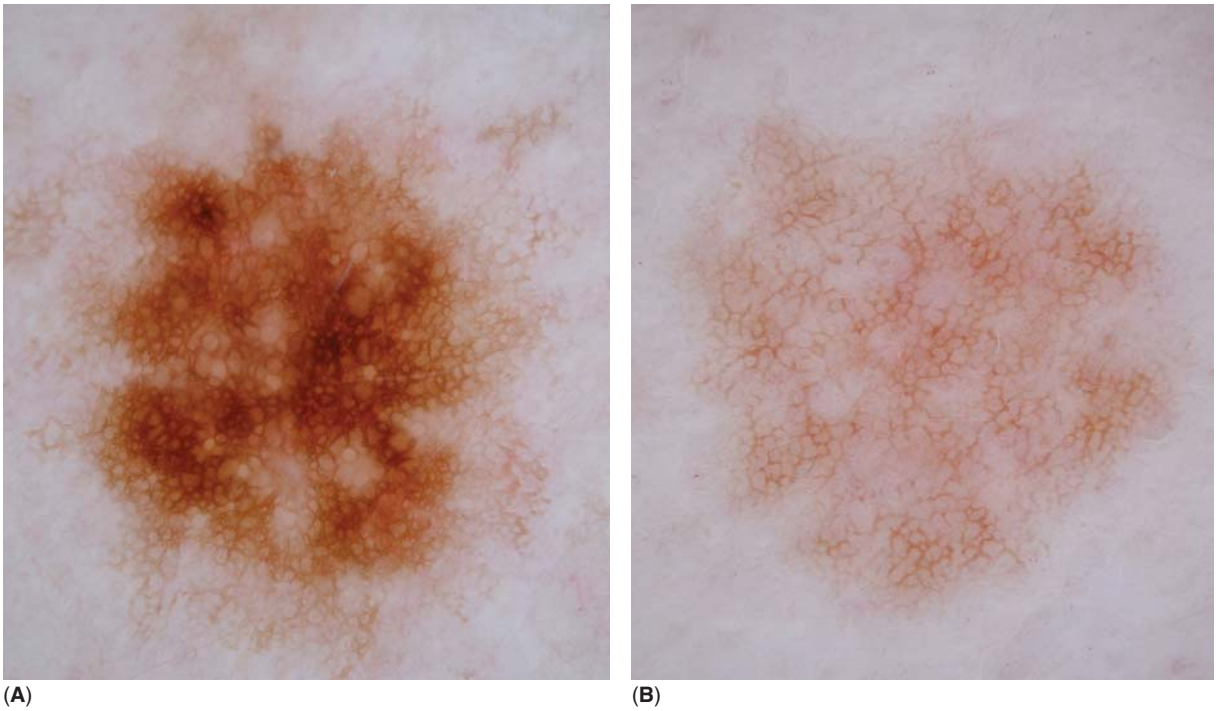
Figure 7c.22 Example of globular-reticular nevus exhibiting in the center predominantly structureless hypopigmentation with a few globules.



(**A**) (**B**)

(**C**) (**D**)

Figure 7c.23 Dermoscopic view of a small congenital nevus (**A**), compound nevus without peripheral reticular pattern (**B**), compound nevus with peripheral network (**C**), and dermal nevus (**D**). All types are typified by a globular/cobblestone pattern underscoring their common histiogenetic background.



(**A**) (**B**)

Figure 7c.24 Epidemiologic studies and new concepts regarding nevogenesis suggest that reticular nevi frequently disappear during one's lifetime. Here is an example of a reticular nevus that is fading.

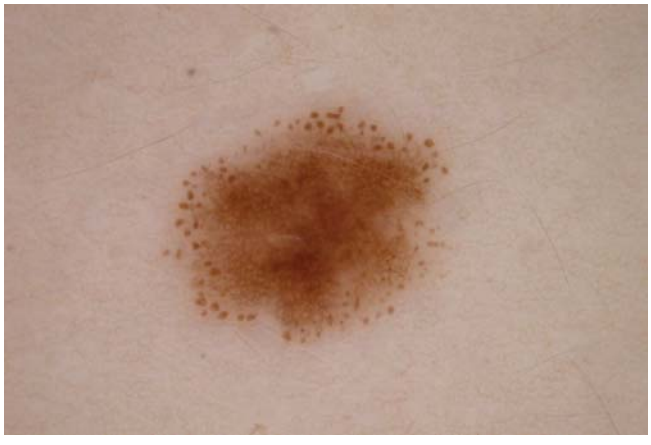


Figure 7c.25 The peripheral rim of small brown globules is indicative for a growing nevus.

recognizable (Fig. 7c.27). These nevi tend to enlarge symmetrically. Although sufficient long-term followup data of single globular or cobblestone nevi are unavailable, many clinicians suspect that after initial proliferation of dermal melanocytes during early childhood, most globular nevi will maintain their clinical and dermoscopic appearance throughout life or acquire the classic appearance of dermal nevi by a progressive loss of pigmentation.

Globular–Reticular Nevi

Similar to their dermoscopic appearance, globular–reticular nevi reveal also overlapping growth patterns of reticular nevi and globular nevi. Similar to reticular nevi, this group may reveal a peripheral rim of globules that eventually results in the creation of a network located toward the periphery of the lesion. The center of this nevus type typically reveals a central brown to gray structureless pattern. Exact morphologic data about the further steps of growth are lacking, but based on personal experiences

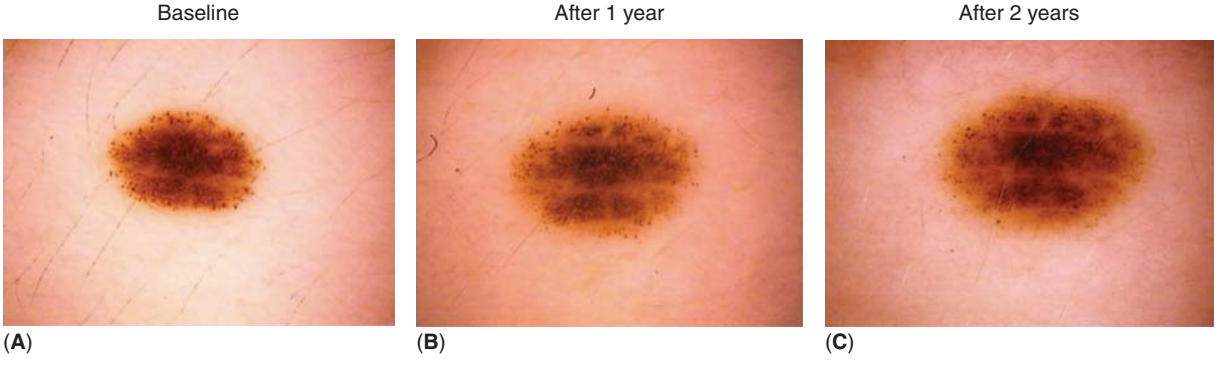


Figure 7c.26 Baseline digital dermoscopic image of a reticular nevus showing a peripheral rim of globules (**A**). During subsequent followup, the nevus shows symmetric enlargement (**B**) until the disappearance of the peripheral globules, which indicates that the nevus has entered senescence (**C**). *Source*: Images courtesy by Dr. Harald Kittler.

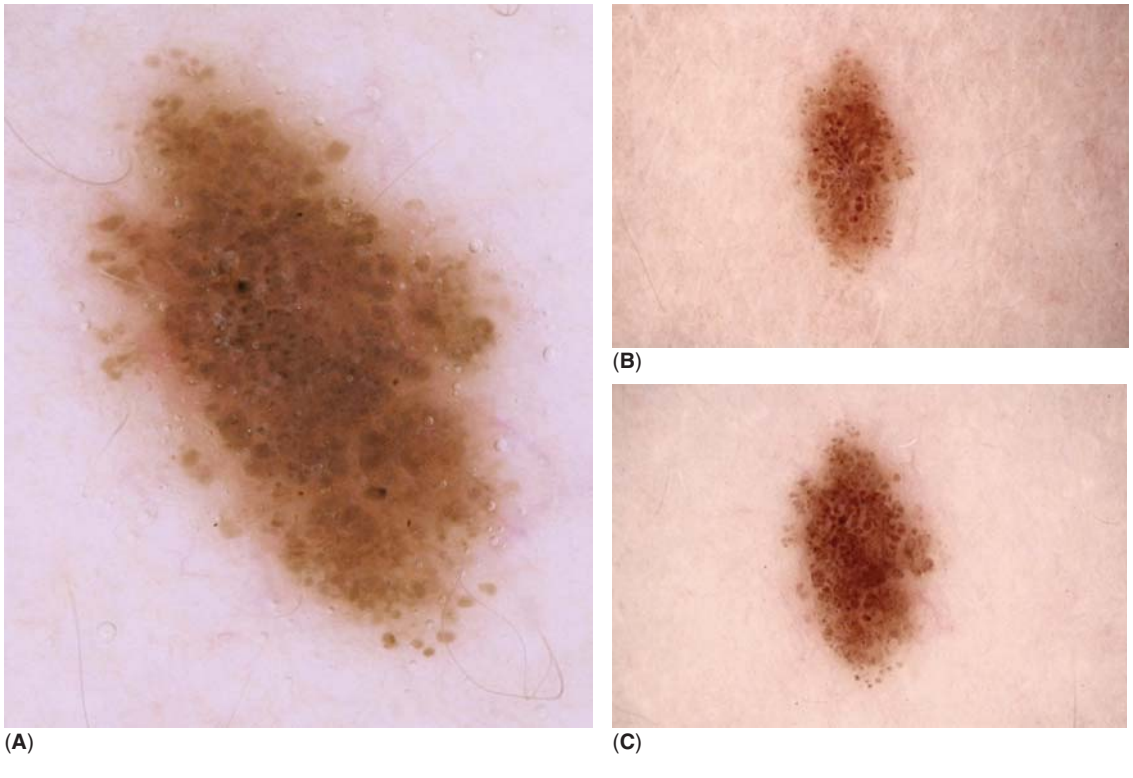


Figure 7c.27 (**A**) Dermoscopic image of a globular/cobblestone nevus. Side-by-side comparison of the baseline image (**B**) and the followup image taken after one year (**C**) reveal a symmetric enlargement in the absence of a clearly visible peripheral rim of small globules as typically seen in growing reticular nevi.

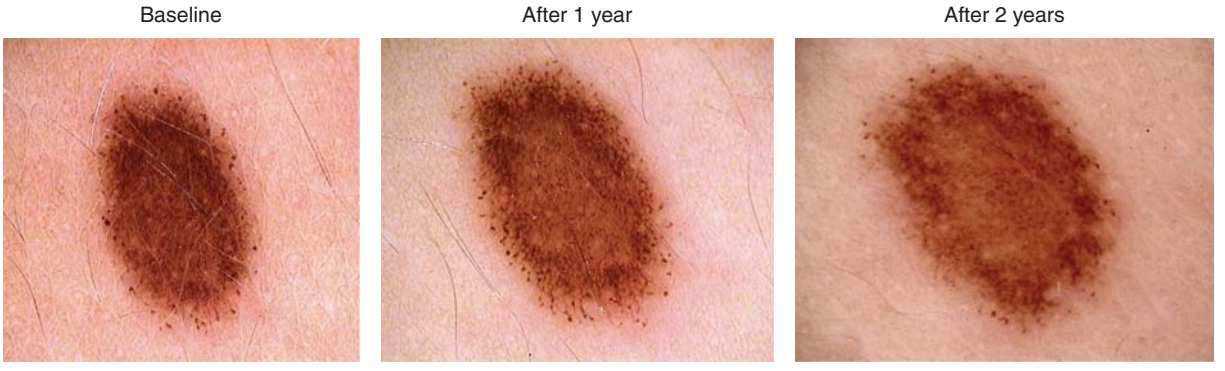


Figure 7c.28 Digital dermoscopic followup of a globular–reticular nevus showing a progressive loss of the central pigmentation.

the central component becomes more elevated and progressively loses pigmentation (Fig. 7c.28).

CONCLUSION

Banal nevi are common melanocytic neoplasms that are dermoscopically characterized by a striking symmetry of colors and structures. The knowledge of the underlying histopathologic correlates of dermoscopic patterns and colors as well as other factors associated with these nevi are a prerequisite for improved identification and management of these common neoplasms on human skin.

Key Points

- Reticular nevi correlate histopathologically with nevi possessing a prominent junctional or lentiginous component.
- Reticular nevi are the most frequent nevus type encountered in adults.
- The color and pigment distribution of nevi is influenced by the skin type of a given individual.
- Reticular nevi start developing around puberty and during their active growth phase many of these nevi will manifest a peripheral rim of brown globules.
- Followup of nevi with a peripheral rim of globules will reveal symmetric enlargement until senescence, at which point the peripheral rim of globules will no longer be visible.
- Globular and cobblestone nevi represent primary dermal melanocytic proliferations and are the hallmark of small congenital melanocytic, compound, and intradermal nevi.
- The globular pattern is the prevailing nevus pattern in children.
- The dermoscopic hallmark of hypopigmented variants of nevi with a globular or cobblestone pattern are comma-like vessels.

REFERENCES

Arevalo, A., Altamura, D., Avramidis, M., Blum, A. & Menzies, S., 2008, The significance of eccentric and central hyperpigmentation, multifocal hyper/hypopigmentation, and the multicomponent pattern in melanocytic lesions lacking specific dermoscopic features of melanoma. *Arch Dermatol*, 144, 1440–4.

Argenziano, G., Soyer, H.P., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Argenziano, G., Zalaudek, I., Ferrara, G., Hofmann-Wellenhof, R. & Soyer, H.P., 2007, Proposal of a new classification system for melanocytic naevi. *Br J Dermatol*, 157, 217–27.

Braun, R.P., Gaide, O., Oliviero, M., et al., 2007, The significance of multiple blue-grey dots(granularity) for the dermoscopic diagnosis of melanoma. *Br J Dermatol*, 157, 907–13.

Gachon, J., Beaulieu, P., Sei, J.F., et al., 2005 First prospective study of the recognition process of melanoma in dermatological practice. *Arch Dermatol*, 141, 434–8.

Grob, J.J., and Bonerandi, J.J., 1998, "The 'ugly Duckling' Sign: Identification of the Common Characteristics of Nevi in An Individual As a Basis for Melanoma Screening." *Arch Dermatol*, 134, 103–4.

Hofmann-Wellenhof, R., Blum, A., Wolf, I.H., et al., 2001, Dermoscopic classification of atypical melanocytic nevi (Clark nevi). *Arch Dermatol*, 137, 1575–80.

Kincannon, J. & Boutzale, C., 1999, The physiology of pigmented nevi. *Pediatrics*, 104, 1042–5.

Kittler, H., Pehamberger, H., Wolff, K. & Binder, M., 2000, Follow-up of melanocytic skin lesions with digital epiluminescence microscopy: patterns of modifications observed in early melanoma, atypical nevi, and common nevi. *J Am Acad Dermatol*, 43, 467–76.

Kittler, H., Seltenheim, M., Dawid, M., et al., 2000, Frequency and characteristics of enlarging common melanocytic nevi. *Arch Dermatol*, 136, 316–20.

Oliveria, S.A., Geller, A.C., Dusza, S.W., et al., 2004, The Framingham school nevus study: a pilot study. *Arch Dermatol*, 140, 545–51.

Scope, A., Dusza, S.W., Halpern, A.C., et al., 2008, The "ugly duckling" sign: agreement between observers. *Arch Dermatol*, 144, 58–64.

Scope, A., Marghoob, A.A., Dusza, S.W., et al., 2008, Dermoscopic patterns of naevi in fifth grade children of the Framingham school system. *Br J Dermatol*, 158, 1041–9.

Zalaudek, I., Argenziano, G., Ferrara, G., et al., 2004, Clinically equivocal melanocytic skin lesions with features of regression: a dermoscopic-pathological study. *Br J Dermatol*, 150, 64–71.

Zalaudek, I., Argenziano, G., Mordente, I., et al., 2007, Nevus type in dermoscopy is related to skin type in white persons. *Arch Dermatol*, 143, 351–6.

Zalaudek, I., Grinschgl, S., Argenziano, G., et al., 2006, Age-related prevalence of dermoscopy patterns in acquired melanocytic naevi. *Br J Dermatol*, 154, 299–304.

Zalaudek, I., Hofmann-Wellenhof, R., Kittler, H., et al., 2007, A dual concept of nevogenesis: theoretical considerations based on dermoscopic features of melanocytic nevi. *J Dtsch Dermatol Ges*, 5, 985–92.

Zalaudek, I., Kittler, H., Marghoob, A.A., et al., 2008, Time required for a complete skin examination with and without dermoscopy: a prospective, randomized multicenter study. *Arch Dermatol*, 144, 509–13.

Zalaudek, I., Leinweber, B., Hofmann-Wellenhof, R., et al., 2008, The epidermal and dermal origin of melanocytic tumors: theoretical considerations based on epidemiologic, clinical, and histopathologic findings. *Am J Dermatopathol*, 30, 403–6.

Zalaudek, I., Leinweber, B., Hofmann-Wellenhof, R. & Soyer, H.P., 2006, The impact of dermoscopic-pathologic correlates in the diagnosis and management of pigmented skin tumors. *Expert Rev Dermatol*, 4, 579–87.

7d Blue nevi and variants

Cristina Carrera, Josep Malvehy, and Susana Puig

INTRODUCTION

Differentiating benign from malignant blue melanocytic tumors can pose a diagnostic challenge since their clinical morphology can overlap greatly. For example, blue nevi (BN) are relatively easy to diagnose on histopathology, however, clinically and sometimes dermoscopically they may be difficult to differentiate from nodular melanoma, dermal melanoma, epidermatropic melanoma metastases, and subcutaneous melanoma metastases. To complicate matters further, BN belong to a diverse family of cutaneous blue tumors including "atypical" BN, sclerosing BN, and deep penetrating BN. Unfortunately, the biologic potential of these rarer variants of BN to develop into malignancy remains unknown. However, the use of dermoscopic–pathologic correlation may contribute to the better understanding, recognition, and management of such BN variants.

BLUE NEVUS

BN are considered a type of dermal dendritic melanocytosis. It is believed that they form as a result of aberrant arrested migration within the dermis of the neural crest–derived melanocytes during embryogenesis. They usually become clinically apparent after the second decade of age, and thereafter tend to remain unchanged during lifetime. The prevalence of BN in adult Caucasians is approximately 1–2% and in adult Asians is about 3–5%.

Generally, BN are subdivided into the common form and the cellular variant. Further histopathologic subdivisions are based on the cellularity and stromal fibrotic reaction within the BN. The term malignant BN refers to a rare and heterogenous group of melanomas that have a highly aggressive biology, and includes melanomas arising in association with a common or cellular blue nevus, and those arising "de novo" and resembling cellular BN.

Clinically, BN usually present as solitary small, grey to bluish-black firm, flat to slightly elevated maculae-papules. The cellular BN variant is usually larger, consisting of a plaque that is up to 1–3 cm in diameter. Aside from taking into account the size of the lesion, it is normally not possible to distinguish among BN variants based only on their clinical and dermoscopic appearance. The most frequent location of BN is on limbs, mostly over the dorsum of hands and feet, but they are also often located on the head, neck, and sacral region.

Recognizing the dermoscopic characteristics of BN requires an understanding of their histopathology. The BN variants are characterized histopathologically by three main features: the presence of heavily pigmented bipolar dendritic melanocytes, numerous melanophages, and variable dermal fibrosis. These cells form ill-defined dermal proliferations that are often localized in the midreticular dermis, but BN may on occasion be located in the superficial or in the deep reticular dermis. The common BN is composed of bipolar spindle-shaped melanocytes with long dendritic processes that contain abundant melanin. Characteristically, these cells are grouped in fascicles arranged parallel to the epidermis, with the dermoepidermal junction (DEJ) being spared of any melanocytic proliferations. It is also common to see numerous melanophages and fibrosis. Cellular BN present with the same features but in addition, they also reveal aggregates or islands of spindle-shaped and epithelioid cells, with abundant pale cytoplasm and scant melanin. The nevus cells in cellular BN may almost completely occupy the dermis and may even extend into subcutaneous fat. Cellular BN nodules are relatively well demarcated and often appear encapsulated because of compression of the fibrous stroma around them. Mitotic figures are not uncommonly encountered in such lesions.

In most cases BN can be diagnosed easily based on their typical clinical presentation and clear history of being biologically stable lesions. However, without a clear history, dermoscopy can be useful in distinguishing BN from malignancy.

DERMOSCOPY

The most frequent and characteristic pattern of BN is the homogenous structureless bluish pigmentation or white-blue, steel blue-gray to blue-black pigment pattern (Figs. 7d.1–7d.6). Other patterns found vary from brown to polychromatic structureless patterns, and sometimes whitish

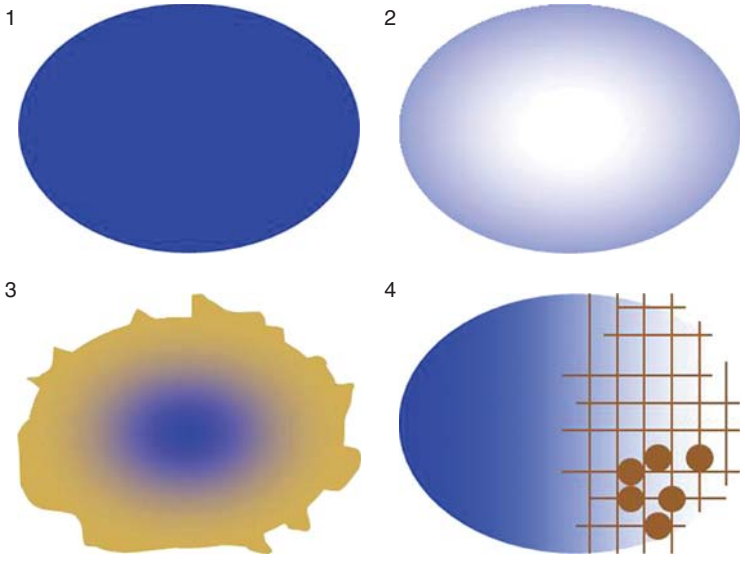


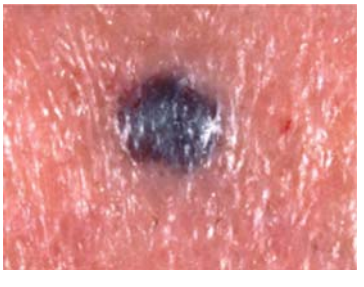
Figure 7d.1 Schematic representation of dermoscopy features seen in blue melanocytic lesions. 1. Typical homogenous blue pattern in blue nevus; 2. blue and white homogenous pattern in a sclerotic-type blue nevus; 3. blue nevus with brownish projections; 3. combined nevus with blue nevus component and benign-acquired nevus/Clark-type pigment network and aggregated globules.

▲ **Figure 7d.2a** Small, pigmented papule on the forearm.

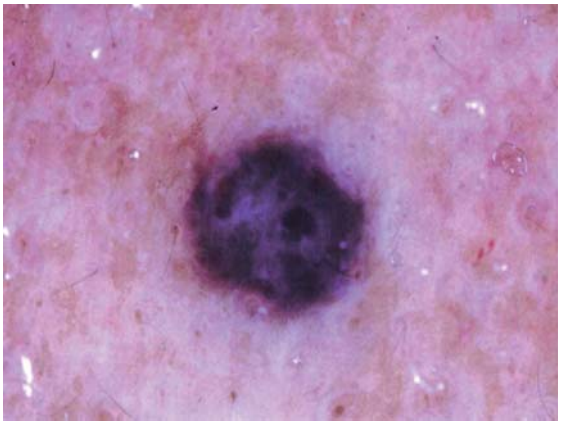
◀ **Figure 7d.2b** Dermoscopy: blue nevus with the homogenous steel bluish pigmentation with faded border.

▲ **Figure 7d.3a** An 8 mm bluish plaque on scapular region.

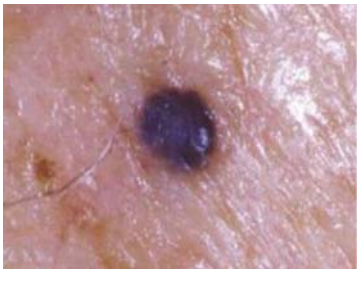
◀ **Figure 7d.3b** Dermoscopy: blue nevus: homogenous blue-white pigmentation with blue roundish globules present toward the center of the lesion. A light brownish hue or brownish veil can also be seen.



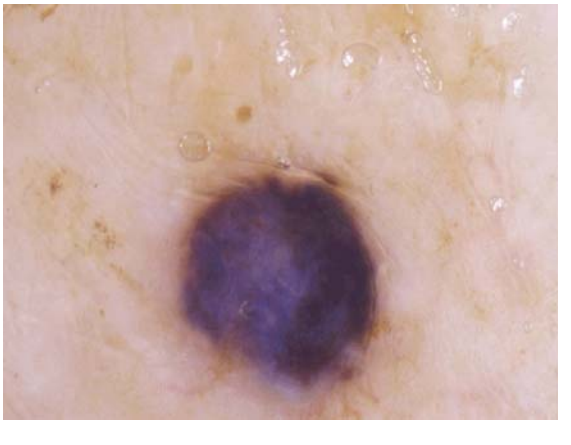
▲ **Figure 7d.4a** Clinical image of a blue nevus.



◀ **Figure 7d.4b** This blue nevus manifests a homogenous pattern with two shades of blue. Although the pattern is homogenous, the distribution of the different shades of blue is somewhat disorganized. Without a reliable history it may be difficult to exclude a diagnosis of melanoma in such blue nevi without a biopsy.



▲ **Figure 7d.5a** Clinical image of a blue nevus.



◀ **Figure 7d.5b** This blue nevus manifests a homogenous pattern with two shades of blue. The distribution of the different shades of blue is fairly organized.

areas corresponding to fibrosis can also be seen (Figs. 7d.7–7d.10). The pigment in BN is usually confluent throughout the lesion and fades toward the periphery (Figs. 7d.2, 7d.3 and 7d.6). Sometimes BN manifest focal bluish projections (Fig. 7d.11) at the periphery of the lesion. These projections appear blurry or out of focus, and they correspond to focal pigment extensions composed of the nevus cells or melanophages within the dermis. The absence of additional dermoscopic features, such as atypical vessels, streaks, dots/globules, and network, is crucial in helping to distinguish BN from other melanocytic lesions, such as nodular melanoma, Reed nevus, or metastases mimicking BN.

The aforementioned dermoscopic features of BN can be seen with both polarized and nonpolarized light dermoscopy. However, it is important to be aware that in some BN a few additional features can be seen when the lesion is viewed with polarized dermoscopy. The homogenous blue-pigmented area as seen with nonpolarized dermoscopy may appear darker and more heterogenous (i.e., differing shades of blue) and may also reveal bluish globules/dots, bluish network-like structures, chrysalis/crystalline structures (corresponding to fibrosis), and/or the peripheral projections mentioned above (Fig. 7d.11). Thus, although the classic homogenous steel blue pattern of BN can be seen with either polarized or nonpolarized dermoscopy, it is not uncommon for BN to appear differently with polarized light. The most common difference is that with polarized light a more heterogenous brownish or polychromatic pattern can be identified (Figs. 7d.4 and 7d.5).

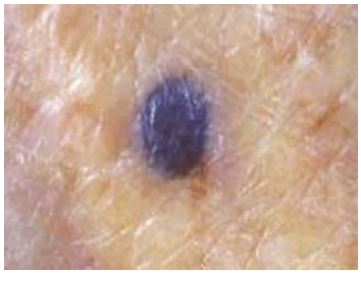
BLUE NEVUS VARIANTS

Dermoscopic–histopathologic correlation enables us to better understand and recognize BN variants. In *sclerotic or desmoplastic BN*, the fibrosis is predominant and the clinical and dermoscopic appearance may resemble a dermatofibroma, with whitish areas or even whitish scar-like depigmentation, which under polarized dermoscopy may reveal crystalline structures. (Fig. 7d.10). In contrast, a homogenous blue-to-black pigmentation, sometimes associated with globules, is the dermoscopic pattern seen in *compound BN*, which is a specific and rare variant of BN described by Kamino and Tam (1990). This entity is characterized by intensely pigmented dendritic melanocytes at the DEJ and within the dermis. Another variant of BN *is the deep penetrating blue nevus*. Dermoscopy shows a more polychromatic and heterogenous pattern making it difficult to differentiate them from melanoma. *A combined blue nevus* has two different cell populations (Figs. 7d.8, 7d.9 and 7d.12–7d.14). Most commonly one population of cells results in BN and the other population of cells results in a conventional compound/junctional nevus. Less frequently the association of BN with Spitz/Reed nevus can be observed (Fig. 7d.15).

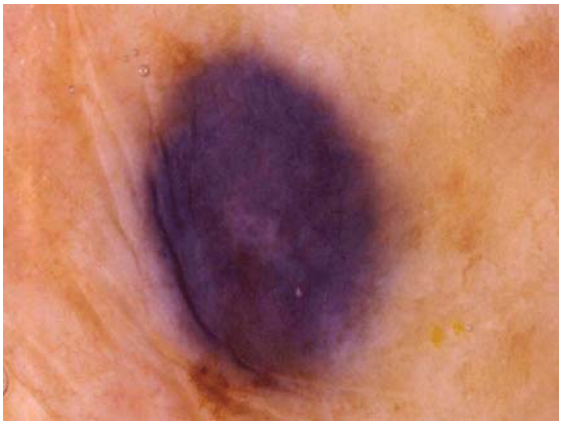
Aside from compound and combined BN, histopathologically all BN variants are defined by a lack of a DEJ component, resulting in a "Grenz zone" separating the dermal proliferation from the epidermis. In contrast, the DEJ is involved in compound and combined BN with nests of melanocytes visible at the DEJ. These lesions often resemble melanoma clinically and dermoscopically, and therefore biopsy and histopathologic examination remain the gold standard to rule out the possibility of melanoma. With that said, dermoscopically they manifest features of the two melanocytic components (Figs. 7d.8, 7d.9, 7d.12–7d.14). The most frequent finding is brown pigmentation or a brown veil in combination with homogenous bluish pigmentation (Figs. 7d.8, 7d.9 and 7d.14). Sometimes a whitish pigmentation similar to the blue-white veil described in melanomas can be seen, making it virtually impossible to exclude the diagnosis of melanoma based on dermoscopic examination alone (Figs. 7d.9 and 7d.12–7d.15).

DIFFERENTIAL DIAGNOSIS OF BLUISH LESIONS

Not all lesions with a bluish homogenous pattern represent BN. Malignant BN (Fig. 7d.16), nodular melanoma (Fig. 7d.17), dermal melanoma (Fig. 7d.18), melanoma metastasis (Fig. 7d.19), exogenous

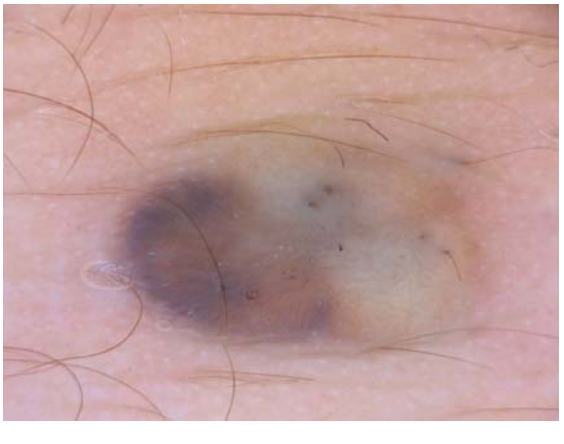


▲ **Figure 7d.6a** Clinical image of a blue nevus.



◀ **Figure 7d.6b** Dermoscopic image: homogenous blue-gray to blue-black pigmentation in the absence of network, branched streaks, and globules.

▲ **Figure 7d.7a** Asymmetrically pigmented in a raised tumor on dorsum of the hand.



◀ **Figure 7d.7b** Dermoscopy: blue nevus (with neuroid differentiation or Masson neuronevus): Bipolar heterogenous blue-brownish pigmentation with an adjacent whitish area. Follicular openings and faint fine lines forming a brown network-like structure can be distinguished.

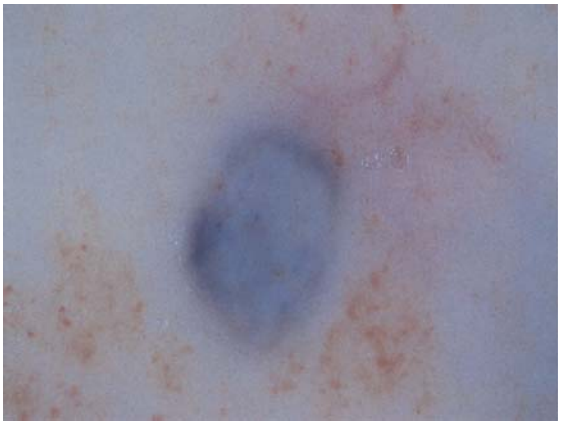
▲ **Figure 7d.8a** Pigmented lesion on the leg with a subtle white halo.

◀ **Figure 7d.8b** Dermoscopy: targetoid combined blue nevus with a compound nevus and with an inflammatory halo reaction. Polychromic lesion with a brown globular–homogenous pattern and a bluish to black central hyperpigmentation area. Discrete halo-like depigmentation and faded borders are present.

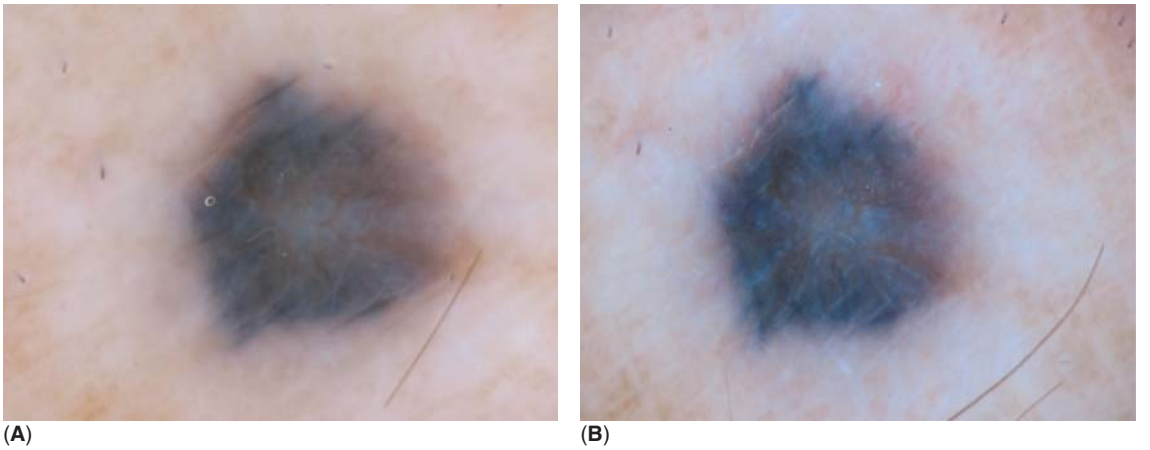
▲ **Figure 7d.9a** Raised pigmented tumor on the cheek.

◀ **Figure 7d.9b** Dermoscopy: combined nevus (deep penetrating nevus with intradermal nevus): heterogenous polychromic blue-brownish and whitish pigmentation, with some lineal vessels present.

▲ **Figure 7d.10a** Clinical image of a sclerotic blue nevus.

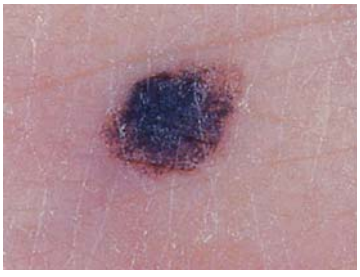


◀ **Figure 7d.10b** Dermoscopy reveals features of a blue nevus with a prominent white component. The white reflects the fibrosis within sclerosing blue nevi.



(**A**) (**B**)

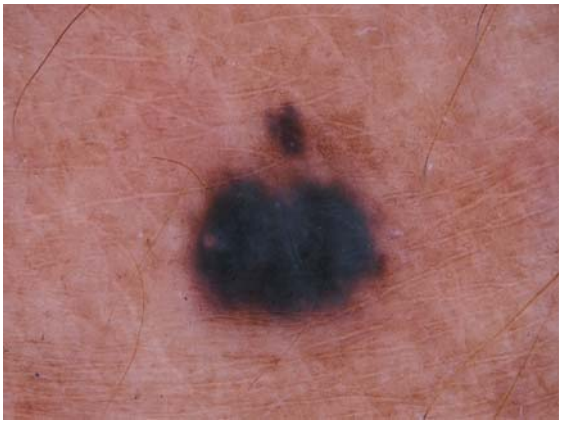
Figure 7d.11 (**A**) This image of a BN was obtained using nonpolarized dermoscopy. The image reveals the classic homogenous blue pigment normally seen in BN. Also note that this lesion has a few blurry peripheral projections. These out-of-focus pigment projections should not be confused for streaks. (**B**) The same BN imaged using polarized dermoscopy reveals an image with a deeper blue color and a few short white lines (chrysalis/crystalline structures corresponding to fibrosis). The presence of these short white lines should always raise suspicion for melanoma. The biopsy of this lesion was consistent with a BN. *Abbreviation*: BN, blue nevi.



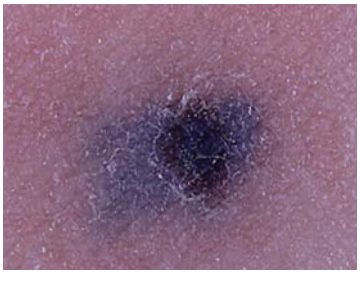
▲ **Figure 7d.12a** Clinical image of a combined BN.

◀ **Figure 7d.12b** Dermoscopy reveals a central homogenous blue area corresponding to the BN component. Surrounding the BN is a network, which corresponds to the combined junctional nevus. *Abbreviation*: BN, blue nevi.

▲ **Figure 7d.13a** Clinical image of a combined blue nevi.



◀ **Figure 7d.13b** Combined nevus. Faint, regular, patchy pigmented network with superimposed homogeneous blue-gray pigmentation extended throughout the entire lesion.



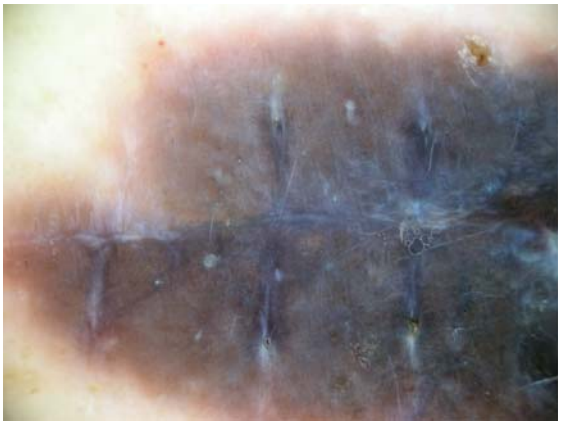
▲ **Figure 7d.14a** Clinical image of a combined blue nevus.

◀ **Figure 7d.14b** Homogenous blue pigmentation extending throughout the entire lesion corresponds to the BN component of this lesion. In addition, a focal brown area can be seen within the center of the lesion, which corresponds to the compound nevus component in this combined BN. *Abbreviation*: BN, blue nevi.

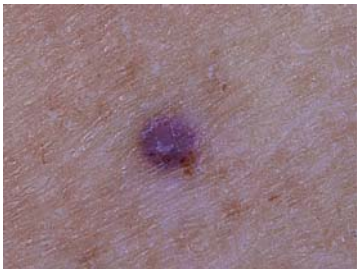
▲ **Figure 7d.15a** Blue pigmented lesion on the arm of a young male.

◀ **Figure 7d.15b** Dermoscopy: combined blue nevus with a Spitz/Reed nevus. Blue-to-black pigmentation with peripheral faded projections and bluish globules.

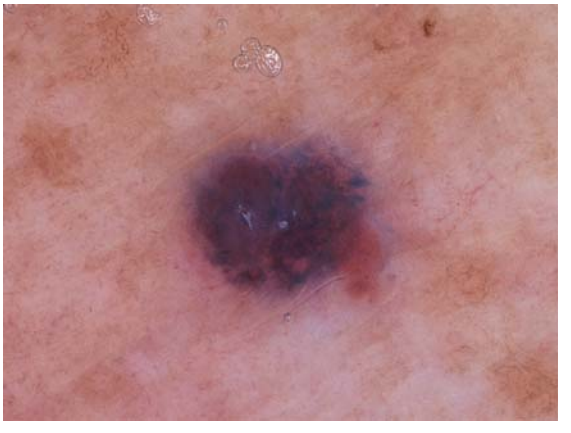
▲ **Figure 7d.16a** A large blue tumor (30 × 15 mm) on the back of a 46-year-old woman corresponding to malignant blue nevus.



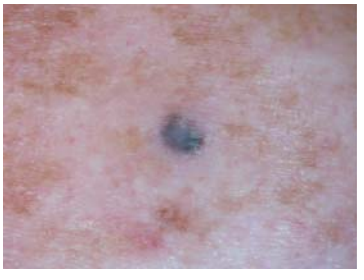
◀ **Figure 7d.16b** Dermoscopy: heterogenous polychromic pigmentation, with blue-white veil and brown pigmentation. Dermoscopy features are indistinguishable from melanoma.



▲ **Figure 7d.17a** Clinical image of a small nodular melanoma.



◀ **Figure 7d.17b** Dermoscopy reveals heterogenous (not homogenous) patchy bluish pigmentation intermixed with brown pigment. This 0.8 mm nodular melanoma can easily be mistaken for a blue nevi.



▲ **Figure 7d.18a** A new 6 mm bluish papule was noted on the shoulder of this 73 years old.

◀ **Figure 7d.18b** Nonpolarized dermoscopy reveals a polychromatic lesion with features of a BN. However, the lesion also has multiple linear irregular vessels, which is a feature not commonly seen in BN.

◀ **Figure 7d.18c** Polarized dermoscopy of the same lesion reveals numerous chrysalis/crystalline structures. The presence of irregular vessels and crystalline structures in a BN-like lesion should raise suspicion for malignancy. An excisional biopsy was performed and the histopathology of this lesion was consistent with a primary dermal melanoma. *Abbreviation*: BN, blue nevi.

tattoo (radiation therapy tattoo), pigmented spindle-cell (Reed nevus) nevus, and congenital melanocytic nevus (Fig. 7d.20) can at times be indistinguishable from BN. However, a careful dermoscopic examination will usually help identify clues to make the diagnosis, such as atypical vessels, regression structures, or streaks. Needless to say, the history of the patient is vital and any lesion with blue white structures, resembling BN, should be biopsied if the history reveals that the lesion is new or has recently changed in an adult patient or in patients with history of melanoma.

Other nonmelanocytic tumors, such as basal cell carcinomas, hemangiomas, angiokeratomas, and up to 20% of pilomatricomas may present with confluent blue-hue pigmentation but, usually in these cases, other clinical and dermoscopic characteristics are present making their recognition easy.

Lastly, we want to highlight that BN on the face may reveal a pseudonetwork pattern (Fig. 7d.21). In essence, such lesions can still be considered to have a homogenous blue color with the clear spaces representing voids created by the numerous adnexal openings normally present on facial skin.

▲ **Figure 7d.19a** Multiple-pigmented maculae-papules corresponding to epidermotropic metastasis on the limb of a young patient with a history of a previously excised primary melanoma on the same leg.

◀ **Figure 7d.19b** Dermoscopy: blue-white homogenous pigmentation mimicking a blue nevus. Note the reddish halo surrounding the tumor. Clinical history and the presence of multiple lesions make rendering a diagnosis of metastasis easy.

▲ **Figure 7d.20a** Clinical image of a small congenital melanocytic nevus that was documented to be present at birth.

◀ **Figure 7d.20b** Dermoscopy of this congenital nevus reveals a homogenous blue pigment pattern. This pattern is usually associated with blue nevi, but as highlighted in this case, congenital nevi can on occasion manifest a similar pattern.

▲ **Figure 7d.21a** A 3 mm black spot on the forehead of an elderly male.

◀ **Figure 7d.21b** Dermoscopy: blue nevus on the face. Bluish homogenous pigmentation, which spares the adnexal openings, creating a pseudonetwork pattern can be seen.

Key Points

1. The blue homogenous pigmentation is the most important dermoscopic finding in blue nevi (BN).
2. BN can exhibit combinations of homogenous pigmentation with tones of brown, blue, and white coloration.
3. Melanoma metastasis, dermal melanoma, and nodular melanoma can mimic blue nevus under dermoscopy.

BIBLIOGRAPHY

Ackerman, A.B., Cerroni, L. & Kerl, H., 1994, *Pitfalls in the Diagnosis of Malignant Melanoma*. Philadelphia: Lea & Febiger,182–266.

Argenziano, G., Soyer, H.P., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions. Results of a Consensus Meeting via Internet. *J Am Acad Dermatol*, 48, 679–93.

Barnhill, R.L., Argenyi, Z., Berwick, M., et al., 2008, Atypical cellular blue nevi (cellular blue nevi with atypical features): lack of consensus for diagnosis and distinction from cellular blue nevi and malignant melanoma ("malignant blue nevus"). *Am J Surg Pathol*, 32, 36–44.

Benvenuto-Andrade, C., Dusza, S.W., Agero, A.L., et al., 2007, Differences between polarized light dermoscopy and immersion contact dermoscopy for the evaluation of skin lesions. *Arch Dermatol*, 143, 329–38.

Carrera, C., Ferrer, B., Mascaró, J.M., Jr. & Palou, J., 2006, Compound blue naevus: a potential simulator of melanoma. *Br J Dermatol*, 155, 207–8.

Cooper, P.H., 1992, Deep penetrating (plexiform spindle cell) nevus. A frequent participant in combined nevus. *J Cutan Pathol*, 19, 172.

de Giorgi, V., Massi, D., Salvini, C., et al., 2004, Dermoscopic features of combined melanocytic nevi. *J Cutan Pathol*, 31, 600–4.

Ferrara, G., Argenziano, G., Zgavec, B., et al., 2002, "Compound blue nevus": a reappraisal of "superficial blue nevus wit prominent intraepidermal dendritic melanocytes" with emphasis on dermoscopic and histopathologic features. *J Am Acad Dermatol*, 46, 85–9.

Ferrara, G., Soyer, H.P., Malvehy, J., et al., 2007, The many faces of blue nevus: a clinicopathologic study. *J Cutan Pathol*, 34, 543–51.

Flauta, V.S., Lingamfelter, D.C., Dang, L.M. & Lankachandra, K.M., 2006, Deep penetrating nevus: a case report and brief literature review. *Diagn Pathol*, 1, 31.

Garrido-Ríos, A.A., Carrera, C., Puig, S., et al., 2008, Homogeneous blue pattern in an acral congenital melanocytic nevus. *Dermatology*, 217, 315–17.

Granter, S.R., McKee, P.H., Calonje, E., Mihm, M.C., Jr. & Busam, K., 2001, Melanoma associated with blue nevus and melanoma mimicking cellular blue nevus. A clinicopathologic study of 10 cases on the spectrum of so-called "malignant blue nevus." *Am J Surg Pathol*, 25, 316–23.

Kamino, H. & Tam, S.T., 1990, Compound blue nevus: a variant of blue nevus with an additional junctional dendritic component: a clinical, histopathologic, and immunohistochemical study of six cases. *Arch Dermatol*, 126, 1330–3.

Magro, C.M., Crowson, A.N. & Mihm, M.C., 2006, Unusual variants of malignant melanoma. *Mod Pathol*, 19, S41–70.

Malvehy, J. & Puig, S., 2002, *Principles of Dermoscopy*. Barcelona, CEGE.

Piccolo, D., Altamura, D., Lozzi, G.P. & Peris, K., 2006, Blue-whitish veil-like structure as the primary dermoscopic feature of combined nevus. *Dermatol Surg*, 32, 1176–8.

Schulz, H., 2000, Epiluminescence microscopy features of cutaneous malignant melanoma metastases. *Melanoma Res*, 10, 273–80.

Seab, J.A., Jr., Graham, J.H. & Helwig, E.B., 1989, Deep penetrating nevus. *Am J Surg Pathol*, 13, 39.

Tsunemi, Y., Saeki, H. & Tamaki, K., 2008, Blue naevus with pigment network-like structure on dermoscopy. *Acta Derm Venereol*, 88, 412–13.

Wang, S.Q., Dusza, S.W., Scope, A., et al., 2008, Differences in dermoscopic images from nonpolarized dermoscope and polarized dermoscope influence the diagnostic accuracy and confidence level: a pilot study. *Dermatol Surg*, 34, 1389–95.

Zaballos, P., Llambrich, A., Puig, S. & Malvehy, J., 2008, Dermoscopic findings of pilomatricomas. *Dermatology*, 217, 225–30.

Zembowicz, A. & Mihm, M.C., 2004, Dermal dendritic melanocytic proliferations: an update. *Histopathology*, 45, 433–51.

7e Spitz and Reed nevi

Gerardo Ferrara and Giuseppe Argenziano

INTRODUCTION

The eponymic designation "Spitz nevus" refers to a benign melanocytic proliferation, which was first described in 1948 by Sophie Spitz as "melanoma of the childhood" (Spitz, 1948). Along with this original description, we now consider as "classical" Spitz nevus a rapidly growing, pink or flesh-colored papule or nodule of the lower extremities or the face in childhood or early adulthood (Weedon & Little, 1977); its histopathologic hallmark is the presence of large spindle and/or epithelioid cells, usually in the paucity or absence of melanin.

"Reed nevus" is another eponymic designation for a benign melanocytic lesion described by Reed et al. (1975) as "pigmented spindle cell nevus." It is mostly found in young adults on the lower extremities as a rapidly growing brownish-black macule or papule; histopathologically, it has interconnecting junctional fascicles of heavily pigmented spindle cells. The nosologic autonomy of Reed nevus from Spitz nevus has been questioning because of the occurrence of cases of spindle and/or epithelioid cell nevi with heavy pigmentation, thereby ascribing Reed nevus to the morphologic spectrum of Spitz nevus. At present, some authors still maintain that Reed nevus is an entity, which can be clearly differentiated from pigmented spindle cell Spitz nevus (Smith, 1987; Barnhill & Mihm, 1989; Barnhill et al., 1991). Although the clinicopathologic evaluation of a large case series has shown that the histopathologic distinction between these two diagnostic categories is often a matter of debate, it has no clinical and dermoscopic relevance (Ferrara et al., 2005). We can therefore refer to Spitz nevus by classifying it into two clinical variants, namely, the *classical* and the *pigmented* type (the latter also comprising Reed nevus).

Indisputably, some melanomas histopathologically may resemble Spitz nevi to varying extent. A morphologic spectrum of melanomas with "Spitzoid" features probably exists, with one end showing lesions that are readily identified as malignant on histopathologic examination; at the opposite edge of this spectrum, one may on rare occasion discover cases, which can be diagnosed as malignant only retrospectively, that is, after the development of metastases (Smith et al., 1989; Barnhill et al., 1999; Barnhill, 2006). These lesions are often referred to as "atypical Spitz nevi/tumors" (Barnhill et al., 1999). These tumors can be considered as neoplasms with "bland" ("low-grade") histopathologic features that appear to have metastatic potential with an affinity to metastasize to the regional lymph nodes (Smith et al., 1989; Barnhill, 2006).

DERMOSCOPIC CRITERIA

Six main dermoscopic patterns can be ascribed to Spitz nevi, namely, vascular (pink homogenous), globular, starburst, reticular, atypical, and homogenous (pigmented) (Fig. 7e.1) (Ferrara et al., 2005). However, most of these different dermoscopic patterns probably represent different phases of the natural evolution of Spitz nevi. It has been demonstrated that a pigmented Spitz nevus can evolve from a globular pattern to a "starburst" pattern, and finally when it enters an apparent state of senescence it manifests a homogenous pattern (Pizzichetta et al., 2002). The colors manifested by Spitz nevi range from pink to brown to blue to black. However, many pigmented Spitz nevi will reveal blue to blue-white colors due to the presence of melanin in the deeper dermis (Peris et al., 2002).

Vascular Pattern

Classical Spitz nevus is an amelanotic or hypopigmented lesions with a vascular pattern composed most often of dotted vessels (Argenziano et al., 2004), which imparts the "definitional" pink color to these lesions (Figs. 7e.2a, b and 7e.3a, b). These dotted vessels tend to be monomorphic and regularly distributed throughout the lesion. However, it is not uncommon to see vessels with a nondotted morphology and in such lesions it is difficult to rule out melanoma without performing a biopsy (Figs. 7e.4a, b and 7e.5a, b). In addition, it is not uncommon for pink Spitz nevi to also manifest intersecting white lines, the so-called reticular depigmentation (Fig. 7e.6a, b). Reticular depigmentation appears to be a combination of a negative network and chrysalis-like (also known as crystalline or shiny white lines) structures. Although commonly seen together, they can also be seen independently, one from the other. It is important to point out that, whereas the negative network can be visualized with both polarized and nonpolarized dermoscopy (Fig. 7e.7a, b), the crystalline structure can only be seen with polarized dermoscopy (Fig. 7e.8a, b).

Globular Pattern

Pigmented Spitz nevi often present with a diffuse brownish hue with widely spaced gray-brown, small-to-medium–sized globules (Fig. 7e.9a, b).

In heavily pigmented lesions, globules are brown to bluish to black, large and distributed throughout the lesion or at the periphery (Fig. 7e.10a, b of blue Spitz globular Magipinto). Globular pattern Spitz nevi can also reveal reticular depigmentation (Fig. 7e.11A–D). On occasion, the globules in a Spitz nevus are arranged in a centrifugal fashion and reminiscent of an exploding star (Fig. 7e.12a, b). This pattern differs from the peripheral globular pattern seen in growing Clark nevi (see chap. 7C) in that the globules in a growing Clark nevus are distributed in a single row at the periphery of the lesion. In contrast, in Spitz nevi there are multiple rows of globules (i.e., tiered) at the periphery.

Starburst Pattern

As stated above, the starburst pattern can be seen with tiered globules at the periphery. However, in most cases of pigmented Spitz nevi, peripheral globules are fused with the central body of the lesion; these regular, "in focus" radial projections (so-called streaks) are responsible for a "starburst" appearance (Fig. 7e.13A–D). The streaks in a Spitz can be composed of pseudopods or as radial streaming (Fig. 7e.14a, b). The starburst pattern corresponds to the radial growth phase of the tumor.

Reticular Pattern

In rare cases, heavy pigmentation may give rise to a black network. The black color is due to the presence of excessive amounts of melanin in the stratum corneum. This black pigment can often be diminished or removed by tape stripping ("superficial black network") (Fig. 7e.15a, b) (Argenziano et al., 2001).

Atypical Pattern

Several of the aforementioned features can be simultaneously present and/or irregularly distributed within a given lesion, thus giving an atypical or "melanoma-like" pattern (Figs. 7e.16A–D and 7e.17a, b). Dermoscopic atypia can also be heightened by virtue of the presence of a blue-white veil. This veil is due to the presence of deep dermal pigmentation with an overlying epidermal hyperplasia/orthokeratosis (Fig. 7e.18a, b).

Homogenous Pattern

The homogenous pigmented pattern is characterized by a diffuse dark brown to black-bluish color, which lacks evidence of clear-cut streaks at the periphery (Fig. 7e.19a, b). A reddish periphery is not uncommonly seen in such "homogenous" Spitz nevi. Parenthetically, some "dermal" nevi revealing a homogenous light brown pattern may represent the end phase in the natural evolution of classical Spitz nevi. Although the

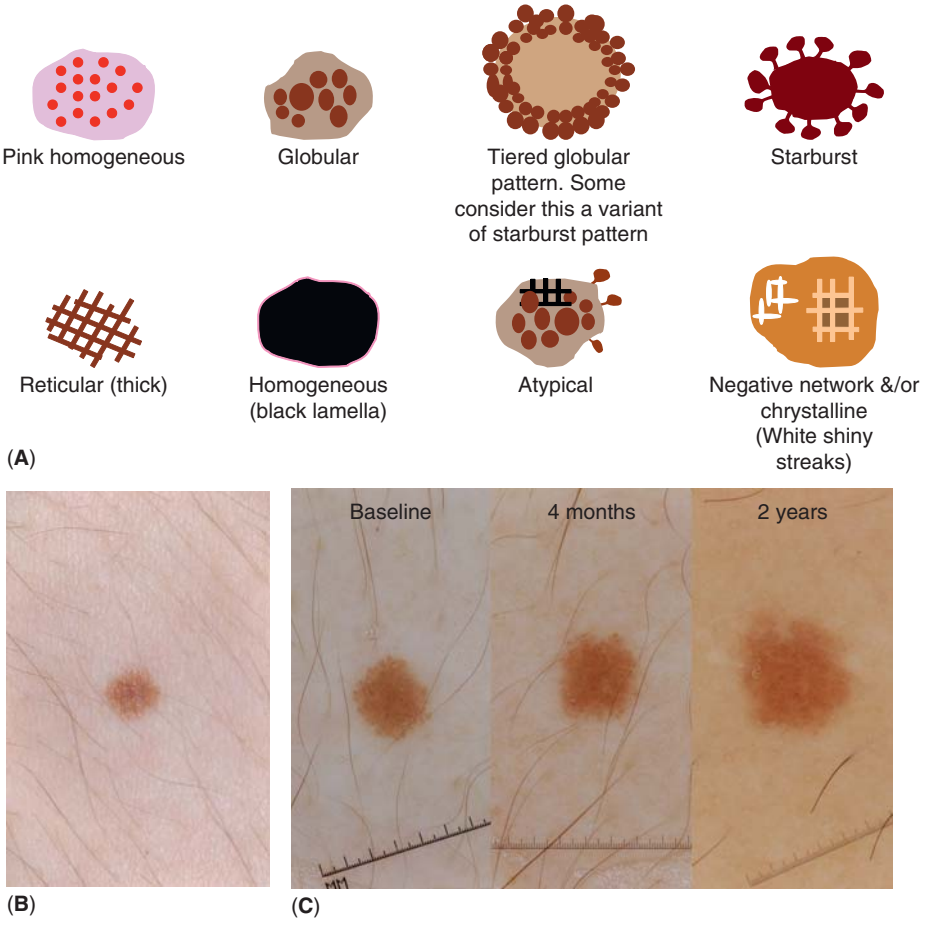
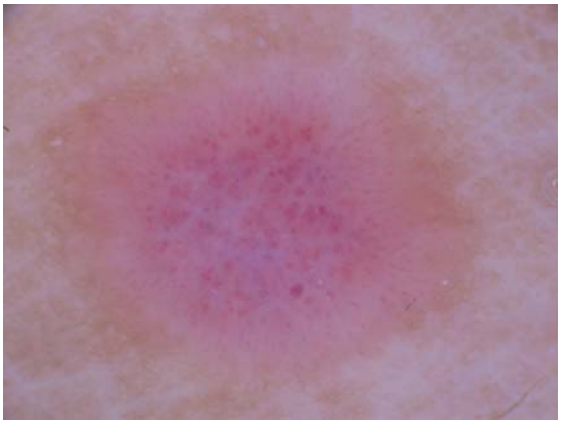


Figure 7e.1 (**A**) Schematic drawing of features of Spitz nevus. (**B**) Clinical image of Spitz nevus. (**C**) This Spitz nevus had a starburst pattern when first seen. The nevus enlarged symmetrically over a period of two years. It eventually stopped growing, at which point it manifested a homogenous pattern. It has remained unchanged now for more than one year.

▲ **Figure 7e.2a** Clinical image of a pink (classic) Spitz nevus.

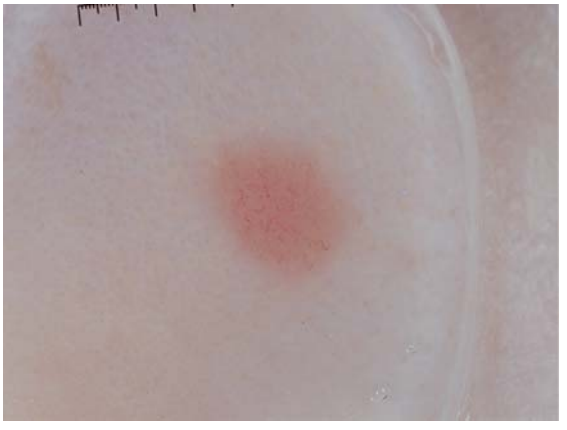
◀ **Figure 7e.2b** Dermoscopy reveals a pink lesion with numerous dotted vessels.

▲ **Figure 7e.3a** A small pink Spitz nevus.



◀ **Figure 7e.3b** Dermoscopically this lesion reveals dotted vessels. This lesion also has vessels manifesting varied morphologies, including glomerular vessels, linear and hairpin vessels. The vessels are distributed in an almost "starburst" configuration.

▲ **Figure 7e.4a** Clinical image of a pink Spitz nevus on the nose of a three-year-old girl.



◀ **Figure 7e.4b** Dermoscopically this lesion reveals linear, irregular (serpentine) vessels. Such a pattern can also be seen in amelanotic melanoma. However, the pre-test probability of this lesion being a melanoma in a three-year-old child is very low.

▲ **Figure 7e.5a** Clinical image of a Spitzoid lesion in a 56-year-old woman.

◀ **Figure 7e.5b** Dermoscopy reveals irregular vessels. This lesion was excised and the diagnosis was consistent with an atypical Spitz nevus. The pre-test probability that this Spitzoid lesion will prove to be melanoma remains high in older patients.

▲ **Figure 7e.6a** Clinical image of Spitz nevus.

◀ **Figure 7e.6b** A partially pigmented Spitz nevus dermoscopically characterized by brown to gray globules and dotted vessels together with reticular depigmentation.

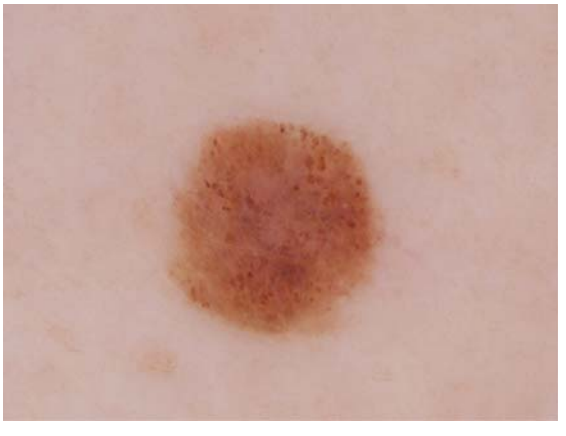
▲ **Figure 7e.7a** Clinical image of a lightly pigmented Spitz nevus.

◀ **Figure 7e.7b** This Spitz nevus manifests a negative network pattern.

▲ **Figure 7e.8a** Clinical image of a Spitz nevus.

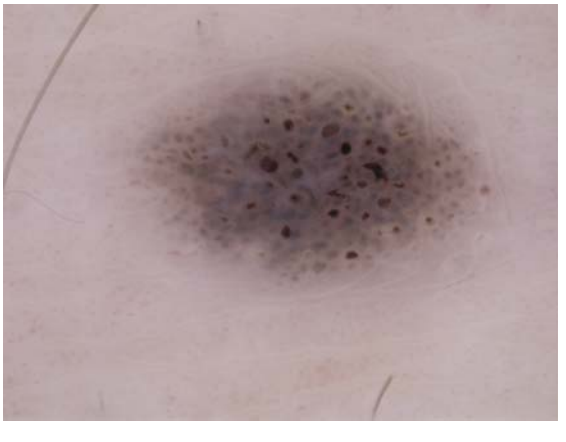
◀ **Figure 7e.8b** This image is taken with polarized light. Crystalline structures can clearly be seen within the center of the lesion.

▲ **Figure 7e.9a** Clinical image of a Spitz nevus.



◀ **Figure 7e.9b** Dermoscopy of this Spitz nevus reveals a diffuse brown background with multiple widely spaced globules.

▲ **Figure 7e.10a** Clinical image of a pigmented Spitz nevus.



◀ **Figure 7e.10b** Dermoscopy reveals multiple globules of differing colors. The deeper nests will appear bluish in color.

long-term longitudinal natural history of Spitz nevi remains unknown, some speculate that the final stage in the natural evolution of Spitz nevi is complete involution of the lesion (Argenziano et al., 2007).

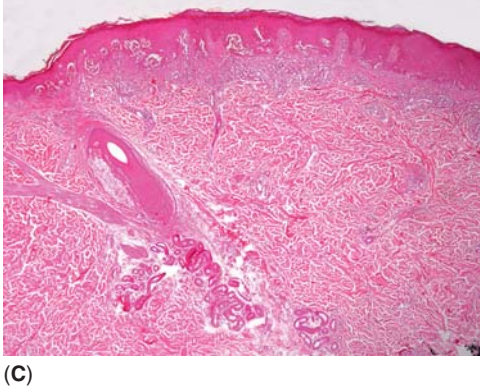
Overall, the "starburst," the "globular," and the "atypical" patterns are the most common dermoscopic patterns in surgically excised Spitz nevi (Ferrara et al., 2005). Such a high frequency of pigmented variants among excised lesions could be the result of improved clinical recognition of these lesions through dermoscopy coupled with low-excision rates of classical "pink" Spitz nevi in children. However, we feel that "pink" nodular lesions have the highest chances of harboring histopathologic features of atypia found in metastasizing "atypical Spitz nevi/tumors," such as nodular dermal growth, deep extension, deep dermal mitoses, and epidermal consumption (ulceration). The increasing dermoscopic recognition of pigmented Spitz nevi may result in us categorizing "classical" (see above) Spitz nevus as an uncommon and often histopathologically atypical variant (Fig. 7e.20A–D).

DIAGNOSIS AND MANAGEMENT

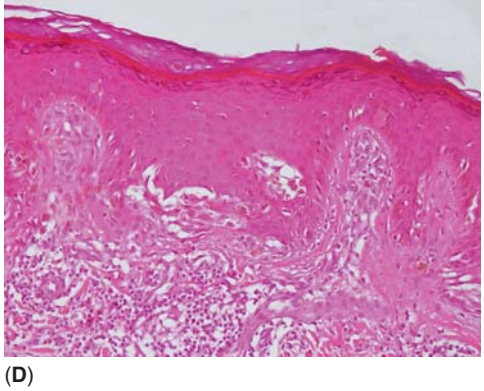
As a general rule, Spitz nevi can manifest any of the melanoma-specific structures listed in chapter 17, figure 17.5., but in Spitz nevi these structures tend to be distributed in a more or less *tidy or organized* fashion.

▲ **Figure 7e.11a** Clinical image of a Spitz nevus.

(**B**)

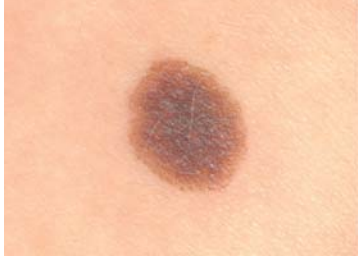


(**C**)

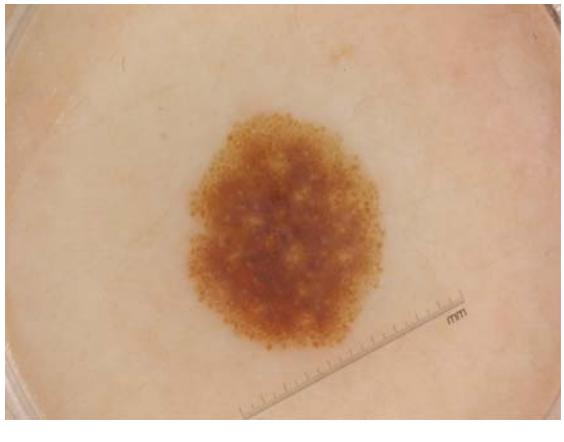


(**D**)

Figure 7e.11 (B) Dermoscopy reveals a pigmented Spitz nevus, with large brown globules and dotted vessels surrounded by reticular depigmentation. (C and D) Histology of this Spitz nevus is shown in these two images. A plaque-like melanocytic proliferation composed of regularly sized, shaped, and spaced junctional nests within a regularly hyperplastic epidermis (hematoxylin–eosin, ×40) (C). At closer examination (D), the nests of spindle and epithelioid melanocytes are accompanied by eosinophilic Kamino bodies (hematoxylin–eosin, ×200). Histopathologic diagnosis: Spitz nevus.



▲ **Figure 7e.12a** Clinical image of a Spitz nevus.



◀ **Figure 7e.12b** Dermoscopy reveals a starburst pattern consisting of tiered peripheral globules.

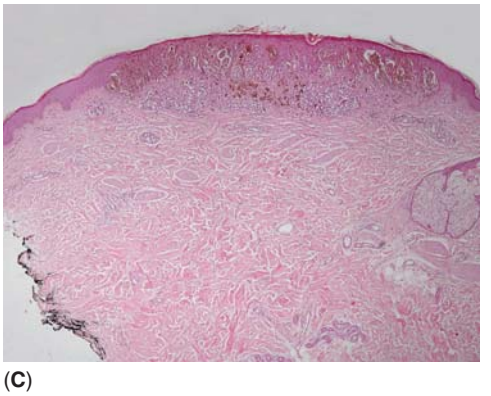
However, the occurrence of an atypical dermoscopic pattern in Spitz nevi is well recognized (Ferrara et al., 2005). In addition, the occurrence of melanomas exhibiting Spitzoid features with a globular or starburst or homogeneous or vascular pattern have been described (Argenziano et al., 1999).

Based on these considerations, a classic pink or pigmented Spitz nevus appearing before the age of 12 years can be managed conservatively if it is relatively small (up to 1 cm) and shows no atypical clinical and dermoscopic features (Brunetti et al., 2005). Under these circumstances, a followup can be scheduled every three to six months to insure that its biological behavior is benign (Brunetti et al., 2005). In the absence of dramatic and irregular changes in color, shape, or size, such a followup protocol can be continued until the lesion enters senescence and/or manifests a homogenous pattern. After the lesion enters senescence, annual followup of such lesions should suffice.

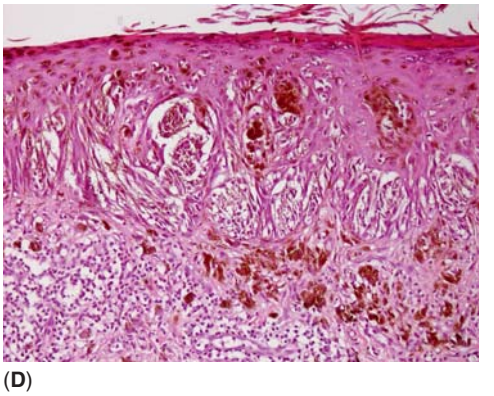
Spitz nevi developing in individuals above the age of 12 years and those lesions that are large (>1 cm), nodular, ulcerated, rapidly changing, or otherwise atypical, even if seen during childhood, should be excised. Surgical excision should also be contemplated for any Spitz nevus appear during adulthood, irrespective of the presence or absence of atypical clinical or dermoscopic features.

▲ **Figure 7e.13a** Clinical image of a pigmented Spitz nevus.

(**B**)



(**C**)



(**D**)

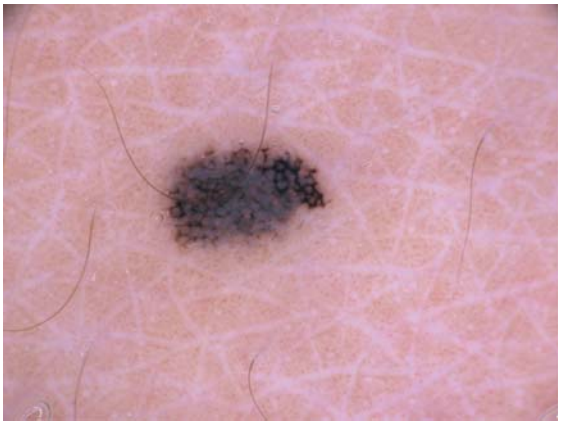
Figure 7e.13 (**B**) A small, heavily pigmented Spitz nevus with stereotypical starburst pattern. The starburst pattern in this lesion consists of streaks (pseudopods) around the entire perimeter of the lesion. (**C, D**) A small, sharply circumscribed, junctional melanocytic proliferation with an underlying band-like infiltrate of lymphocytes and melanophages [(**C**), hematoxylin–eosin, ×40]. The lesion is composed of small and monomorphic spindle-shaped melanocytes [(**D**), hematoxylin–eosin, ×200]. Histopathologic diagnosis: Reed nevus.

(**A**)

(**B**)

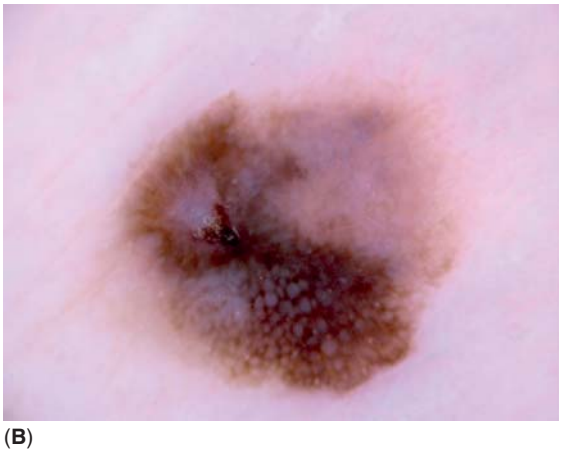
Figure 7e.14 (**A**) Dermoscopy of a Spitz nevus with a starburst pattern composed of pseudopods. (**B**) Dermoscopy of a Spitz nevus with a starburst pattern composed or radial streaming. *Source*: Image courtesy of Adam Korzenko.

▲ **Figure 7e.15a** Clinical image of a Spitz nevus.



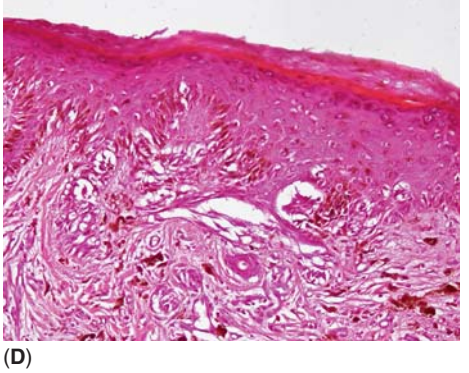
◀ **Figure 7e.15b** Dermoscopy of a small, flat, hyperpigmented Spitz nevus with superficial black network superimposed on a blue-gray pigmented background.

▲ **Figure 7e.16a** Clinical image of an atypical Spitz nevus.



(**B**)

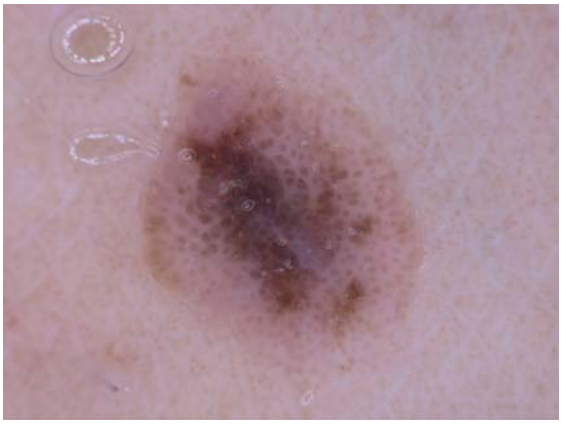
(**C**)



(**D**)

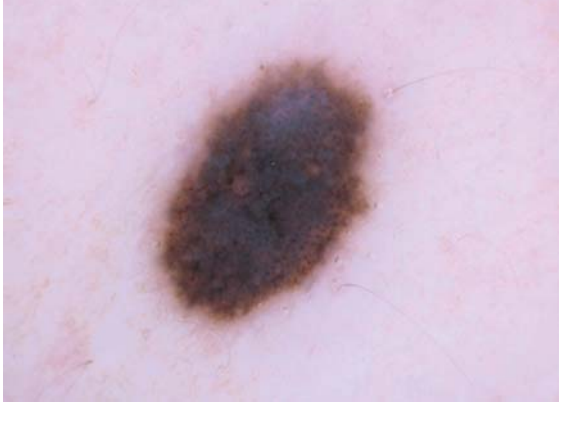
Figure 7e.16 (**B**) Pigmented Spitz nevus with melanoma-like pattern, typified by an atypical black network and irregular blue-white structures. (**C**, **D**) A slightly raised, mostly junctional melanocytic proliferation with epidermal hyperplasia (hyperkeratosis–hypergranulosis) associated with telangiectasias (hematoxylin–eosin, 40×) (**C**); junctional nests are predominantly made by spindle melanocytes (**D**). Histopathologic diagnosis: Spitz nevus.

▲ **Figure 7e.17a** Clinical image of an atypical Spitz nevus.



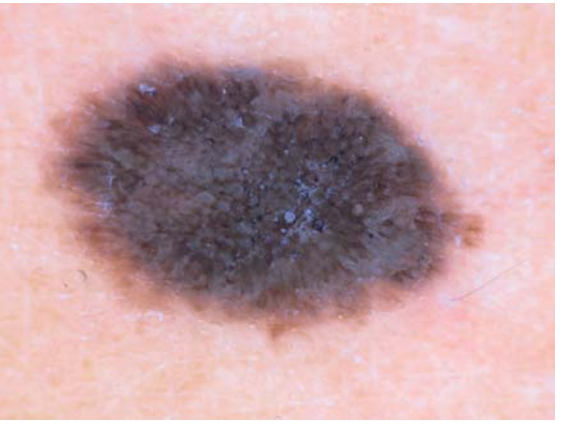
◀ **Figure 7e.17b** Pigmented Spitz nevus with melanoma-like pattern, typified by irregular globules and blue-white veil.

▲ **Figure 7e.18a** Clinical image of a pigmented Spitz nevus.

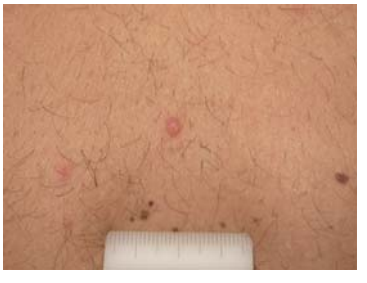


◀ **Figure 7e.18b** Pigmented Spitz nevus with a homogenous/globular overall pattern. The presence of the blue-white veil makes this lesion appear atypical under dermoscopy.

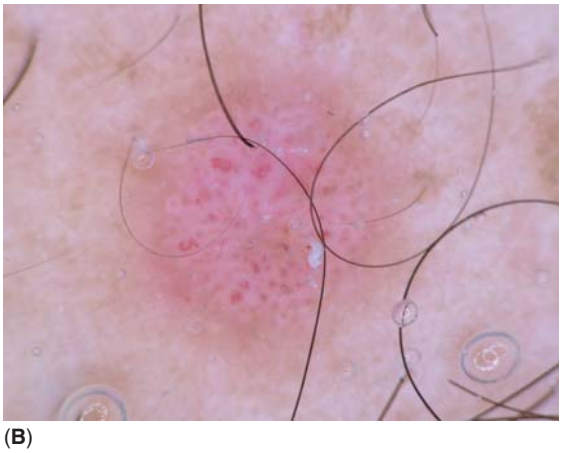
▲ **Figure 7e.19a** Clinical image of a pigmented Spitz nevus.



◀ **Figure 7e.19b** Pigmented Spitz nevus in which streaks are not clearly visible at the periphery. However, there is a superficial black network giving rise to a starburst-like appearance.

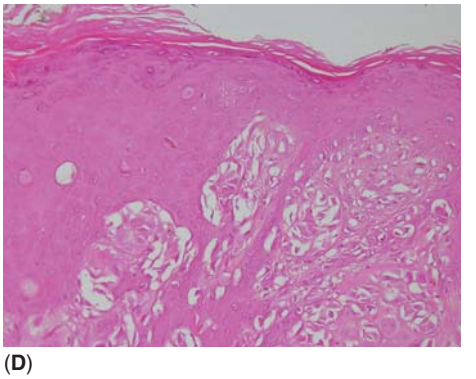


▲ **Figure 7e.20a** Clinical image of a Spitz nevus.



(**B**)

(**C**)



(**D**)

Figure 7e.20 (**B**) A small pink Spitz nevus with atypical vascular pattern and reticular depigmentation. (**C, D**) A small, dome-shaped, compound melanocytic proliferation with a striking epidermal hyperplasia [(**C**), hematoxylin–eosin, ×40]. Melanocytes are large, with an abundant, deeply eosinophilic cytoplasm; the higher-power-field examination also discloses some Kamino bodies as well as some ectatic blood vessels within the superficial dermis [(**D**), hematoxylin–eosin, ×200]. Histopathologic diagnosis: Spitz nevus.

Key Points

- Spitz nevus has two clinical variants: the *classical* (homogenous pink) and the *pigmented* type (the latter also comprising Reed nevus).
- Six main dermoscopic patterns can be ascribed to Spitz nevus: vascular (pink homogenous), globular, starburst, reticular, atypical, and homogenous pigmented.
- Most of these differing dermoscopic patterns may reflect different phases of the natural evolution of Spitz nevi.
- Currently, pigmented Spitz nevi are excised more frequently than are classical pink Spitz nevi. This may be due to the improved ability to recognize pigmented Spitz nevi with dermoscopy.
- It appears that the "pink" nodular Spitz nevi have the highest chances of manifesting atypical histopathologic features. Although infrequent, these pink Spitz nevi are also the ones that most frequently contribute to the group of metastasizing "atypical Spitz nevi/tumors."
- As a general rule, Spitz nevi can reveal any of the dermoscopic features and structures encountered in melanoma, but in Spitz nevi the distribution of these structures appears more organized.
- Surgical excision is usually the norm when Spitz nevi appear in the adulthood, irrespective of the presence or absence of atypical clinical or dermoscopic features.
- Atypical Spitz nevi and Spitz nevi that are large (>1 cm), nodular, ulcerated, rapidly changing, or otherwise atypical should be excised, irrespective of the patient's age.

REFERENCES

Argenziano, G., Scalvenzi, M., Staibano, S., et al., 1999, Dermatoscopic pitfalls in differentiating pigmented Spitz nevi from cutaneous melanomas. *Br J Dermatol*, 141, 788–93.

Argenziano, G., Zalaudek, I., Ferrara, G., et al., 2007, Involution: the natural evolution of pigmented Spitz and Reed nevi? *Arch Dermatol*, 143, 549–51.

Argenziano, G., Soyer, H.P., Ferrara, G., et al., 2001, Superficial black network: an additional dermoscopic clue for the diagnosis of spindle and/or epithelioid cell nevus. *Dermatology*, 203, 333–5.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Barnhill, R.L., 2006, The Spitzoid lesion: the importance of atypical variants and risk assessment. *Am J Dermatopathol*, 28, 75–83.

Barnhill, R.L., Argenyi, Z.B., From, L., et al., 1999, Atypical Spitz nevi/tumor: lack of consensus for diagnosis, discrimination from melanoma, and prediction of outcome. *Hum Pathol*, 30, 513–20.

Barnhill, R.L., Barnhill, M.A., Berwick, M. & Mihm, M.C., Jr., 1991, The histologic spectrum of pigmented spindle cell nevus: a review of 120 cases with emphasis on atypical variants. *Hum Pathol*, 22, 53–8.

Barnhill, R.L. & Mihm, M.C., Jr., 1989, Pigmented spindle cell nevus and its variants distinction from melanoma. *Br J Dermatol*, 121, 717–26.

Brunetti, B., Nino, M., Sammarco, E. & Scalvenzi, M., 2005, Spitz naevus: a proposal for management. *J Eur Acad Dermatol Venereol*, 19, 391.

Ferrara, G., Argenziano, G., Soyer, H.P., et al., 2005, The spectrum of Spitz nevi: a clinicopathologic study of 83 cases. *Arch Dermatol*, 141, 1381–7.

Peris, K., Ferrari, A., Argenziano, G., et al., 2002, Dermoscopic classification of Spitz/Reed nevi. *Clin Dermatol*, 20, 259–62.

Pizzichetta, M.A., Argenziano, G., Grandi, G., et al., Morphologic changes of a pigmented Spitz nevus assessed by dermoscopy. *J Am Acad Dermatol*, 47, 137–9.

Reed, R.J., Ichinose, H., Clark, W.H., et al., 1975, Common and uncommon melanocytic nevi and borderline melanomas. *Semin Oncol*, 2, 119–47.

Smith, K., Skelton, H., Lupton, G. & Graham, J., 1989, Spindle cell and epithelioid cell nevi with atypia and metastasis (malignant Spitz nevus). *Am J Surg Pathol*, 13, 931–9.

Smith, N.P., 1987, The Pigmented Spindle Cell Tumor of Reed: An Underdiagnosed Lesion. Semin Diagn Pathol 4, 75–87.

Spitz, S., 1948, Melanomas of childhood. *Am J Pathol*, 24, 591–609.

Weedon, D. & Little, J.H., 1977, Spindle and epithelioid cell nevi in children and adults: a review of 211 cases of the Spitz nevus. *Cancer*, 40, 217–25.

7f Recurrent (persistent) nevi

Ashfaq A. Marghoob

Persistent nevi, also called recurrent nevi or pseudomelanoma, are defined as recurrences of pigmentation that appear after incomplete removal of a compound (Fig. 7f.1) or intradermal melanocytic nevus (Fig. 7f.2) (Harvell & White, 1999; Harvell et al., 2002; Sexton & Sexton, 1991). Many mechanisms have been proposed for the pathogenesis of these nevi; however, most theories suggest that persistent nevi arise from residual nevomelanocytes found in hair follicles, sweat glands, dermis, or epidermis (Sexton & Sexton, 1991). Although most persistent nevi arise after incomplete surgical removal, some can arise after laser treatment or after non–biopsy-related trauma to a melanocytic nevus (Figs. 7f.3 and 7f.4) (Langel & White, 2000).

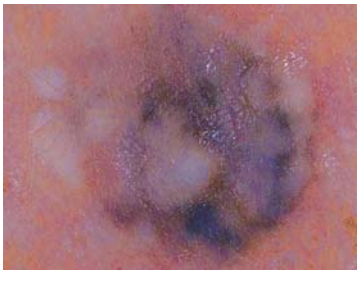
As the term "pseudomelanoma" implies, it may be difficult to differentiate recurrent nevi from melanoma at the clinical, dermoscopic, and histopathologic levels (Figs. 7f.4–7f.6). Obviously, a history of a previous biopsy of a benign nevus at the location of the now recurrent lesion is an important clue to the diagnosis of a recurrent nevus. In such scenarios it is important to review the original pathology slides to insure that the biopsied lesion was indeed benign (Figs. 7f.7 and 7f.8). With that said, there are subtle differences that may enable one to distinguish between a recurrent nevus *versus* a recurrent melanoma. A historical clue is that in recurrent nevi the appearance of the pigmentation usually develops within three to six months (Park et al., 1987). In contrast, the pigment in locally recurrent melanomas characteristically becomes apparent after six months from the time of the biopsy; in fact, most recur years after the initial biopsy. In addition, in persistent nevi the pigment almost never extends beyond the scar (i.e., the pigment is usually confined to within the scar), whereas recurrent melanoma often manifests as a pigmented macule, papule, or nodule at the edge of a scar, frequently extending beyond the scar—extending onto normal uninvolved skin (Figs. 7f.5–7f.9).

The dermoscopic features of persistent nevi include the following: asymmetry, sharp borders, homogenous or multicomponent pattern, atypical pigment network, irregular streaks, black dots, globules, and blue-gray or red colors (Marghoob & Kopf, 1997). It is not uncommon for the pigment of recurrent nevi to fade over time (Figs. 7f.10 and 7f.11). The same dermoscopic features seen in persistent nevi can also be seen in primary melanoma. The dermoscopic features of local recurrent melanoma are described as globular or diffuse nonhomogenous pigmentation in the absence of a pigment network (Ferrari et al., 2000). However, pigment network, regression structures, crystalline structures, or other melanoma-specific structures can also be seen.

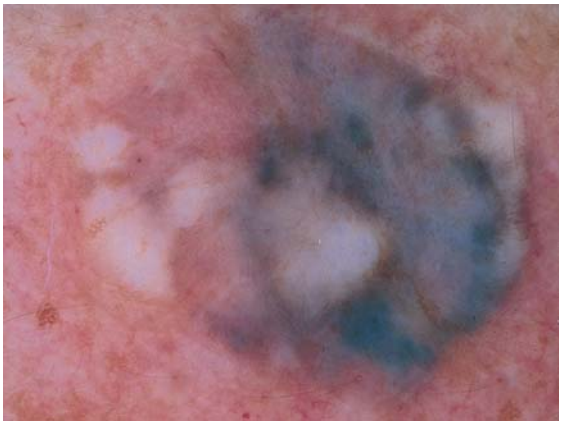
In conclusion, it is often impossible to differentiate recurrent nevi from melanoma. As a general rule, in recurrent nevi the pigment will not extend beyond the white biopsy scar, the pigment will recur within three to six months from the time of the biopsy, the entire scar will often be surrounded by a light brown halo of pigment, and the pigment will often fade over time (Figs. 7f.1, 7f.5, and 7f.12).

▲ **Figure 7f.1a** Clinical image.

◀ **Figure 7f.1b** Dermoscopic image of recurrence of pigmentation after shave biopsy of a compound nevus. Notice that the pigment recurrence is confined to within the white scar and also notice that the white scar is surrounded by a light brown halo.

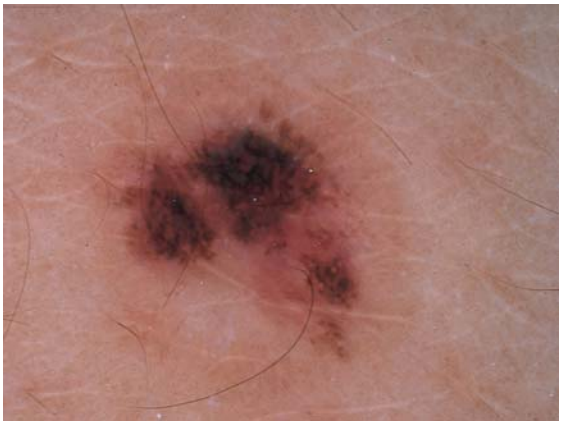


▲ **Figure 7f.2a** Clinical image.

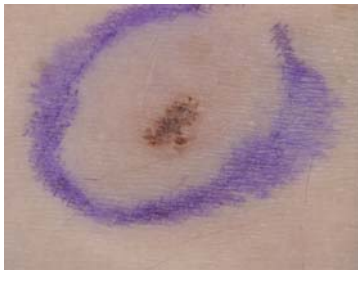


◀ **Figure 7f.2b** Recurrence of a blue nevus (intradermal). The dermoscopic image has features that can be seen in melanoma, such as blue color and areas reminiscent of regression (white scar-like areas).

▲ **Figure 7f.3a** Clinical image.



◀ **Figure 7f.3b** Recurrent nevus that developed after trauma. Dermoscopic structures, such as streaks, thickened network, globules, and asymmetry, are all features that are also seen in melanoma.



▲ **Figure 7f.4a** Clinical closeup of this recurrent nevus.

◀ **Figure 7f.4b** As can be seen in the upper panel, the patient had a skin-colored intradermal nevus on the medial aspect of his upper arm. The lesion was traumatically scratched off and shortly thereafter the site developed a pigmented macule, as evident in the lower panel.

◀ **Figure 7f.4c** Dermoscopy reveals peripheral streaks and irregular dots, which are structures commonly associated with melanoma. The lesion was biopsied and pathology confirmed this to be a recurrent nevus.

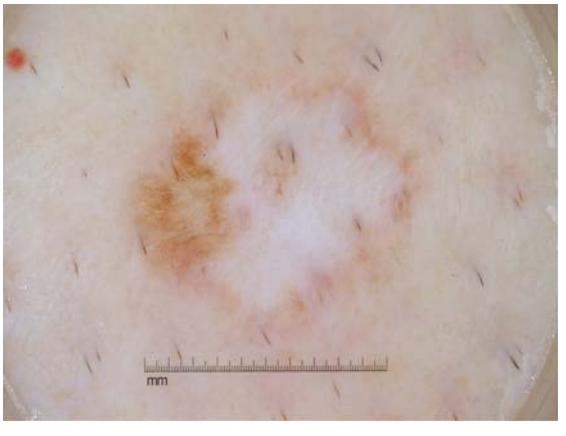
▲ **Figure 7f.5a** Clinical image.

◀ **Figure 7f.5b** Recurrent nevus manifesting asymmetry and streaks, both features commonly seen in melanoma. As a general rule, the recurrent pigment in persistent nevi will not extend beyond the white-scarred skin and the entire scar will often be surrounded by a light brown halo of pigment (Fig. 7f.2).

▲ **Figure 7f.6a** Clinical image.

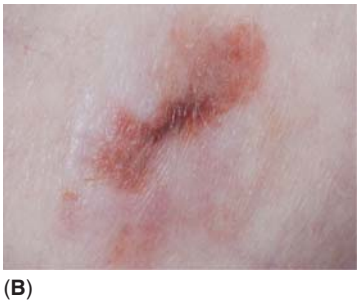
◀ **Figure 7f.6b** The morphology of persistent nevi overlap with melanoma. The dermoscopic image of this recurrent nevus reveals asymmetry, multicomponent pattern, atypical pigment network, irregular streaks, globules, and areas suggestive of regression (regression structures).

▲ **Figure 7f.7a** Clinical image of recurrent pigment in association with a scar. The patient had a shave biopsy performed two years prior to the onset of the recurrent pigmentation.



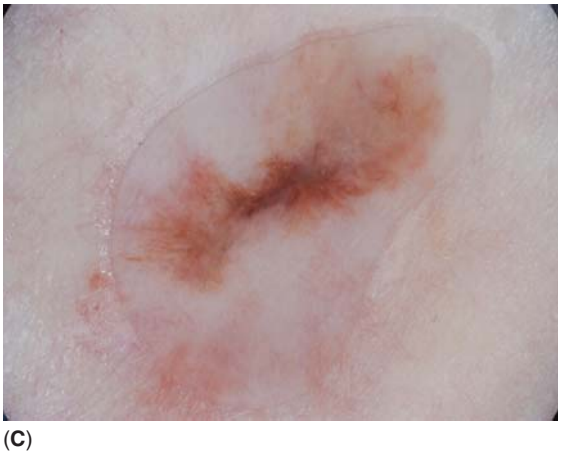
◀ **Figure 7f.7b** Dermoscopy reveals pigment network within the scar; however, the pigment network is also traversing from the scar onto normal skin. The original biopsy report was that of a dysplastic nevus. The original biopsy slides were re-reviewed and the diagnosis of a dysplastic nevus with moderate atypia was confirmed. However, this recurrent lesion was completely excised and the pathology was consistent with a melanoma. It is possible that this melanoma may have arisen from residual nevus cell or from a focus of melanoma that was missed on partial biopsy or step-sectioning of the tissue.

▶ **Figure 7f.8a** This patient had a biopsy performed on a lesion on her breast (*left panel*). Approximately 3.5 years after the biopsy there was pigment noted to be developing within the scar (*right panel*).

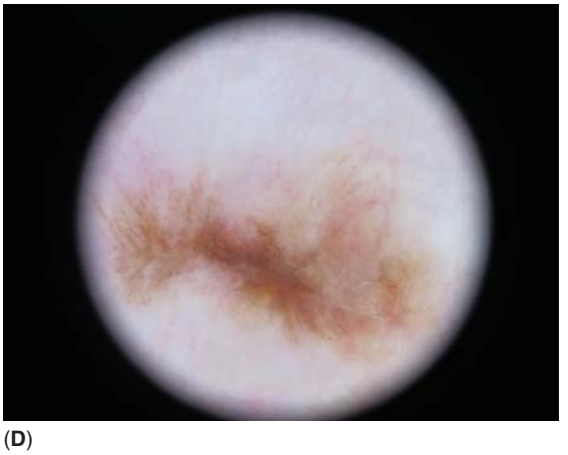


◀ **Figure 7f.8b** Closeup clinical image of recurrent pigment.

(**B**)



(**C**)



(**D**)

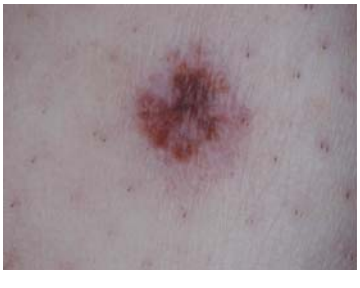
Figure 7f.8 (**C**) Nonpolarized dermoscopy reveals tan structureless areas and regression structures. (**D**) Polarized dermoscopy reveals chrysalis/crystalline/shiny white lines. The combined features seen in polarized and nonpolarized dermoscopy are suggestive of melanoma. The original biopsy report stated that the lesion was a dysplastic nevus with severe atypia. The original biopsy slides were re-reviewed and the diagnosis rendered was not dysplastic nevus but rather melanoma. This area was re-excised and revealed melanoma with a thickness of 0.45 mm. Thus, this lesion was a locally recurrent melanoma.

▲ **Figure 7f.9a** Clinical image.

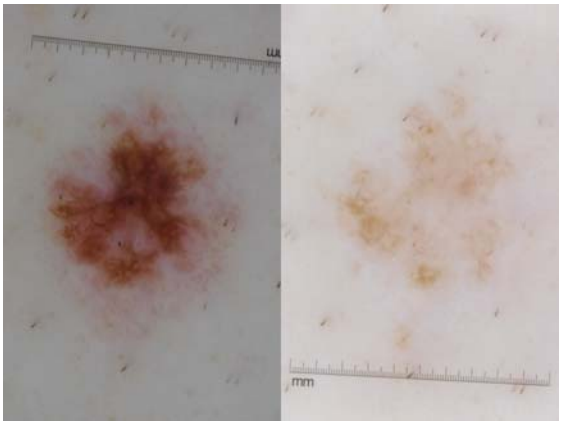
◀ **Figure 7f.9b** Recurrent nevus that reveals many of the features discussed in this chapter. This lesion manifests streaks, blotch, and regression structures (all of which are commonly seen in melanoma). However, notice that the pigment is confined to the white scar, and that the white scar is surrounded by a light brown halo (both features commonly seen in recurrent nevi).

▲ **Figure 7f.10a** A superficial congenital nevus was biopsied and approximately two months later recurrence of pigment was noted within the scar.

◀ **Figure 7f.10b** The lesion was followed dermoscopically. The initial recurrent nevus revealed pigment confined to within the scar with the presence of irregular dots and globules (*left panel*). Three months later (*right panel*) the dots and globules were no longer visible, the recurrent pigment consisted of a tan homogenous color and the lesion had become lighter in color.



▲ **Figure 7f.11a** Clinical image of a recurrent superficial congenital nevus.



◀ **Figure 7f.11b** Dermoscopy reveals focal atypical network within the scar (left panel). Approximately six months later the recurrent pigment has almost completely faded away.

▲ **Figure 7f.12a** Clinical image of recurrent nevus.

◀ **Figure 7f.12b** Dermoscopy reveals blue white veil and globules confined to within the scar. This nevus recurred less than three months after the original biopsy. The recurrent pigment is confined to within the scar and the scar is surrounded by a light brown halo of pigment.

Key Points

1. Incomplete removal of a melanocytic neoplasm can result in recurrence of pigmentation within the scar.
2. If a nevus were to recur, it tends to recur within 6 months and the pigment tends to be confined to within the scared area.
3. The dermoscopic features of a recurrent nevus can resemble melanoma.
4. If a melanoma were to recur, it tends to re-pigment more than 6 months after the biopsy and the pigment often transverses the boundary between the scar and normal skin.

REFERENCES

Ferrari, A., Peris, K., Piccolo, D. & Chimenti, S., 2000, Dermoscopic features of cutaneous local recurrent melanoma. *J Am Acad Dermatol*, 43, 722–4.

Harvell, J.D. & White, W.L., 1999, Persistent and recurrent blue nevi. *Am J Dermatopathol*, 21, 506–17.

Harvell, J.D., Bastian, B.C. & LeBoit, P.E., 2002, Persistent (recurrent) Spitz nevi: a histopathologic, immunohistochemical, and molecular pathologic study of 22 cases. *Am J Surg Pathol*, 26, 654–61.

Langel, D.J. & White, W.L., 2000, Pseudomelanoma after non-biopsy trauma: expanding the spectrum of persistent nevi. *J Cutan Pathol*, 27, 562.

Marghoob, A.A. & Kopf, A.W., 1997, Persistent nevus: an exception to the ABCD rule of dermoscopy. *J Am Acad Dermatol*, 36, 474–5.

Park, H.K., Leonard, D.D., Arrington, J.H. & Lund, H.Z., 1987, Recurrent melanocytic nevi: clinical and histologic review of 175 cases. *J Am Acad Dermatol*, 17, 285–92.

Sexton, M. & Sexton, C.W., 1991, Recurrent pigmented melanocytic nevus. A benign lesion, not to be mistaken for malignant melanoma. *Arch Pathol Lab Med*, 115, 122–6.

8 Melanoma

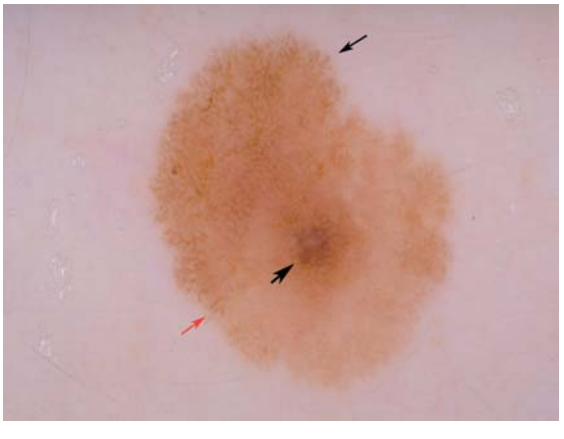
8a Superficial spreading melanoma

Scott W. Menzies

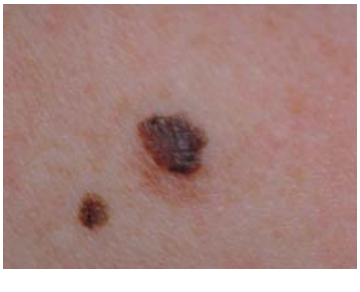
Superficial spreading melanoma (SSM) represent 66% of all invasive melanomas (Chamberlain et al., 2002). An SSM is defined as an invasive melanoma that has an in situ component beyond three rete ridges of its invasive component. Invasion of malignant melanocytes both singly and in nests upward within the epidermis (pagetoid spread) and radially at the dermoepidermal junction (DEJ) is characteristic of these malignancies (Argenziano et al., 1997). These histologic features correlate with the dermoscopic features found at the edge of an SSM (Figs. 8a.1–8a.19).

1. *Pseudopods and radial streaming*. Their presence represents confluent radial nests of melanoma at the DEJ and is indicative of radial growth (Figs. 8a.1, 8a.5, 8a.7–8a.9, 8a.14 and 8a.15).
2. *Peripheral black dots/globules* represent malignant melanocytes found at or near the stratum corneum (Figs. 8a.15 and 8a.19). Multiple *brown dots* correlate with suprabasal epidermal malignant melanocytes and represent the pagetoid spread of an SSM (Figs. 8a.8 and 8a.9).
3. *Blue-gray fine dots (peppering)* represent the common occurrence of regression in SSM. Regression correlates with the dermoscopy findings of multiple blue-gray fine dots also known as blue-gray peppering (melanophages in the early–intermediate phase of regression) and scar-like depigmentation (chronic phase of regression) (Figs. 8a.3, 8a.6–8a.8, 8a.10, 8a.14 and 8a.17).
4. *Atypical broadened network* correlates with the expansion of malignant melanocytes at the rete ridges and can often be found focally at or near the edge of an SSM (Menzies et al., 1996a; Menzies et al., 1996b; Menzies et al., 2003). The broadened atypical network may be the only specific feature of early thin SSM (Figs. 8a.1, 8a.2, 8a.4–8a.6, 8a.9, 8a.12 8a.13).
5. *Blue-white veil*, which is due to melanin in the mid-dermis with overlying epidermal compact orthokeratosis is also frequently observed in melanomas (Figs. 8a.6, 8a.7, 8a.9, 8a.10, 8a.12, 8a.13 and 8a.15).
6. *Multiple colors*, due to melanin at various levels within the dermis and epidermis, are commonly seen in SSM (Figs. 8a.9, 8a.11, 8a.15, 8a.17 8a.19).
7. *Negative pigment network* is seen as a "negative" of the pigmented network, with light areas making up the grids of the network and the dark areas filling the "holes." Histology reveals elongated hypomelanotic rete ridges. It can be seen in melanoma, Spitz nevi, and dysplastic nevi.
8. *Peripheral light brown structureless areas* are seen as light brown, variable sized and shaped areas found at the periphery of a lesion and occupying more than 10% of its surface (Annessi et al., 2007). Histologically the areas are due to relative flattening of the rete ridges in combination with a prepon-

▲ **Figure 8a.1a** Clinical image.

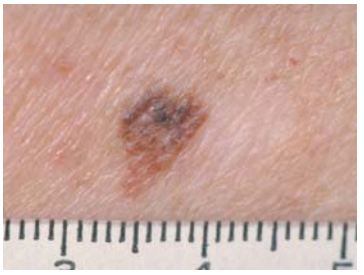


◀ **Figure 8a.1b** This is an asymmetrically patterned multicolored lesion. It lacks symmetry of pattern over every axis through the center of the lesion (see chap. 7b) and has more than one color; scored from tan, dark brown, gray, black, blue, and red. It has the positive melanoma features of a broadened atypical network (*thick arrow*), and the pseudopod (*thin arrow*), and radial streaming (*red arrow*) are very subtle. Note the peripheral light brown structureless area occupying more than 10% of the lesion surface from 3 to 7 o'clock in position. Diagnosis: in situ superficial spreading melanoma.

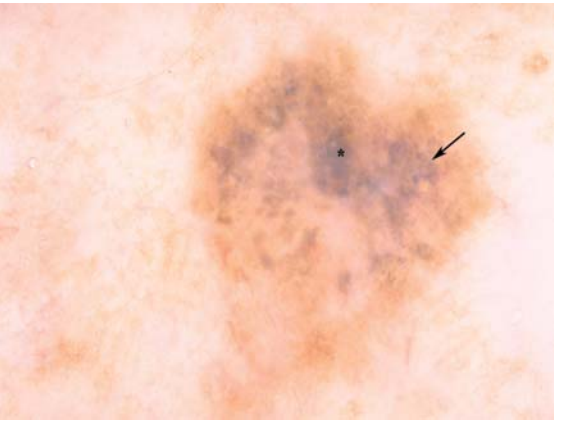


▲ **Figure 8a.2a** Clinical image.

◀ **Figure 8a.2b** This asymmetrically patterned multicolored lesion has the positive melanoma feature of broadened atypical network (*arrows*). Broadened network is usually seen focally rather than in a uniform distribution. It is probably the most important (sensitive) feature of early nonregressing superficial spreading melanoma (SSM). Note the blue pigmentation formed by confluent melanophages in the dermis. Diagnosis: in situ SSM.

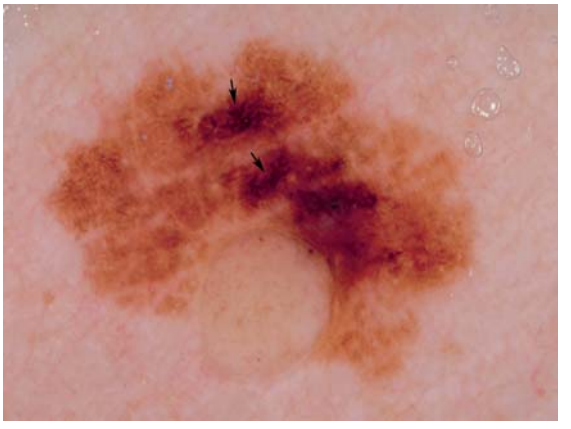


▲ **Figure 8a.3a** Clinical image.

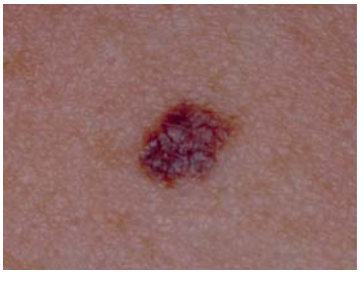


◀ **Figure 8a.3b** This asymmetrically patterned multicolored lesion has both the positive melanoma features of regression (scar-like depigmentation and multiple blue-gray dots; the latter indicated by the *arrow*). Confluence of melanophages is seen in this lesion as blue-white veil (*asterisk*). Diagnosis: regressing superficial spreading melanoma, Breslow thickness 0.3 mm.

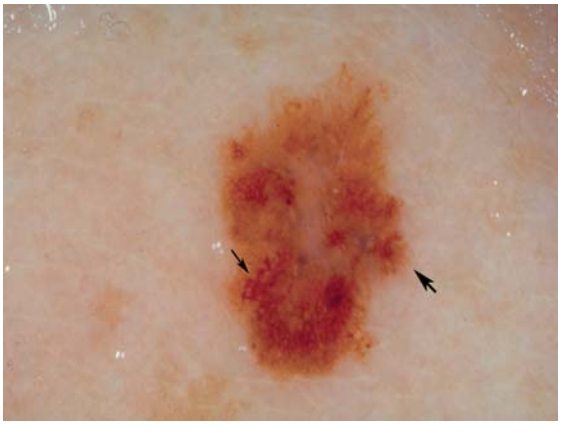
▲ **Figure 8a.4a** Clinical image.



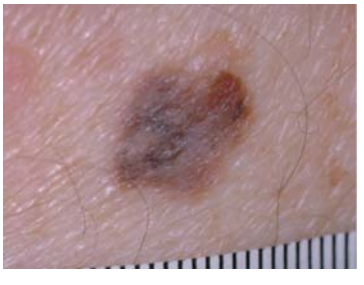
◀ **Figure 8a.4b** This asymmetrically patterned multicolored lesion has the one positive melanoma feature of focal broadened network (*arrows*). Note the amelanotic contiguous nevus. Diagnosis: superficial spreading melanoma, Breslow thickness 0.35 mm with a contiguous compound nevus.



▲ **Figure 8a.5a** Clinical image.

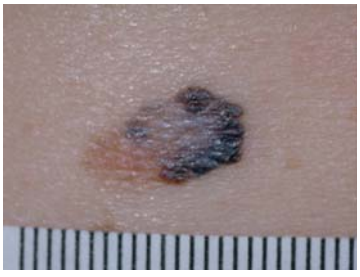


◀ **Figure 8a.5b** This asymmetrically patterned multicolored lesion (dark brown, tan, and gray) has the positive features of focal broadened network (*thin arrow*) and subtle radial streaming (*large arrow*). Diagnosis: superficial spreading melanoma, Breslow thickness 0.35 mm.

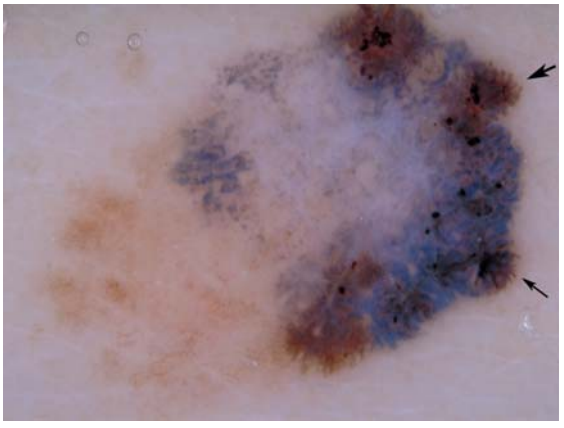


▲ **Figure 8a.6a** Clinical image.

◀ **Figure 8a.6b** This asymmetrically patterned multicolored lesion has the positive features of scar-like depigmentation, blue-white veil, and focal broadened network (*arrow*). In addition, note the widespread peripheral light brown structureless areas occupying more than 10% of the lesion surface. Diagnosis: regressing superficial spreading melanoma, Breslow thickness 0.4 mm.

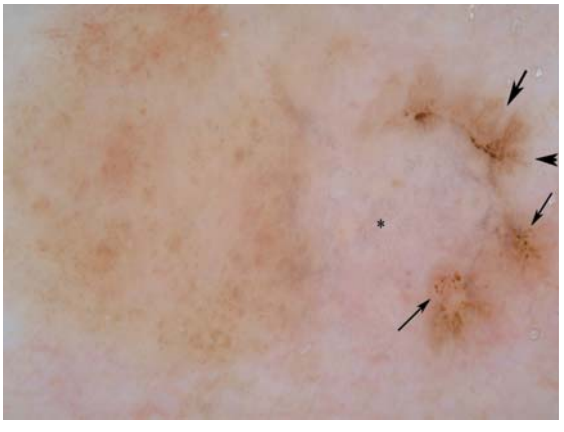


▲ **Figure 8a.7a** Clinical image.

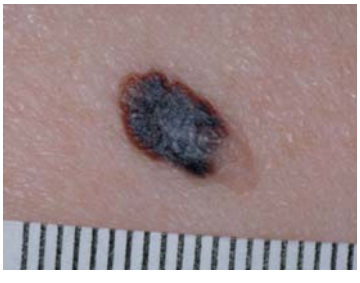


◀ **Figure 8a.7b** This asymmetrically patterned multicolored lesion has the positive melanoma features of blue-white veil, radial streaming (*thin arrow*), pseudopods (*thick arrow*), scar-like depigmentation, multiple blue-gray dots, and multiple (5–6) colors (scored from tan, dark brown, gray, blue, black, and red). Note the contiguous nevus at the left pole. Diagnosis: superficial spreading melanoma, Breslow thickness 0.42 mm.

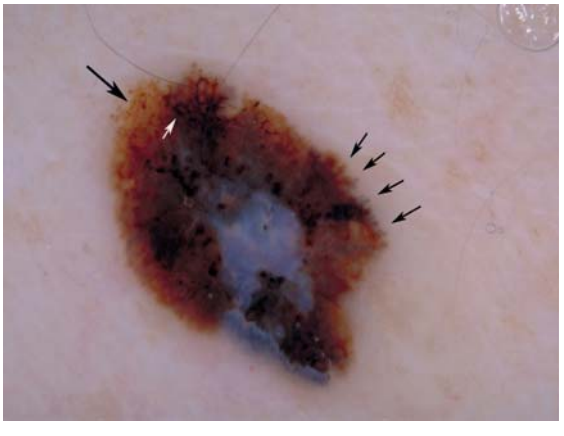
▲ **Figure 8a.8a** Clinical image.



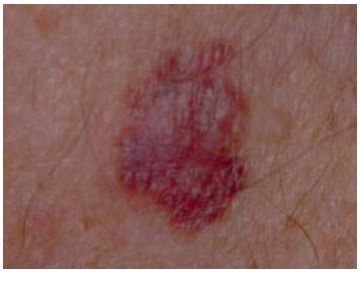
◀ **Figure 8a.8b** This asymmetrically patterned multicolored lesion has the positive melanoma features of multiple brown dots, found in the classical focal distribution (*thin arrows*), radial streaming (*thick arrows*), and multiple blue-gray dots (*asterisk*). Note the contiguous banal nevus at the left half of the lesion. Diagnosis: regressing superficial spreading melanoma, Breslow thickness 0.45 mm with a contiguous compound nevus.



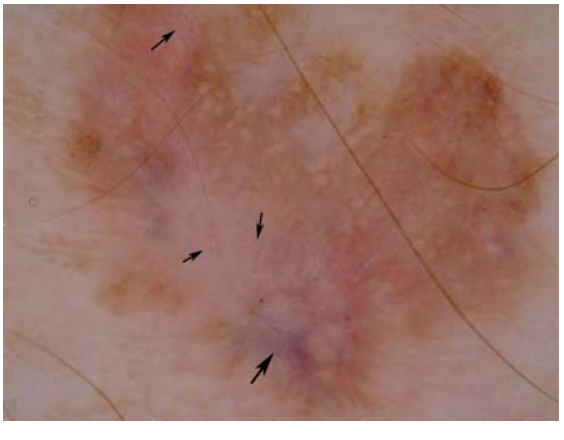
▲ **Figure 8a.9a** Clinical image.



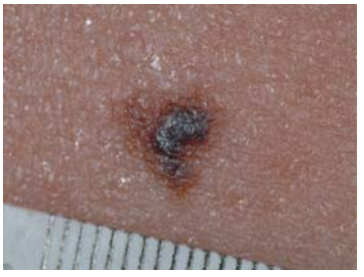
◀ **Figure 8a.9b** This asymmetrically patterned multicolored lesion has the positive melanoma features of blue-white veil, radial streaming and pseudopods (*thin arrows*), multiple brown dots (*thick arrow*), focal broadened network (*white arrow*), and multiple (5–6) colors. Diagnosis: superficial spreading melanoma, Breslow thickness 0.5 mm with a contiguous dermal nevus.



▲ **Figure 8a.10a** Clinical image.



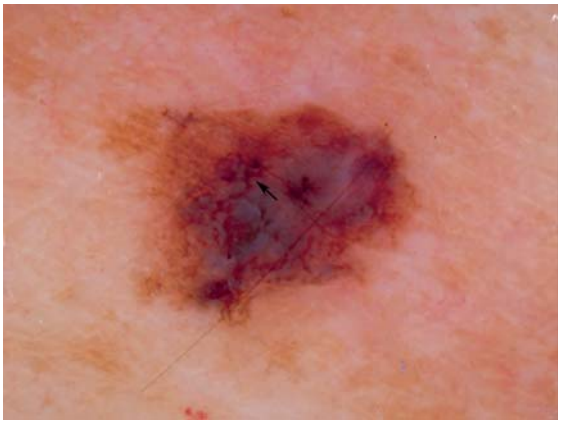
◀ **Figure 8a.10b** This lesion is identified as melanocytic because of the areas of network and brown globules. It is multicolored, has an asymmetric pattern and has the positive features of scar-like depigmentation and blue-white veil (*thick arrow*). Note the pin-point (dotted) vessels in the hypomelanotic areas (*thin arrows*). The presence of dotted vessels is suggestive that the lesion is a melanocytic tumor, and since the lesion is asymmetric the diagnosis of melanoma must be ruled out. Also seen are widespread peripheral light brown structureless areas. Diagnosis: regressing superficial spreading melanoma, Breslow thickness 0.5 mm.



▲ **Figure 8a.11a** Clinical image.

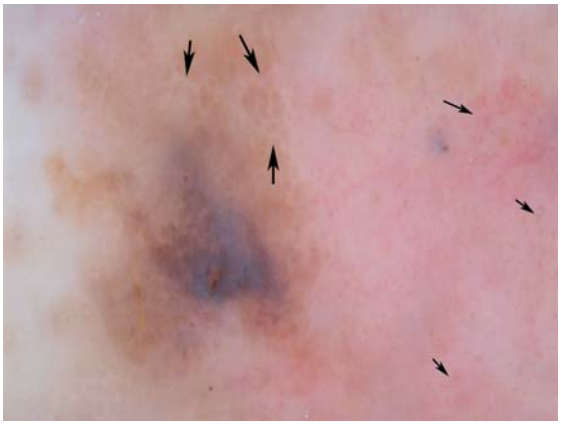
◀ **Figure 8a.11b** This melanoma has the positive feature of multiple (5–6) colors. Diagnosis: superficial spreading melanoma, Breslow thickness 0.55 mm.

▲ **Figure 8a.12a** Clinical image.

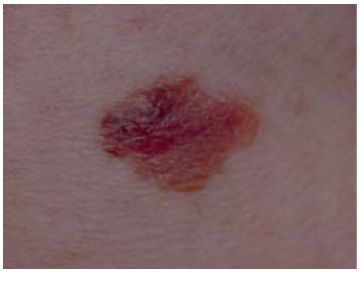


◀ **Figure 8a.12b** This asymmetrically patterned multicolored lesion has the positive features of blue-white veil and broadened network (*arrow*). Diagnosis: superficial spreading melanoma, Breslow thickness 0.6 mm.

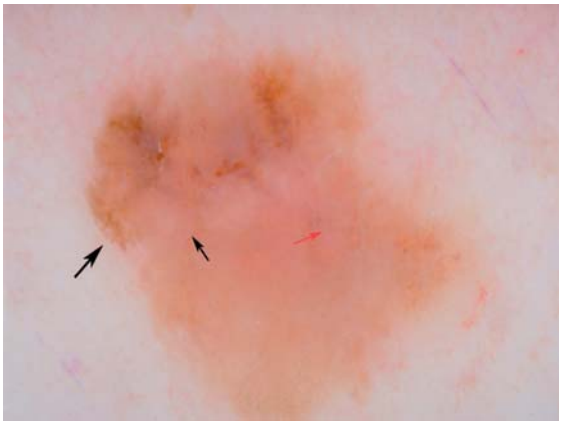
▲ **Figure 8a.13a** Clinical image.



◀ **Figure 8a.13b** This hypomelanotic asymmetrically patterned multicolored lesion has the positive features of extensive scar-like depigmentation and blue-white veil. Note the pin-point (dotted) vessels within the amelanotic component (*small arrow*). Also note the negative pigment network (*large arrow*), which is a significant finding in both Spitz nevi and invasive melanoma (Menzies et al., 1996b). Diagnosis: superficial spreading melanoma, Breslow thickness 0.7 mm.

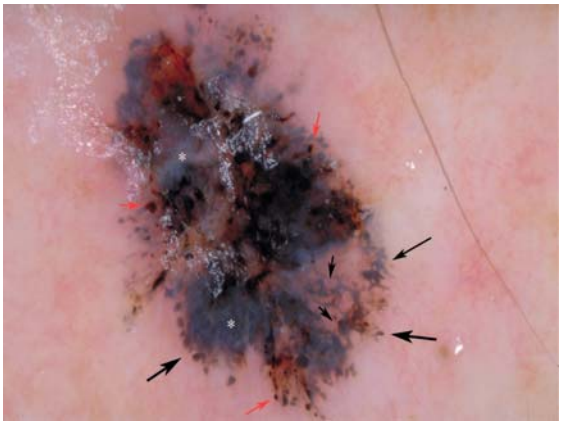


▲ **Figure 8a.14a** Clinical image.



◀ **Figure 8a.14b** This asymmetric multicolored lesion (tan and dark brown) has the positive features of scar-like depigmentation (*fine arrow*) and subtle radial streaming (*thick arrow*). Diagnosis: superficial spreading melanoma, Breslow thickness 0.7 mm.

▲ **Figure 8a.15a** Clinical image.

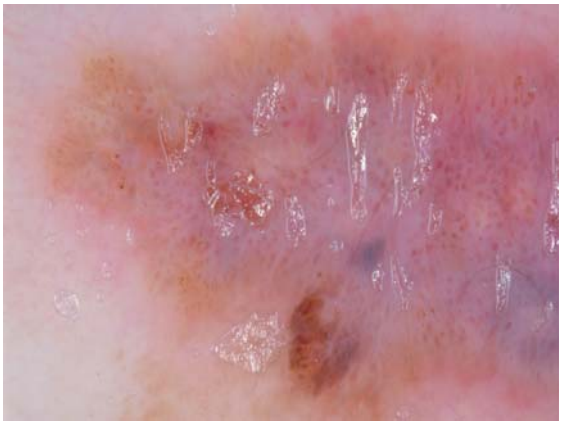


◀ **Figure 8a.15b** This asymmetrically patterned multicolored lesion has the positive melanoma features of broadened network (*thin arrow*), blue-white veil (*asterisk*), peripheral black dots/globules (*red arrow*), pseudopods (*thick arrow*), and multiple (5–6) colors. Diagnosis: superficial spreading melanoma, Breslow thickness 0.8 mm.

▲ **Figure 8a.16a** Clinical image.

◀ **Figure 8a.16b** This amelanotic lesion has some linear irregular and arborising vessels. Because of overlap between amelanotic melanoma and other malignant amelanotic lesions, it is easier to distinguish all malignant amelanotic/hypomelanotic lesions from all benign lesions rather than to attempt to discriminate melanoma from other malignant lesions, such as basal cell carcinoma. This illustrates the importance of biopsy prior to any nonsurgical treatment of amelanotic lesions. Diagnosis: amelanotic superficial spreading melanoma, Breslow thickness 0.8 mm.

▲ **Figure 8a.17a** Clinical image.



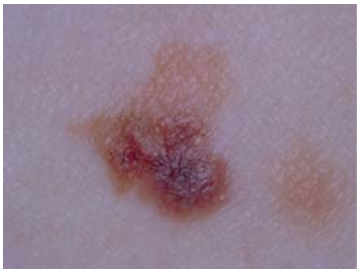
◀ **Figure 8a.17b** This hypomelanotic lesion is asymmetric in pattern and multicolored. It has foci of brown dots and globules indicating its melanocytic origin. In addition, it has the positive features of scar-like depigmentation and blue-white veil. Note the extensive pin-point (dotted) vessels in the amelanotic component. Also seen are widespread peripheral light brown structureless areas (especially at the superior lesion border). Diagnosis: superficial spreading melanoma, Breslow thickness 1.1 mm.

derance of single-cell pagetoid melanoma cells and pigmented keratinocytes rather than the formation of nests in the epidermis (Figs. 8a.1, 8a.6, 8a.10, 8a.11, 8a.17, 8a.19).

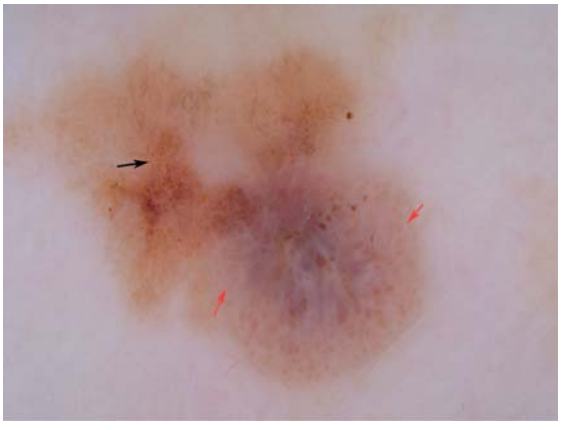
9. Crystalline structures consist of shiny white lines that are often oriented orthogonal to each other (see chapter 6a). This structure can only be seen with polarized light and correlates with an altered stromal matrix. The presence of crystalline structures is suggestive of an invasive melanoma (Balagula et al., 2011).
10. Other structures commonly seen in SSM include blotches and atypical vessels. The most predictive vascular pattern for melanoma is the combination of dotted and linear-irregular (serpentine) vessels.

Table 8a.1 shows the specificity and sensitivity of the important dermoscopic features of invasive SSM. The morphologic definitions of the above features have been described in detail in chapter 7b. SSMs have a number of specific dermoscopic features that are less commonly found in nodular melanoma. Indeed, the vast majority of pigmented SSMs are easily identified using dermoscopic criteria.

In contrast to pigmented SSMs, fewer descriptions of the dermoscopy of hypomelanotic or amelanotic SSMs are published (Bono et al., 2001; Pizzichetta et al., 2004; Menzies et al., 2008). These latter lesions can be due to widespread regression, in which case their diagnosis is less difficult because of the positive specific features of scar-like depigmentation with or without multiple blue-gray fine dots (melanophages) (Figs. 8a.3, 8a.6, 8a.7). More difficult



▲ **Figure 8a.18a** Clinical image.



◀ **Figure 8a.18b** This asymmetrically patterned multicolored SSM has the positive melanoma features of focal multiple brown dots (*arrows*) and small areas of blue-white veil. Note also the extensive negative pigment network (*red arrow*). Diagnosis: SSM, Breslow thickness 1.2 mm with associated compound nevus. *Abbreviation*: SSM, superficial spreading melanoma.

▲ **Figure 8a.19a** Clinical image.

◀ **Figure 8a.19b** This asymmetrically patterned multicolored lesion has the positive melanoma features of blue-white veil, peripheral black dots/globules, and multiple (5–6) colors. Also seen are peripheral light brown structureless areas at the left border of the lesion. Diagnosis: superficial spreading melanoma, Breslow thickness 1.4 mm.

Table 8a.1 The Major Dermoscopic Features of Invasive Superficial Spreading Melanoma

Melanoma specific structure/feature	Sensitivity (highest reported; %)	Specificity (highest reported; %)	Odds ratio (highest reported)
Atypical network	77	89	9.0
Irregular streaks	23	99	5.8
Negative network	22	95	2.0
Chrysalis/ crystalline	5	99	9.7
Atypical dots and globules	88	97	4.8
Irregular blotch	38	88	4.1
Blue-white veil (raised)	51	99	13
Regression structures	46	94	8.0
Atypical vessels	63	96	12.5
Peripheral brown structureless areas[a]	63	96	28
5–6 colors	53	95	3.2

[a]Data were derived from both in situ and thin invasive melanoma (Annessi et al., 2007).
Source: Adapted from Menzies et al. (1996a), with additions.

are the true amelanotic/hypomelanotic SSMs. In the largest series published where more than 80% were SSMs, the most significant positive predictive nonregressing features were (in order) blue-white veil, irregularly shaped depigmentation, irregularly distributed and shaped brown dots/globules, 5–6 colors (in partially pigmented lesions), predominant central vessels, peripheral light brown structureless areas, asymmetrical pigmentation pattern, milky red pink areas, greater than one shade of pink, asymmetrical shape, dotted and linear irregular vessels in combination, and linear irregular vessels as the predominant vessel type (Menzies et al., 2008). Features that were uncommon in amelanotic/hypomelanotic melanomas were multiple (>3) milia-like cysts (1%), regularly distributed comma vessels (1%) or comma vessels as the predominant vessel type (2.9%), blue-gray globules of irregular size or distribution (1.9%), arborizing small diameter vessels (6.7%), arborizing vessels as the predominant vessel type (8.6%), and symmetrical pigmentation pattern (7.6%) (Menzies et al., 2008). More details on the dermoscopy of hypomelanotic melanoma can be found in chapters 8e and 12.

Key Points

1. SSM manifest an asymmetric pattern that is multicolored.
2. Atypical network is one of the earliest features seen in SSM.
3. Streaks in a SSM is indicative of radial growth.
4. Dotted and liner vessels within the same lesion is highly suggestive of melanoma.
5. Other structures commonly seen in SSM include negative network, crystalline structures, atypical dots and globules, irregular blotch, blue white veil, regression structures, and peripheral brown structureless areas.
6. Crystalline structures correlates with an altered stromal matrix and is suggestive of invasion. This structure can only be seen with polarized light (see chapter 6A).

REFERENCES

Annessi, G., Bono, R., Sampogna, F., Faraggiana, T. & Abeni, D., 2007, Sensitivity, specificity, and diagnostic accuracy of three dermoscopic algorithmic methods in the diagnosis of doubtful melanocytic lesions: the importance of light brown structureless areas in differentiating atypical melanocytic nevi from thin melanomas. *J Am Acad Dermatol*, 56, 759–67.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1997, Epiluminescence microscopy: criteria of cutaneous melanoma progression. *J Am Acad Dermatol*, 37, 68–74.

Balagula Y., Braun R.P., Rabinovitz H.S., et al., 2011, The significance of crystalline/chrysalis structures in the diagnosis of melanocytic and nonmelanocytic lesions. *J Am Acad Dermatol*.

Bono, A., Maurichi, A., Moglia, D., et al., 2001, Clinical and dermatoscopic diagnosis of early amelanotic melanoma. *Melanoma Res*, 11, 491–4.

Chamberlain, A.J., Fritschi, L., Giles, G.G., et al., 2002, Nodular type and older age as the most significant associations of thick melanoma in Victoria, Australia. *Arch Dermatol*, 138, 609–14.

Menzies, S.W., Crotty, K.A., Ingvar, C. & McCarthy, W.H., 2003, *An Atlas of Surface Microscopy of Pigmented Skin Lesions: Dermoscopy*. 2nd ed. Sydney, McGraw Hill.

Menzies, S.W., Ingvar, C., Crotty, K. & McCarthy, W.H., 1996a, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Menzies, S.W., Ingvar, C. & McCarthy, W.H., 1996b, A sensitivity and specificity analysis of the surface microscopy features of invasive melanoma. *Melanoma Res*, 6, 55–62.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopy of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Pizzichetta, M.A., Talamini, R., Stanganelli, I., et al., 2004, Amelanotic/hypomelanotic melanoma: clinical and dermoscopic features. *Br J Dermatol*, 150, 1117–24.

8b Acrolentiginous melanoma

Josep Malvehy and Susana Puig

INTRODUCTION

The clinical faces of acrolentiginous melanoma (ALM) are quite varied, ranging from a very conspicuous and obvious malignancy to an almost imperceptible callas-like appearing area. According to the evidence in case–control studies, the prognosis of this tumor, controlling for tumor thickness, is worse than for melanomas located on the leg or arms. In addition, delay in diagnosis, which can range from months to years, often compounds the poor prognosis experienced by many patients with ALM. This delay in diagnosis may be attributed to a delay in the patient seeking consultation due to the "out-of-site" location of the lesion or due to a low index of suspicion. Delay in diagnosis by health care providers and dermatologists is also a common occurrence, especially in cases of ALM that are amelanotic/hypomelanotic or ALM manifesting a morphology overlapping with banal entities, such as a callus or a wart.

DERMOSCOPY OF ACRAL LENTIGINOUS MELANOMA

The unique appearance of the skin on palms and soles is due to the presence of alternating furrows and ridges, which are responsible for creating our individualized dermatoglyphic patterns (fingerprints) (Crowson et al., 2003) (Fig. 8b.1). The location of pigment in relationship to the furrows and ridges can help in differentiating benign nevi from melanoma (Fig. 8b.2). Dermoscopy helps more precisely localize the pigment and has been shown to significantly improve the observer's diagnostic accuracy when evaluating volar melanocytic tumors. Numerous specific dermoscopic patterns have been defined for nevi and melanoma located on the palm and plantar regions. In benign melanocytic tumors, the location of the pigment tends to favor the crista limitans, which corresponds to the furrows of the skin. Recent research has revealed that acral nevi may be located at he tips of rete ridges associated with the crista intermedia and limitans; however, they preferentially transfer melanin to the keratinocytes associated with the furrow (Saida et al., 2011). In melanoma the malignant melanocytes tend to cluster around the crista intermedia, which in turn often results in pigment located on the ridges (Saida et al., 1989; Oguchi et al., 1998; Kuchelmeister et al., 2000; Saida et al., 2004; Saida et al., 1995) (Figs. 8b.1 and 8b.2).

Lesions on volar skin that manifest any of the melanoma-specific structures listed in Table 17.5 should be biopsied. With that said, most melanocytic lesions on volar skin will not display any of these structures. Instead, they will predominantly manifest a parallel pigment pattern with pigment visible in the furrows or ridges. The dermoscopic patterns suggestive of benignity in melanocytic tumors on volar skin (Green et al., 1998) include the *parallel furrow pattern, lattice-like pattern, fibrillar or filamentous pattern, globular pattern, homogenous pattern, reticular pattern and globule-streak, and transition pattern* (Saida et al., 2002; Saida et al., 2004; Miyazaki et al., 2005) (Fig. 8b.3). These patterns are described in further detail in the chapter 9a. In contrast to acral nevi, ALM on volar skin most often exhibits a **parallel-ridge pattern** and/or irregular diffuse pigmentation (Fig. 8b.3 and also Figs. 8b.4–8b.9). More advanced ALM tends to manifest a combination of colors and structures producing a **multicomponent pattern** (Fig. 8b.3 and also Figs. 8b.10, 8b.11). A word of caution is warranted here regarding the fibrillar pattern (Fig. 8b.12). The fibrillar pattern is created as a result of the shearing lateral pressure forces placed on the stratum corneum on the weight bearing portions of the sole. In nevi this pattern is created by fine transversely oriented lines in respect to the furrows and ridges. This pattern can also be seen in ALM on the sole but the lines making up the fibrillar pattern in ALM will be thicker, darker, gray, and more irregular. Because there are no shearing forces on the palms, the fibrillar pattern is almost nonexistent on this location and any lesion of the palm manifesting a fibrillar pattern should be viewed with suspicion. Lastly, it is important to be aware that a parallel ridge pattern can also be seen in benign conditions, such as in pigmented

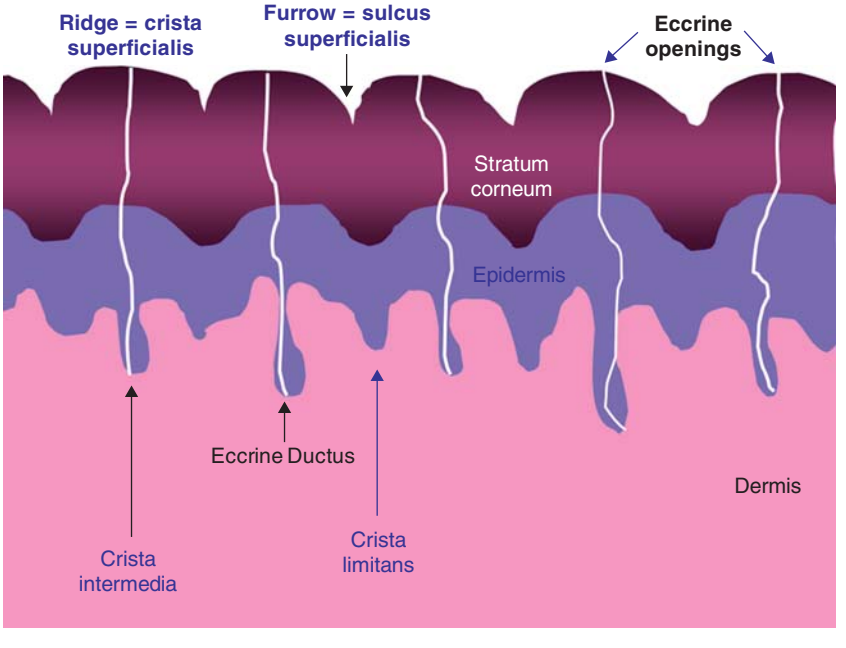


Figure 8b.1 Schematic representation of the anatomy of volar skin.

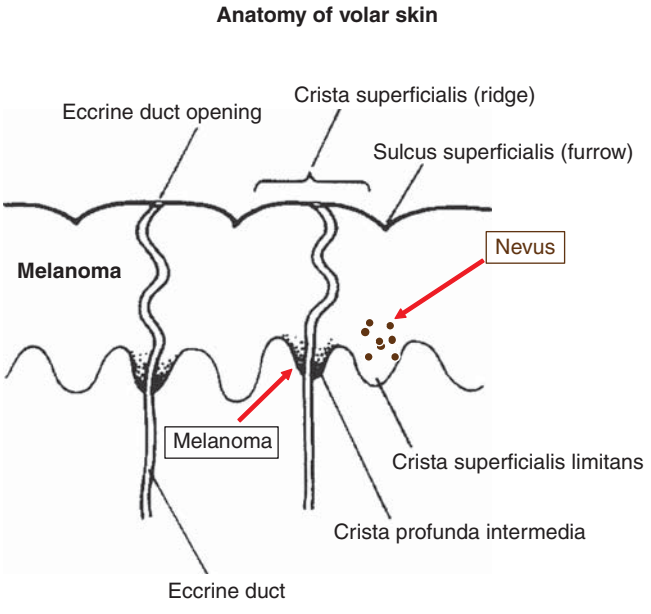


Figure 8b.2 Volar nevi tend to transfer pigment to keratinocytes associated with the crista limitans, which results in a visible parallel furrow pattern. ALM tends to cluster around the crista intermedia, which results in a visible parallel ridge pattern.

lesions on palms and soles of patients with Laugier–Hunziker syndrome Kiling 2007 (Fig. 8b.13), in pigmented macules attributed to ethnic pigmentation, and in conditions resulting in subcorneal hemorrhage (Figs. 8b.14–8b.16). Subcorneal blood on the palms and soles tends to accumulate in the stratum corneum overlying the ridges and can create a parallel ridge pattern (Zalaudek et al., 2004) (Fig. 8b.16) with a rust color or with a pattern known as "pebbles on the ridges" (Fig. 8b.15).

IN SITU ACROLENTIGINOUS MELANOMA

The most common and specific dermoscopic finding in early (including in situ) ALM is the presence of parallel-ridge pattern, which has a specificity of 99%, sensitivity of 86%, and a positive predictive value of 84% (Kwon et al., 2004). This distinct dermoscopic pattern consists of tan-to-dark brown pigmentation that is more prominent on the ridges as compared with the furrows (Figs. 8b.4–8b.9). This pattern is normally detected in the macular portions of melanomas (Braun et al., 2007; Soyer et al., 2000; Washington et al., 2003) on volar skin (Menzies et al., 1996; Stolz et al., 1994). The next most common pattern seen in ALM is the irregular diffuse pigmentation pattern. This pattern consists of pigmented blotches of variegated shades of brown (Figs. 8b.7 and 8b.17). This pattern can be seen in both in situ and invasive ALMs. Another feature occasionally encountered in ALM is the serrated pattern (Fig. 8b.18), which consists of projections (similar to streaks) at the edge of the tumor. As mentioned previously, any fibrillar pattern on the palms or an atypical fibrillar pattern on the sole should also raise suspicion for ALM (Fig. 8b.12). It is not

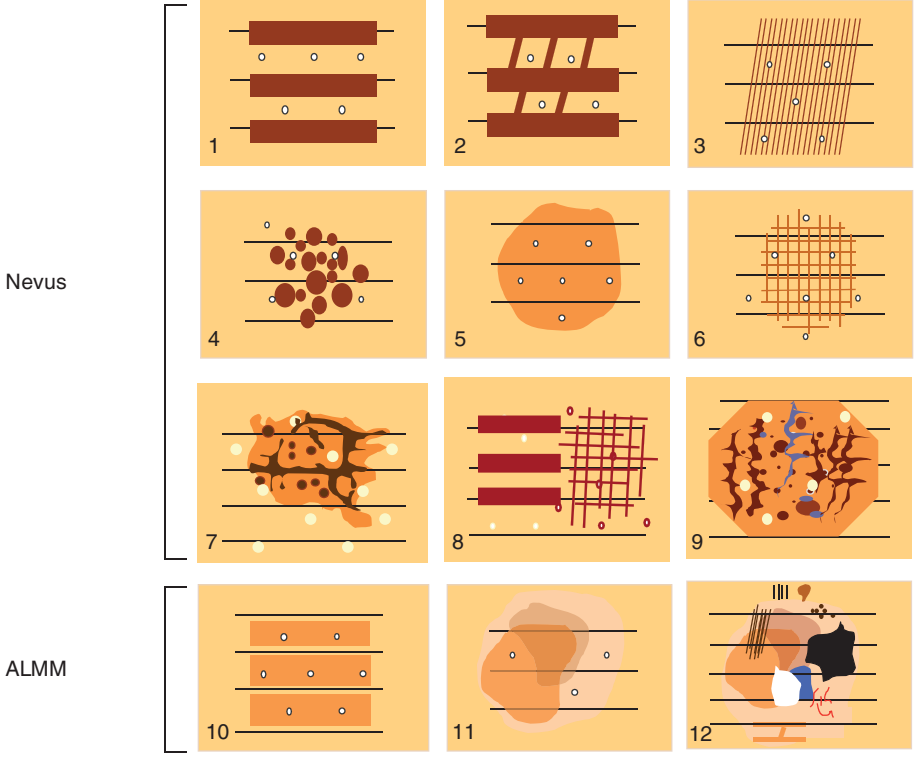
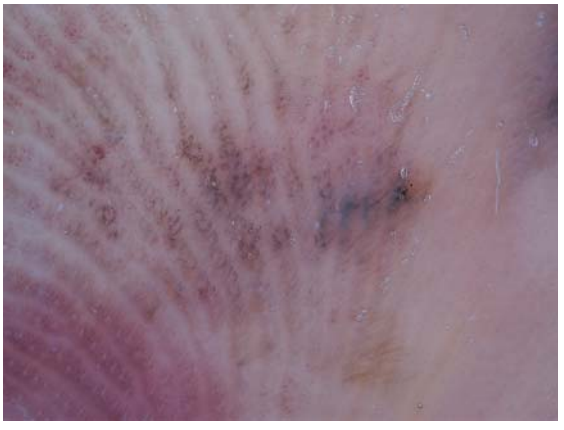


Figure 8b.3 Schematic representation of benign and malignant patterns encountered on volar skin. **Benign patterns***: *Parallel furrow pattern* (1): pigmentation following the furrows; *Lattice-like pattern* (2): pigmentation following the furrows plus linear bands of pigment crossing over the ridge from one furrow to the next like rungs of a ladder; *Fibrillar/filamentous pattern* (3): parallel fine streaks crossing the dermoglyphics in a tangential direction; *Globular pattern* (4): globules not associated with a parallel pattern; *Homogenous pattern* (5): light brown homogenous pigmentation with an amorphous appearance in a lesion that is less than 7–10mm in diameter; *Acral reticular pattern* (6): well-defined pigment network not associated with the skin markings. **Malignant patterns**: *Parallel ridge pattern* (10): linear pigmentation of the ridges; *Diffuse multicomponent pigmentation* (11): pigmented blotches of various shades of brown observed in some portions of the lesion; *Multicomponent pattern* (12): abrupt edge, diffuse pigmentation, peripheral irregular globules and dots, multiple colors, atypical streaks in combination with localized areas exhibiting benign patterns (fibrillar, parallel furrow, or lattice-like). *When pigmentation cannot be classified into any of the aforementioned benign (1–6) or malignant (10–12) patterns then the lesion is classified as having a **"nontypical pattern."**

▲ **Figure 8b.4a** Clinical image.



◀ **Figure 8b.4b** Dermoscopic features of acrolentiginous melanoma on the sole. Band-like pigmentation is seen on the surface ridges of the skin markings, demonstrating the stereotypical parallel ridge pattern. Whitish dots regularly distributed in the pigmented bands corresponding to openings of eccrine ducts. Also note the blue-gray color, irregular dots, and veil. These are all features commonly seen in melanoma. The blue-gray color suggests invasion. This was a 1.3 mm melanoma.

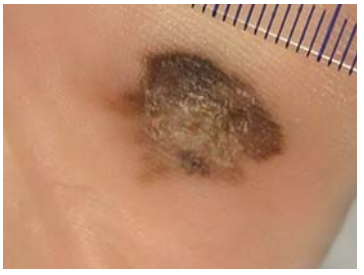
◀ **Figure 8b.5** Dermoscopy of acrolentiginous melanoma in situ on the sole. The parallel ridge pattern with variable shades of brown is well demonstrated. Eccrine pores are recognized as whitish dots regularly distributed within the band-like pigmentation.

▲ **Figure 8b.6a** Clinical image.

◀ **Figure 8b.6b** Dermoscopic features of acrolentiginous melanoma on the sole. Irregular diffuse pigmentation accompanied by subtle features of the parallel ridge pattern is evident. In addition, the parallel furrow pattern and the lattice-like pattern can be detected focally in the left portion of the image.

uncommon for ALM to manifest a combination of a ridge pattern with areas of diffuse pigmentation (Fig. 8b.7), together with other structures, such as focal areas with serration (Fig. 8b.18). Furthermore, it is important to note that ALM can focally exhibit benign patterns, such as parallel furrow or lattice-like pattern, while other focal areas reveal diffuse pigmentation, parallel ridge pattern or other melanoma-specific structures.

Some clinicians posit that lesions classified as atypical melanosis of the foot represent the early phase of the radial growth of ALM. Molecular analyses may prove useful in correctly classifying these atypical proliferations based on the presence or absence of oncogene amplifications characteristic of melanoma. Possibly in the future the use of molecular analyses in combination with other diagnostic information obtained from the clinical, dermoscopic, and histopathologic examination may provide insights into the true biological nature of these lesions. At the present time, it is impossible to predict the biological potential of melanocytic lesions that are equivocal under conventional histopathologic examination. Lesions with an uncertain biological nature should probably be excised. Sequential digital monitoring of equivocal melanocytic lesions on volar skin may be an alternative to excision, but this has not yet been formally studied.

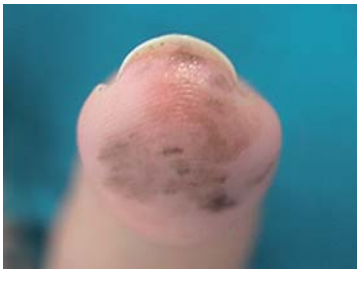


▲ **Figure 8b.7a** Clinical image of an acrolentiginous melanoma.

◀ **Figure 8b.7b** Invasive acrolentiginous melanoma on the foot exhibiting asymmetry, multiple colors, and central hyperkeratosis. Dermoscopy reveals a typical parallel ridge pattern (*arrows*) and irregular diffuse pigmentation (*asterisk*).

▲ **Figure 8b.8a** Invasive acrolentiginous melanoma on the toe with destruction of the nail apparatus.

◀ **Figure 8b.8b** Dermoscopy reveals the stereotypical parallel ridge pattern on the hyponychium corresponding to an area of in situ tumor. Notice the white eccrine ducts opening on top of the pigmented ridge.



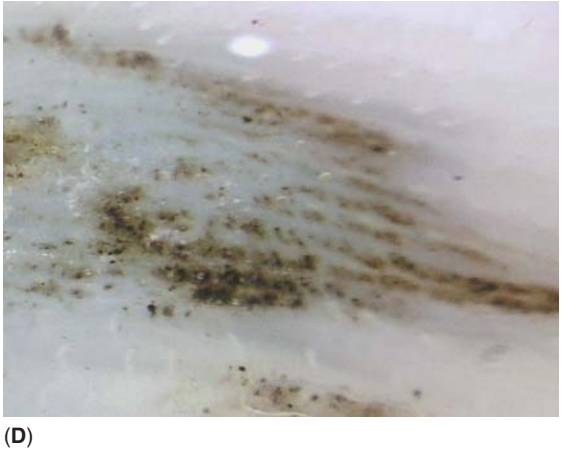
▲ **Figure 8b.9a** In situ acrolentiginous melanoma of the tip of the third finger.

◀ **Figure 8b.9b** Dermoscopy shows a typical irregular brown pigmentation that is located on the ridges (parallel ridge pattern).

Figure 8b.10a Invasive ALM on the heel.

(**B**)

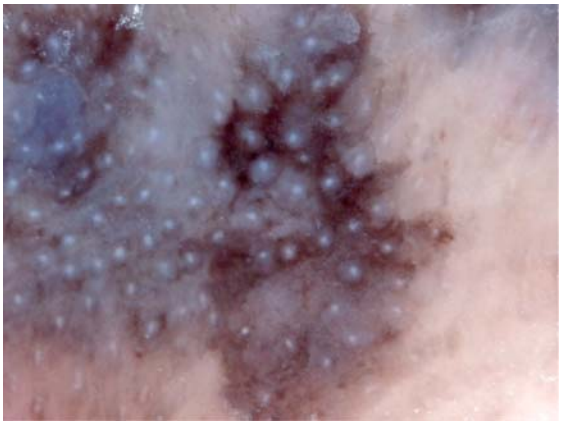
(**C**)



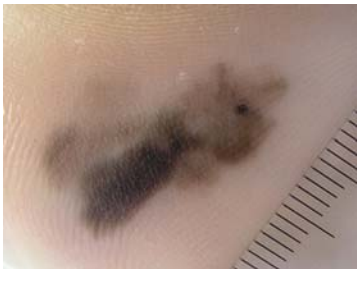
(**D**)

Figure 8b.10 (**B**) Dermoscopy at reduced magnification shows a multicomponent pattern with multiple colors and asymmetry. (**C**) A higher magnification of this ALM also reveals atypical dots and globules and (**D**) a parallel ridge pattern. *Abbreviation*: ALM, acrolentiginous melanoma.

▲ **Figure 8b.11a** Invasive acrolentiginous melanoma on the toe with a nodular component.



◀ **Figure 8b.11b** Dermoscopy reveals a multicomponent pattern with asymmetry and multiple colors (*blue, black, dark brown, and light brown*). In this case the openings of the eccrine ducts are clearly visible (white dots).



▲ **Figure 8b.12a** Clinical image of a ALM.

◀ **Figure 8b.12b** Dermoscopy of an Acral lentiginous malignant melanoma of the sole (early invasive). Notice the fibrillar pattern in combination with parallel ridge pattern.

▲ **Figure 8b.13a** Clinical image.

◀ **Figure 8b.13b** Dermoscopic features of pigmented macule on the finger of a patient with Laugier–Hunziker's syndrome. The parallel ridge pattern is evident on dermoscopy. Misdiagnosing these lesions as melanoma can be avoided by recognizing the unique unique clinical presentation consisting of, multiple small brownish macules on multiple fingers and also on the lip in a patient with Laugier-Hunziker's syndrome. *Source*: Courtesy of Drs S. Shibata and Y. Tomita.

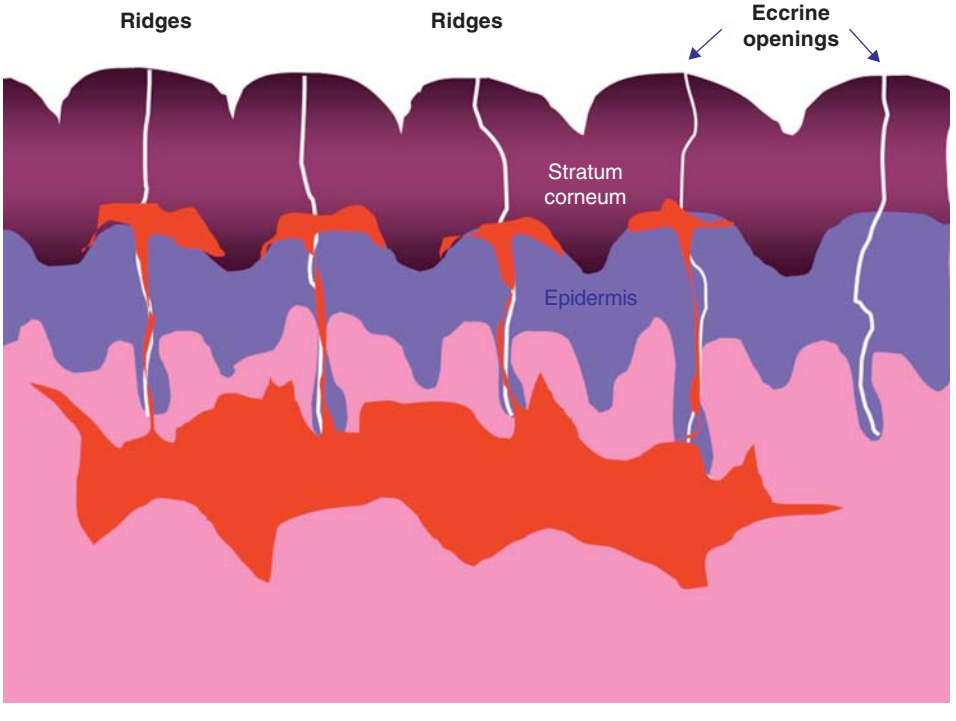
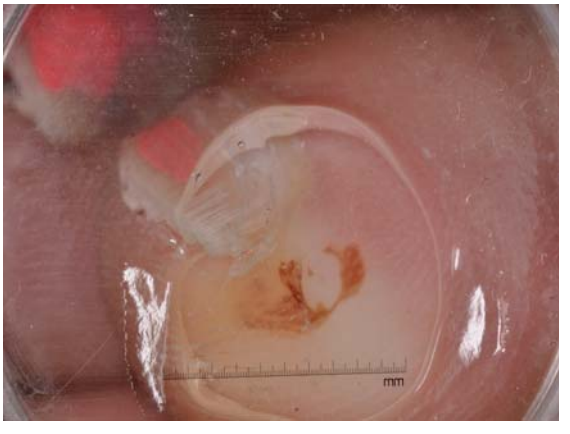


Figure 8b.14 Schematic of subcorneal blood. It is surmised that subcorneal blood will track along the least-resistant tissue planes, which may be along eccrine glands. This results in the accumulation of blood on the ridges, creating a parallel ridge pattern or pebbles on the ridge pattern.

▲ **Figure 8b.15a** Clinical image.

◀ **Figure 8b.15b** Dermoscopic features of "black heel," that is, petechiae on the heel, which is often the result of ill-fitting sport shoes. The pigmentation is prominent on the ridges, somewhat mimicking the parallel ridge pattern. However, it is composed of droplets with smooth margins and the color is reddish black, indicating that this pigmentation is due to bleeding. This dermoscopic feature is peculiar to this condition and is referred to it as "pebbles on the ridges."

▲ **Figure 8b.16a** Clinical image of a pigmented macule on the toe.



▶ **Figure 8b.16** Dermoscopy of this lesion (B)reveals a parallel ridge pattern with a rust color (**B**). This lesion developed after a tennis match. To confirm that this was consistent with subcorneal hemorrhage, the stratum corneum was pared down with a scalpel resulting in the removal of the blood (**C**). Once the stratum corneum with the blood has been removed, it is clear to see that the underlying skin looks normal (**C**).

▲ **Figure 8b.17a** This is a 1cm lesion on the sole.

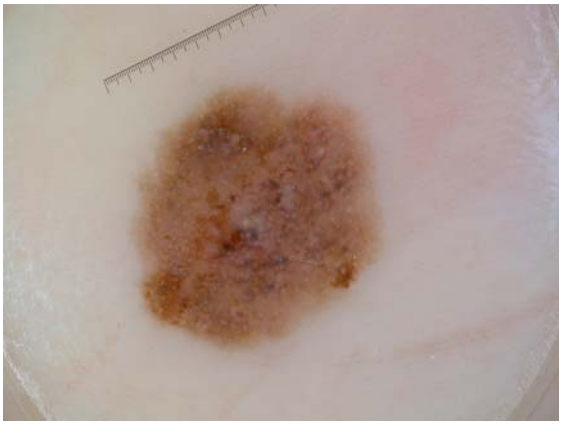


Figure 8b.17b With dermoscopy one can see a homogenous pigment pattern. This lesion was an acrolentiginous melanoma.

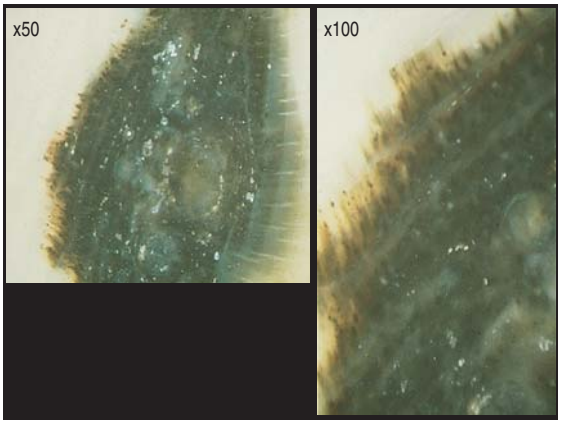
INVASIVE ACROLENTIGINOUS MELANOMA

The pigment in invasive ALM tends to be located on both the ridges and furrows. The invasive melanoma tends to destroy the architecture of furrows and ridges resulting in structureless, pigmented patches (Frankel et al., 1987; Barnhill et al., 2004). Invasive ALM also tends to manifest more dermoscopic colors and structures, such as abrupt edge, irregular dots and globules, multiple colors, atypical streaks, irregular blotches, blue-white veil, regression structures, and atypical vessels (Figs. 8b.19 and 8b.20). In these invasive melanomas on volar skin a multicomponent pattern is quite common.

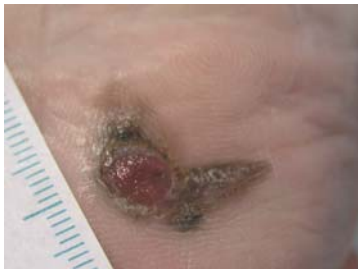
MANAGEMENT ALGORITHM

According to the clinical and dermoscopic information an algorithm for the management of acral lesions has been created (Fig. 8b.21).

▲ **Figure 8b.18a** Clinical image.



◀ **Figure 8b.18b** Dermoscopic features of malignant melanoma on the sole. This small black nodule, 6.5 mm in diameter, has a macular component at the periphery. Dermoscopically, diffuse black pigmentation predominates, and sharp demarcation (i.e., abrupt cutoff of pigment at the periphery) is clearly recognized at the left margin. In addition, irregular streaks and peripheral dots are detected at the margin.



▲ **Figure 8b.19a** Ulcerated invasive acrolentiginous melanoma on the sole.

◀ **Figure 8b.19b** Dermoscopy shows asymmetry, multiple colors, and multicomponent pattern. In the central part an amelanotic nodule with atypical vessels is clearly visible.

◀ **Figure 8b.19c** At the periphery of this ALM, atypical dots and globules with parallel ridge pattern is observable.

▲ **Figure 8b.20a** : Clinical image of an amelanotic ALM.

◀ **Figure 8b.20b** Dermoscopic image of an amelanotic ulcerated acrolentiginous melanoma. In this case the clues to the diagnosis are the presence of atypical vessels under dermoscopy (cork screw) and remnants of pigment associated with a hemorrhage and hyperkeratosis.

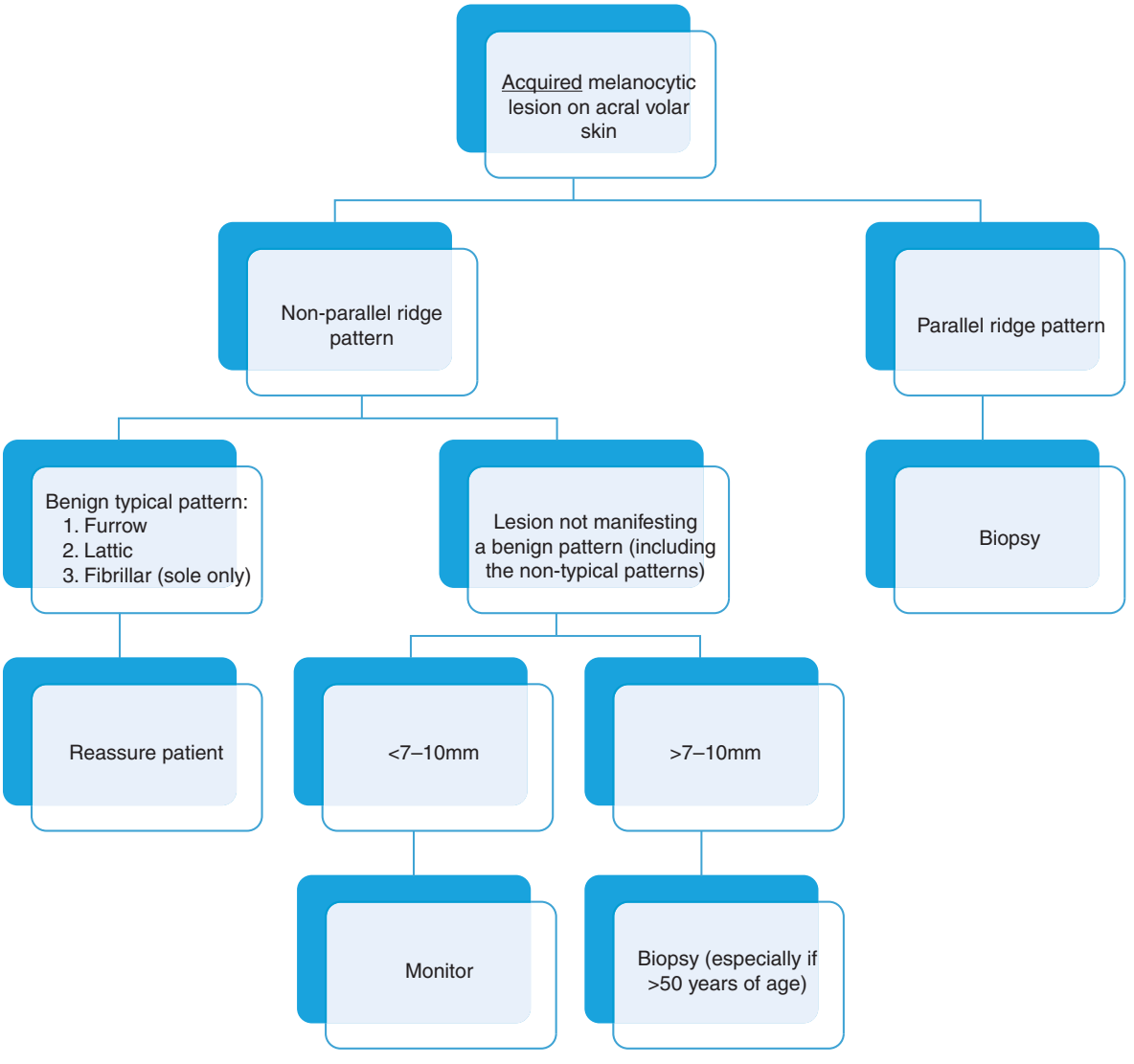


Figure 8b.21 Management algorithm for acral melanocytic lesions based on clinical and dermoscopic information. The lesion should first be evaluated to determine if there are any melanoma-specific structures (such as parallel ridge pattern) present focally anywhere within the lesion. With few exceptions, if a melanoma-specific structure is seen then the lesion must be biopsied. If the lesion does not manifest any melanoma-specific structures, then it needs to be evaluated to determine if it has one of the classic benign nevus patterns (furrow, lattice, or benign fibrillar). If it does have a benign nevus pattern (and no melanoma-specific structures) then the patient can be reassured. If it does not have a benign pattern and it has no melanoma specific structures then the management decision is based on the maximum diameter of the lesion (Fig. 8a.17).

Key Points

- The parallel ridge pattern is the most important dermoscopic clue to the diagnosis of acrolentiginous melanoma (ALM).
- ALM exhibits three major dermoscopic patterns: parallel ridge, irregular diffuse pigmentation, and multicomponent pattern.
- In acral melanoma it is not uncommon to see focal areas with a benign pattern.
- In lesions that do not manifest a classic benign or malignant pattern, the decision to biopsy or monitor is dependent on the maximum diameter of the lesion.

BIBLIOGRAPHY

Altamura, D., Altobelli, E., Micantonio, T., et al., 2006, *Arch Dermatol*, 142, 1123–8.

Barnhill, R.L., 2004, Malignant melanoma. In: R.L. Barnhill, M. Piepkorn & K.J. Busam, eds. *Pathology of Melanocytic Nevi and Malignant Melanoma*. 2nd ed. New York: Springer-Verlag.

Braun, P., Gaide, O., Skaria, A.M., et al., 2007, Exclusively benign dermoscopic pattern in a patient with acral lentiginous malignant melanoma. *Arch Dermatol*, 143, 1213–15.

Crowson, A.N., Magro, C.M., Barnhill, R.L. & Mihn, M.C., Jr., 2003, Pathology. In: C.M. Balch, A.N. Houghton, A.J. Sober & S. Soong, eds. *Cutaneous Melanoma*. St Louis: Missouri, 171–206.

Frankel, K.A., 1987, Intraepithelial melanocytic neoplasia: a classification by pattern analysis of proliferation of atypical melanocytes. *Am J Dermatopathol*, 9, 80–3.

Green, A., McCredie, M., MaacKie, R., et al., 1999, A case-control study of melanomas of the soles and palms (Australia and Scotland). *Cancer Causes Control*, 10, 21–5.

Kiling, I., Akanil, T., Unal, I. & Ozdemir, F., 2007, Atypical melanosis of the foot showing a dermoscopic feature of parallel ridge pattern. *J Dermatol*, 34, 56–9.

Kuchelmeister, C., Schaumburg-Lever, G. & Garbe, C., 2000, Acral cutaneous melanoma in Caucasians: clinical features, histopathology and prognosis in 112 patients. *Br J Dermatol*, 143, 275–80.

Kwon, I.H., Lee, J.H. & Cho, K.H., 2004, Acral lentiginous melanoma in situ: a study of nine cases. *Am J Dermapathol*, 26, 285–96.

Malvehy, J. & Puig, S., 2004, Dermoscopic patterns of benign volar melanocytic lesions in patients with atypical mole syndrome. *Arch Dermatol*, 140, 538–44.

Menzies, S.W., Crotty, K.A., Ingvar, C., et al., 1996, *An Atlas of Surface Microscopy of Pigmented Skin Lesions*. Sidney, Australia: McGraw-Hill.

Oguchi, S., Saida, T., Koganehira, Y., et al., 1998, Characteristic epiluminiscent microscopic features of early malignant melanoma on glabrous skin: a videomicroscopic study. *Arch Dermatol*, 134, 563–8.

Saida, T., Koga, H., Goto, Y., Uhara, H., 2011, Characteristic Distribution of Melanin Columns in the Cornified Layer of Acquired Acral Nevus: An Important Clue for Histopathologic Differentiation From Early Acral Melanoma. *Am J Dermatopathol*.

Saida, T., 1989, Malignant melanoma in situ on the sole of foot. Its clinical and histopathologic characteristics. *Am J Dermatopathol*, 11, 124–30.

Saida, T., Miyazaki, A., Oguchi, S., et al., 2004, Significance of dermoscopic patterns in detecting malignant melanoma on acral volar skin. Results of a multicenter study in Japan. *Arch Dermatol*, 140, 1233–3.

Saida, T., Miyazaki, C.M. & Grin, C.M., 2004, Acrolentiginous melanoma. In: A.A. Marghoob, R.P. Braun & A.W. Kopf, eds. *Atlas of Dermoscopy*. London (UK); Taylor & Francis, 221–33.

Saida, T., Oguchi, S. & Ishihara, Y., 1995, In vivo observation of magnified features of pigmented lesions on volar skin using video macroscope: usefulness of epiluminiscence techniques in clinical diagnosis. *Arch Dermatol*, 131, 298–304.

Saida, T., Oguchi, S. & Miyazaki, A., 2002, Dermoscopy for acral pigmented skin lesions. *Clin Dermatol*, 20, 279–85.

Soyer, P., Argenziano, G., Chimenti, S., et al., 2000, Dermoscopy of pigmented skin lesions: an atlas based on the consensus net meeting on dermoscopy, via the internet, July to November.

Stolz, W., Braun-Falco, O., Bilek, P., Lanthaler, M. & Cognetta, A., 1994, *Colour Atlas of Dermoscopy*. Berlin, Germany: Blackwell Science Ltd.

Washington, C.V., 2003, Acral lentiginous melanoma mimicking benign disease: the Emory experience. *J Am Acad Dermatol*, 48, 183–8.

Zalaudek, I., Giuseppe A., H Peter S., Jean-Hilaire S., and Ralph P.B., 2004, "Dermoscopy of Subcorneal Hematoma." *Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.]* 30, no. 9. doi:10.1111/j.1524-4725.2004.30381.x.

8c Nodular melanoma

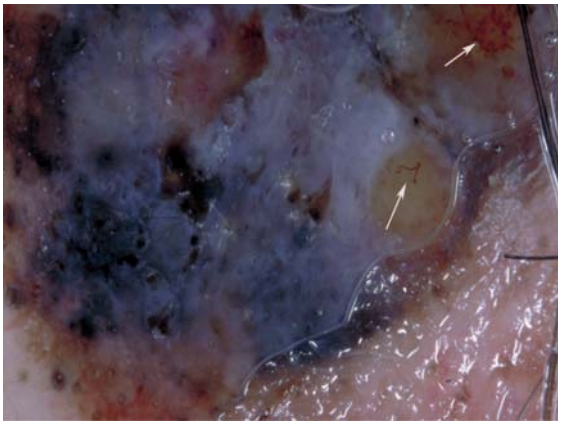
Scott W. Menzies

Nodular melanomas (NMs) are defined as invasive melanomas without a radial growth phase. Specifically, they lack an in situ component beyond three rete ridges of the invasive vertical growth phase. While they represent only 14% of invasive melanomas, thick melanomas (>3 mm Breslow thickness) are predominantly NMs (56%) (Chamberlain et al., 2002)

Clinically, NMs may lack the "ABCD" features more typical of superficial spreading melanomas (SSMs). Similarly, many of the classic dermoscopy features of SSMs (see chap. 8a) are found much less commonly in NMs. Specifically, those features correlating with radial growth and pagetoid spread (pseudopods, radial streaming), and those features found in thin melanoma (atypical broadened network and the early regression feature of multiple blue-gray fine dots or peppering) are often lacking in NMs. However, pigmented NMs more frequently have those dermoscopy features associated with thick melanoma: blue-white veil, multiple (5–6) colors, crystalline structures (seen only with polarized light) and atypical vascular patterns (Menzies et al., 2003; Stolz et al., 2002; Argenziano et al., 1997). In addition, the majority, similar to other melanomas, have an asymmetric pigmentation pattern (see chaps. 6b and 8a). However, the asymmetry of pattern may be less marked compared with SSM. Nevertheless, the majority of pigmented NMs can be diagnosed using standard dermoscopy criteria.

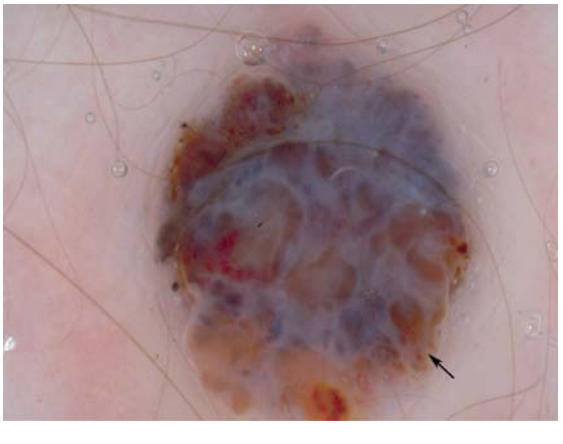
What is diagnostically problematic is the fact that a significant number of NMs are hypomelanotic or amelanotic. In these cases, atypical vascular patterns may be the only clues for the diagnosis of such lesions (see chap. 8e, "Amelanotic melanoma"). While there is yet to be a study which has examined the vascular patterns exclusively of nodular amelanotic/hypomelanotic melanoma, the vascular features more commonly seen in thick light-colored melanoma *versus* thin melanoma include hairpin vessels, large diameter vessels, and ulceration (Figs. 8c.1–8c.7) (Menzies et al., 2008).

▲ **Figure 8c.1a** Clinical image.

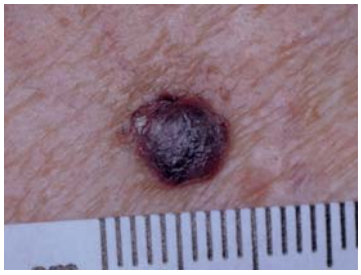


◀ **Figure 8c.1b** This asymmetrically patterned multicolored lesion has the major positive nodular melanoma features of blue-white veil, multiple (5–6) colors (scored from tan, dark brown, black, blue, gray, and red), ulceration (*top arrow*) and a hairpin (looped) vessel (*lower arrow*). Diagnosis: nodular melanoma within a contiguous nevus, Breslow thickness 3.3 mm.

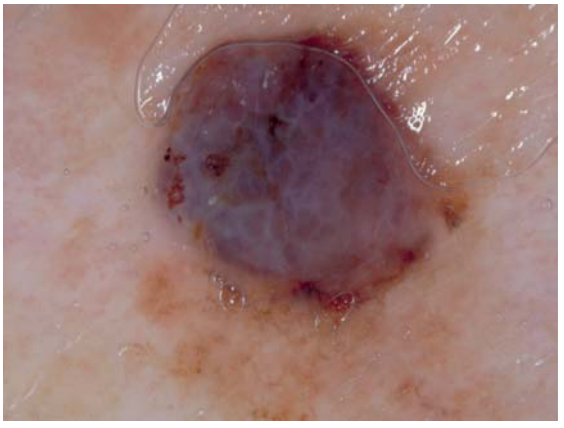
▲ **Figure 8c.2a** Clinical image.



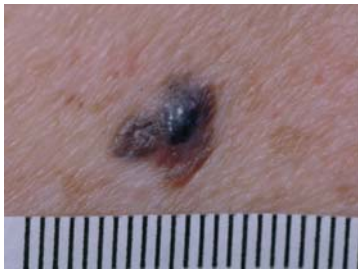
◀ **Figure 8c.2b** This asymmetrically patterned multicolored lesion has extensive blue-white veil and multiple (5–6) colors. The dotted vessels (*arrow*) indicate its melanocytic origin. Diagnosis: nodular melanoma, 2.5 mm Breslow thickness.



▲ **Figure 8c.3a** Clinical image.

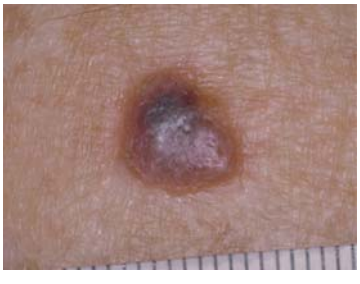


◀ **Figure 8c.3b** This nodule is asymmetrically patterned and multicolored with the positive melanoma feature of extensive blue-white veil. Here, asymmetry of pattern is definitely seen (see chap. 6b), but is less marked than in many superficial spreading melanomas. Diagnosis: nodular melanoma, 1.6 mm Breslow thickness with a contiguous area of atypical lentiginous proliferation of melanocytes.

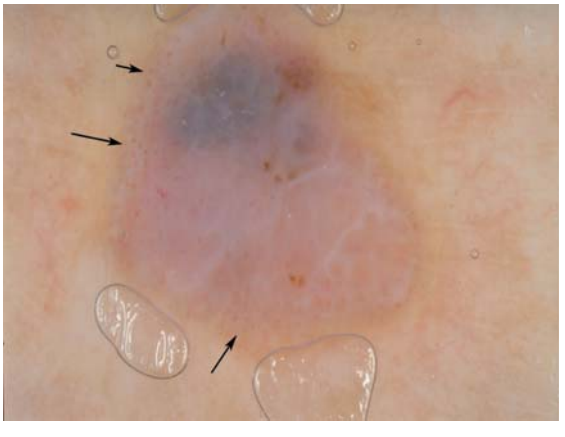


▲ **Figure 8c.4a** Clinical image.

◀ **Figure 8c.4b** This SSM has a distinct nodular component (1.7 mm Breslow thickness) within the center of the lesion. When considering only the nodular component, asymmetry of the pigmentation pattern is present but again less marked than in most SSMs. The presence of blue-white veil remains the defining feature of this nodular melanoma arising within an SSM. *Abbreviation*: SSM, superficial spreading melanomas.

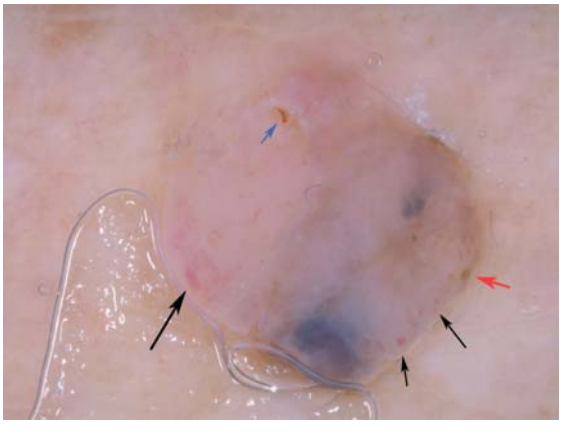


▲ **Figure 8c.5a** Clinical image.



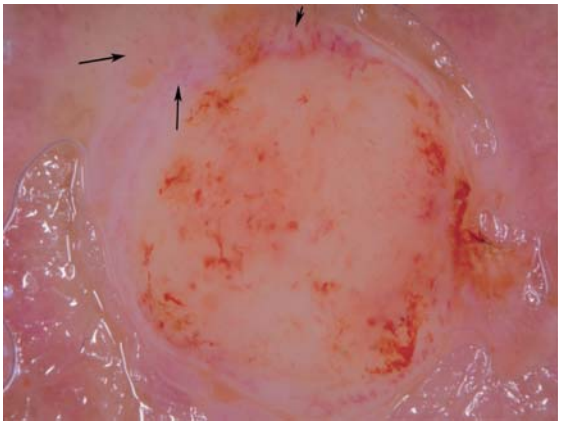
◀ **Figure 8c.5b** This hypomelanotic nodule is multicolored (tan, blue, and red) and has an asymmetric pattern. Note the few but obvious brown globules and widespread dotted (pin-point) vessels (*arrows*) both indicative of its melanocytic origin. It also has the positive melanoma features of blue-white veil . Diagnosis: nodular melanoma, 2.2 mm Breslow thickness.

▲ **Figure 8c.6a** Clinical image.



◀ **Figure 8c.6b** This hypomelanotic nodule is asymmetric in pattern and is multicolored (tan, red, and blue) (Menzies et al., 2000). Although it has features that could be confused for a pigmented BCC with structures resembling large blue-gray ovoid nests and ulceration (*blue arrow*), it lacks arborizing vessels typical of BCC. Instead, it has a solitary brown globule (*red arrow*) and dotted vessels (*thin black arrows*) indicative of a melanocytic lesion. Furthermore, it has a milky-red globule (*thick black arrow*), which is a specific feature of melanoma. Diagnosis: hypomelanotic nodular melanoma, Breslow thickness 1.9 mm. *Abbreviation*: BCC, basal cell carcinoma.

▲ **Figure 8c.7a** Clinical image.



◀ **Figure 8c.7b** This ulcerated amelanotic nodule has dotted (pin-point) vessels suggestive of a melanocytic lesion. Diagnosis: nodular melanomas Breslow thickness 2.8 mm.

Key Points

1. Nodular melanomas (NM) lack network, streaks, and regression structures
2. Pigmented NM often manifest blue-white veil, multiple colors, crystalline structures, and atypical vessels
3. Amelanotic NM reveal atypical vessels and/or crystalline structures
4. The dermoscopic pattern of NM is often homogenous disorganized (dermoscopic asymmetric) or featureless with atypical vessels

REFERENCES

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1997, Epiluminescence microscopy: criteria of cutaneous melanoma progression. *J Am Acad Dermatol*, 37, 8–74.

Chamberlain, A.J., Fritschi, L., Giles, G.G., et al., 2002, Nodular type and older age as the most significant associations of thick melanoma in Victoria, Australia. *Arch Dermatol*, 138, 609–14

Menzies, S.W., Crotty, K.A., Ingvar, C. & McCarthy, W.H., 2003, *An Atlas of Surface Microscopy of Pigmented Skin Lesions: Dermoscopy*. 2nd ed. Sydney, McGraw Hill.

Menzies, S.W., Kreusch, J., Byth, K., Pizzichetta, M.D., et al., 2008, Dermoscopy of amelanotic and hypomelanotic melanoma *Arch Dermatol*, 144, 1120–1127.

Menzies, S.W., Westerhoff, K., Rabinovitz, H., et al., 2000, The surface microscopy of pigmented basal cell carcinoma. *Arch Dermatol*, 136, 1012–16.

Stolz, W., Braun-Falco, O., Bilek, P., et al., 2002, *Color Atlas of Dermatoscopy*. 2nd ed. Berlin, Blackwell.

8d Lentigo maligna melanoma

Alon Scope, Steven Q. Wang, and Harold S. Rabinovitz

Lentigo maligna is a subtype of melanoma that arises on sun-damaged skin. The term lentigo maligna denotes melanoma in situ, whereas lentigo maligna melanoma (LMM) denotes invasive melanoma. In this chapter we use LMM as a term that encompasses all melanomas (in situ and invasive) on sun-damaged skin.

LMMs occur most frequently in the elderly population. The common anatomic sites include the sun-damaged skin of the bald scalp and face. Clinically, LMMs are patches to flat plaques, variegate in colors that range from light brown to black, and asymmetric in shape. These lesions tend to enlarge slowly and if left untreated, cover an area of several centimeters while remaining flat, at times appearing discontinuous and patchy on clinical examination. To appreciate the extent of the clinical lesion, Wood's lamp is an essential part of the examination, and often, it reveals that the lesion is much more extensive than it appears on naked-eye examination. With time, LMM may develop invasive foci clinically evident as papules, nodules, or thicker plaques. LMM at that stage confers risk of metastatic disease.

Histopathologically, findings in LMM include an asymmetric lesion with an abnormal proliferation of single melanocytes in the basal layer of the epidermis, the melanocytes being unevenly spaced and increased in density (crowded), and often extend down follicles. Even few nests of melanocytes in a broad, junctional lesion on the face that displays solar elastosis in the dermis (evidence of sun damage) strongly raise the suspicion of LMM. An irregular scatter of melanocytes in pagetoid fashion (at suprabasal layers of the epidermis) also supports the diagnosis of LMM. Nests and fascicles of melanocytes in the dermis attest that the melanoma is no longer in situ. LMM in the dermis may display at times desmoplastic and neurotropic features.

Early LMM may be clinically subtle and difficult to diagnose on the sun-damaged background that displays many solar lentigines. Other differential diagnoses include pigmented actinic keratosis, lichen plaunus-like keratosis, and early, flat seborrheic keratosis, which are all nonmelanocytic lesions. To this end, dermoscopy may help make the correct diagnosis. While on nonfacial sites, the presence of a pigmented network or globules and dots suggest the lesion is melanocytic, on the face, a pigment network is usually absent due to the flattening of the dermoepidermal junction (DEJ) and effacement of the rete ridges. Thus, additional dermoscopic criteria are applied to diagnose early LMM.

Dermoscopic criteria for the diagnosis of LMM include (Cognetta et al., 2001; Sahin et al., 2004; Schiffner et al., 2000; Stante et al., 2005):

Asymmetrical pigmentation in follicular openings (Figs. 8d.1 and 8d.2): There is crescent-shaped pigmentation that accentuates in only one portion of the follicular opening. On histopathology, this finding correlates with atypical melanocytes as single units or small nests extending down hair follicles. Correlation of dermoscopically identified asymmetric follicular openings using reflectance confocal microscopy (RCM) (Ahlgrimm-Siess et al., 2009) demonstrates a nonuniform infiltration of atypical melanocytes along the circumference of the follicular epithelium, explaining the asymmetric, crescent-shaped pigmentation seen en face by dermoscopy. On occasion one can see asymmetrically pigmented follicular openings in a solar lentigo; however, in a solar lentigo the color of the crescent-shaped area tends to be the same color as the surrounding area. In LMM the follicular openings can be symmetric or asymmetric but the color tends to be darker, often with a grayish hu8e (Fig. 8d.3).

Annular–granular pattern can be divided into dots aggregated around adnexal openings and short and polygonal lines around and between adnexal openings. These two components of the annular–granular pattern can be seen singly or in combination.

Dots aggregated around adnexal openings (Figs. 8d.4 and 8d.5): The findings range from brown dots to blue-gray granularity scattered throughout the lesion, but often appearing to cluster around the adnexal openings (Fig. 8d.6). Based on dermoscopy to RCM and histopathology correlation, these findings are explained by aggregates of melanocytes and small nests at the DEJ between the follicles (brown dots) and by melanophages in the dermis (blue-gray granularity).

Short and polygonal lines around and between adnexal openings. As the density of the brown dots increases, they coalesce to form short pigmented lines around the adnexal openings as well as between the adnexal openings (Figs. 8d.6 and 8d.7). These lines are often polygonal, forming a zig-zag pattern (Fig. 8d.8). Dermoscopy to RCM and histopathology correlation suggest that these structures are due to confluent junctional nests and aggregates of melanocytes.

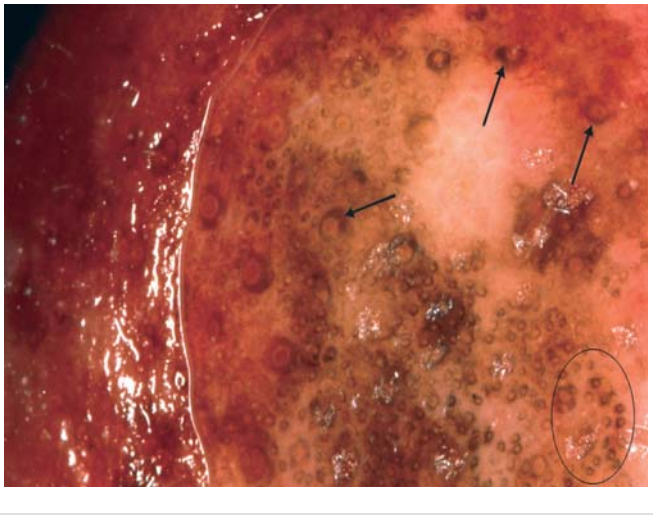


Figure 8d.1 Dark brown or black asymmetrically pigmented follicular openings (*arrows*). Diagnosis: lentigo maligna.

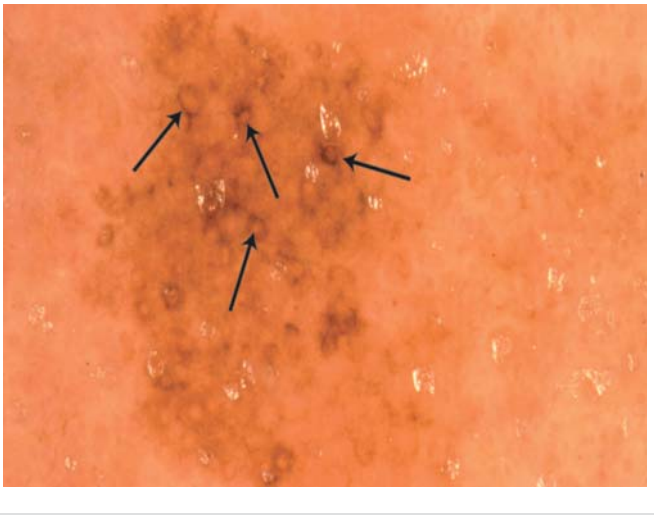
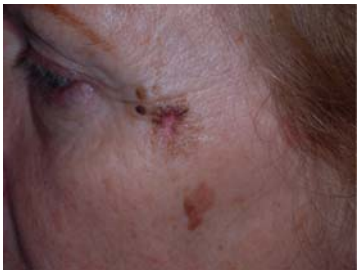
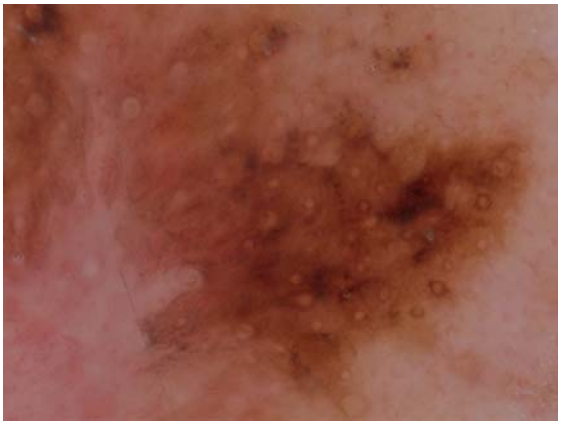


Figure 8d.2 Dark brown or black asymmetrically pigmented follicular openings (*arrows*). Diagnosis: lentigo maligna.



▲ **Figure 8d.3a** Clinical image of a lentigo maligna.



◀ **Figure 8d.3b** The lateral portion of this lesion reveals both symmetric and asymmetric follicular openings. Notice that the color of the follicular openings is darker than the surrounding lesion.

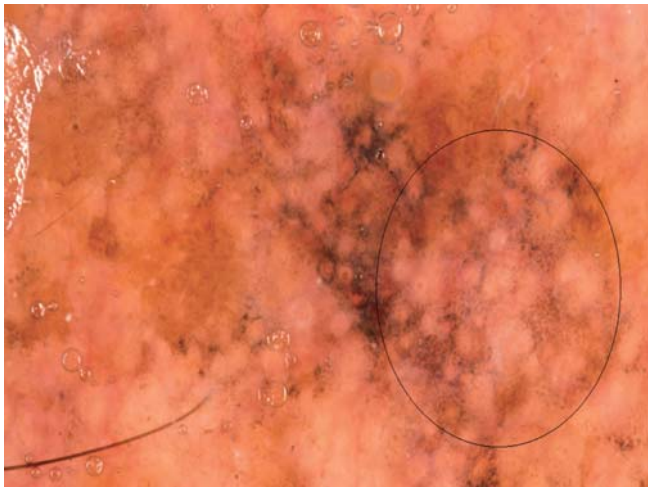


Figure 8d.4 Slate-gray dots and slate-gray globules (*circle*). Diagnosis: lentigo maligna.

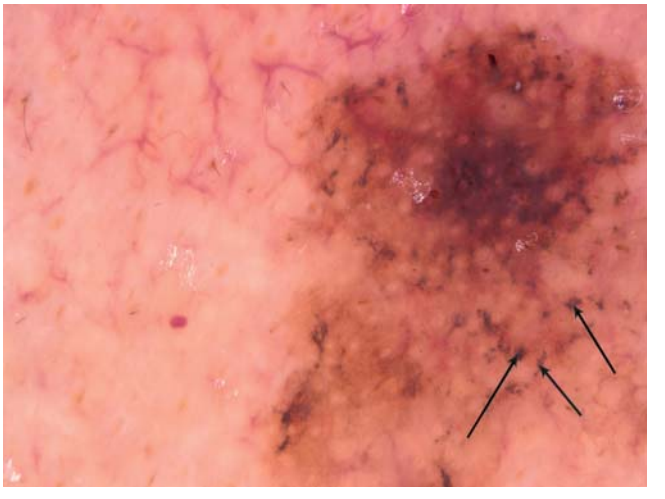
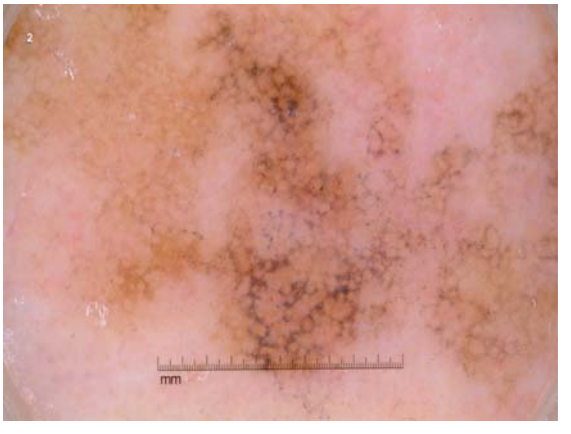


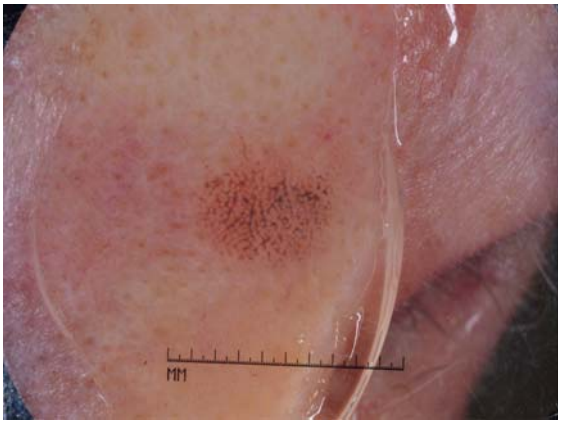
Figure 8d.5 Slate-gray dots and slate-gray globules are evident in this lentigo maligna.

▲ **Figure 8d.6a** Clinical image of a lentigo maligna.



◀ **Figure 8d.6b** This lesion manifests the annular-granular pattern. Notice the granularity around the adnexal openings. In addition, short and polygonal pigmented lines can be seen.

▲ **Figure 8d.7a** Clinical image of a small lentigo maligna.



◀ **Figure 8d.7b** Dermoscopy reveals multiple short polygonal lines.

When asymmetric pigmentation in follicular openings is surrounded by the annular–granular pattern, the concentric dermoscopic appearance has been termed *isobar (also known as circle within a circle)* (Figs. 8d.9 and 8d.10).

Rhomboid structures (Figs. 8d.11–8d.14): Elongation, thickening, and merging of the short polygonal lines around adnexal openings form a polyhedral-shaped structures that have been termed "rhomboidal" (in reality, the shapes vary but are all polygonal). The histopathologic correlation is similar to that of short and polygonal lines, albeit reflecting more extensive infiltration of the DEJ by confluent nests and aggregates of melanocytes.

Dark blotches (also termed "homogenous structures") *with or without obliteration of the adnexal openings.* Dark brown to black blotches are seen, initially with "sparing" of adnexal openings, appearing as light-colored holes within the blotch (Fig. 8d.15), and eventually, as a homogenous black blotch with obliteration of the adnexal openings (Fig. 8d.16).

It should be highlighted that the aforementioned melanoma-specific structures can be seen in lentigo maligna melanomas on the face and also in lentigo maligna melanomas arising on nonfacial chronic sun-damaged skin (Figs. 8d.17–8d.19).

Schiffner et al. (2000) have suggested a model whereby the dermoscopic structures described above represent steps in the progression of LMM (Fig. 8d.20). In many lesions, different areas within the lesion display the various dermoscopic patterns concomitantly. Schiffner et al. (2000) also studied the diagnostic significance of these dermoscopic structures. In a series that included 27 LMM and 50 solar lentigines and seborrheic keratoses, the combination of three dermoscopic structures, namely, asymmetrical follicular openings, annular–granular pattern (termed blue-gray

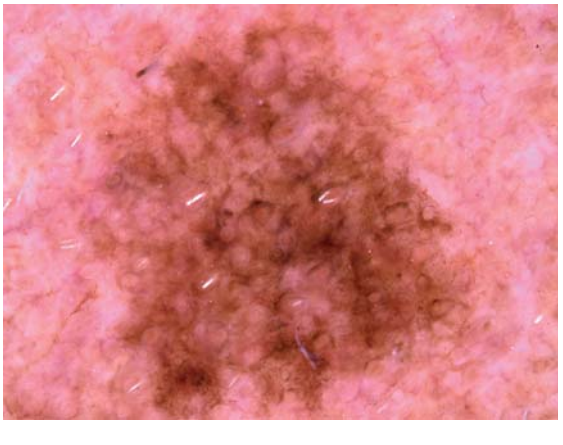
▲ **Figure 8d.8a** Clinical image of a lentigo maligna.

◀ **Figure 8d.8b** Dermoscopy shows polygonal lines that are aligned in a zig-zag pattern.

▲ **Figure 8d.9a** Clinical image of a lentigo maligna.

◀ **Figure 8d.9b** With dermoscopy this lesion reveals one isobar structure at the right lateral edge of the lesion at around the 3 o'clock mark.

▲ **Figure 8d.10a** Clinical image of a lentigo maligna.



◀ **Figure 8d.10b** Dermoscopy reveals a few asymmetric follicular openings, a few dark symmetric follicular openings, and a few isobar or circle within a circle structure.

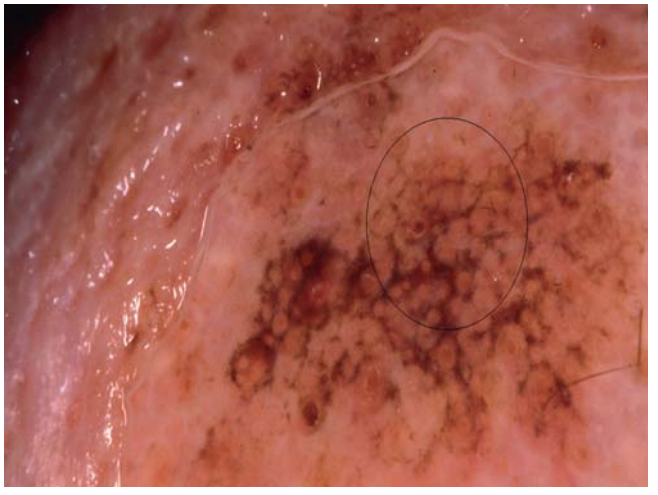


Figure 8d.11 Dark brown or black polygonal lines and rhomboidal structures (*circle*). Diagnosis: lentigo maligna.

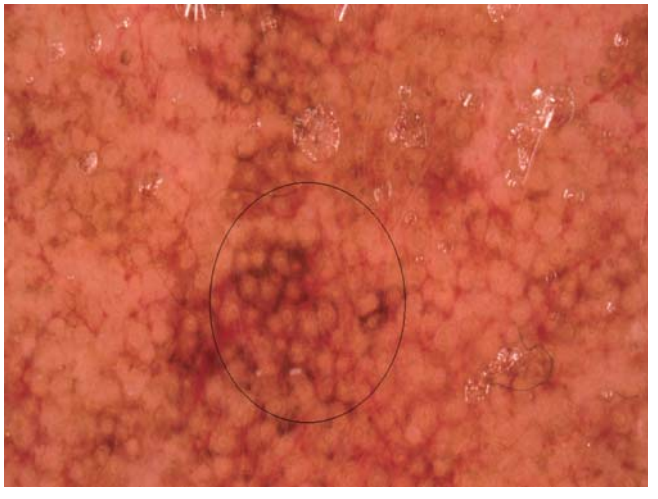


Figure 8d.12 Dark brown or black polygonal lines and rhomboidal structures (*circle*). Diagnosis: lentigo maligna.

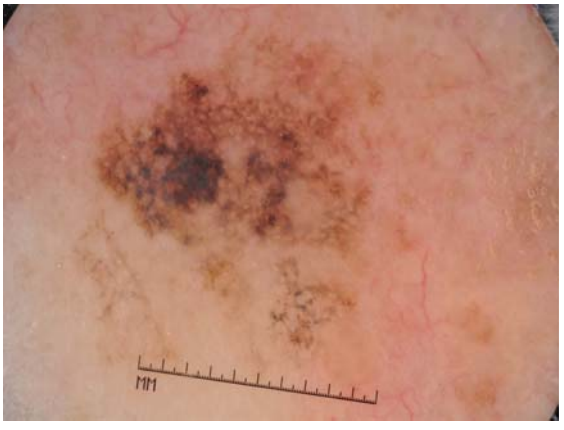
Figure 8d.13 Dark brown or black polygonal lines and rhomboidal structures (*square*). Polygonal lines can be seen within the square. Diagnosis: lentigo maligna.

Figure 8d.14 Dark brown or black polygonal lines and rhomboidal structures (*circle*). Diagnosis: lentigo maligna.

Figure 8d.15 This lentigo maligna has developed darker blotches, but notice that the adnexal openings are still preserved and are clearly visible in this lesion.

dots and globules in their paper), and rhomboidal structures allowed correct classification of 93% of lesions. One proposed algorithm designed to assist in decisions regarding the management of acquired pigmented lesions on the face is shown in Figure 8d.21. The first issue that needs to be addressed when evaluating a pigmented lesion on the face with dermoscopy is whether the lesion possesses any melanoma-specific structures. Although superficial spreading melanoma is rare on the face, they can occur and thus all facial lesions need to be scrutinized for the presence of any of the 10 melanoma-specific structures mentioned in chapter 17, table 17.5 (Fig. 8d.22). In addition, the lesion needs to be evaluated for the presence of the additional melanoma-specific structures encountered on facial skin and/or chronically sun-damaged skin, including asymmetric pigmentation in follicular openings, isobars (also known as circle within circle structures), dots aggregated around adnexal openings, short and polygonal lines (e.g. zig-zag pattern), rhomboidal structures, and dark blotches. If the lesion has any of the aforementioned structures then the lesion needs to be biopsied. If it does not have any of the above-mentioned melanoma-specific structures then the lesion is evaluated for the presence of features diagnostic of basal cell carcinoma, solar lentigo, or seborrheic keratosis. If the lesion has no features to assist in diagnosis then the lesion should either be biopsied or subjected to digital monitoring for at least 6 months to one year. Lastly, one interesting observation made with

▲ **Figure 8d.16a** Clinical image of lentigo maligna.

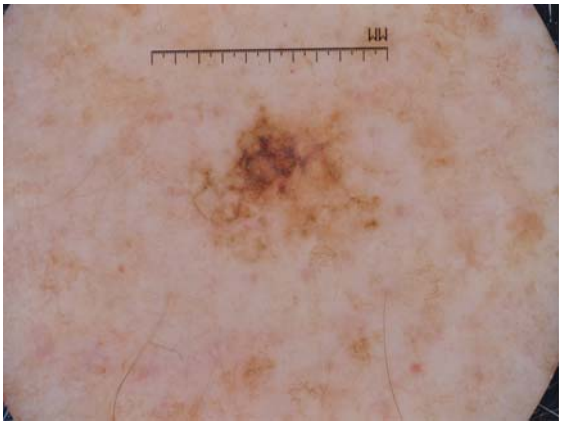


◀ **Figure 8d.16b** Notice that the adnexal openings are almost completely obscured by the dark blotch.

▲ **Figure 8d.17a** Clinical image of a lentigo maligna on the chronic sun-damaged skin of the shoulder.

◀ **Figure 8d.17b** Dermoscopy reveals granularity and polygonal lines.

▲ **Figure 8d.18a** Clinical image of a lentigo maligna on the chronic sun-damaged skin of the chest.



◀ **Figure 8d.18b** Dermoscopy reveals polygonal lines forming rhomboidal structures.

▲ **Figure 8d.19a** Clinical image of a lentigo maligna on the chronic sun damaged skin of the forearm.

◀ **Figure 8d.19b** Dermoscopy reveals lines forming polygonal structures.

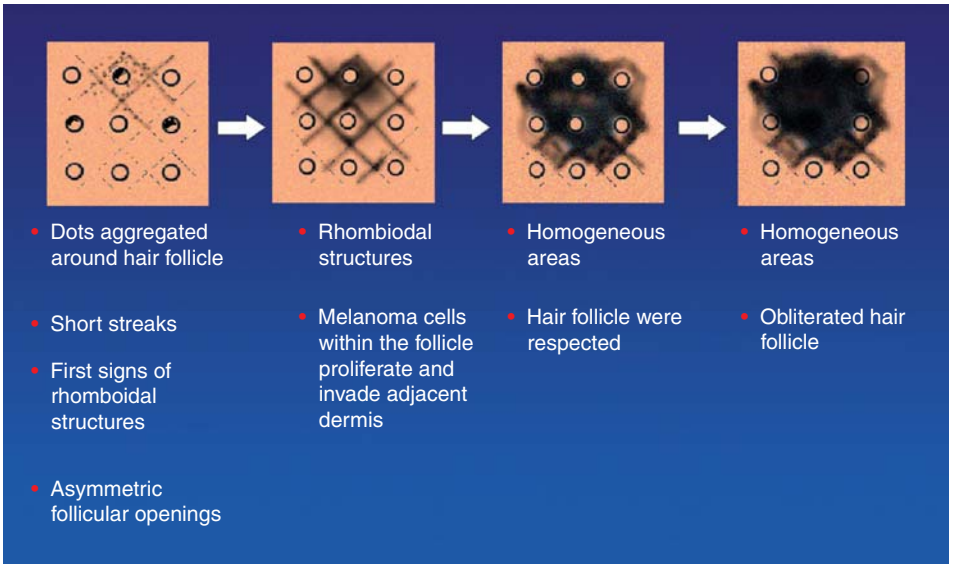


Figure 8d.20 Progression model of lentigo maligna.

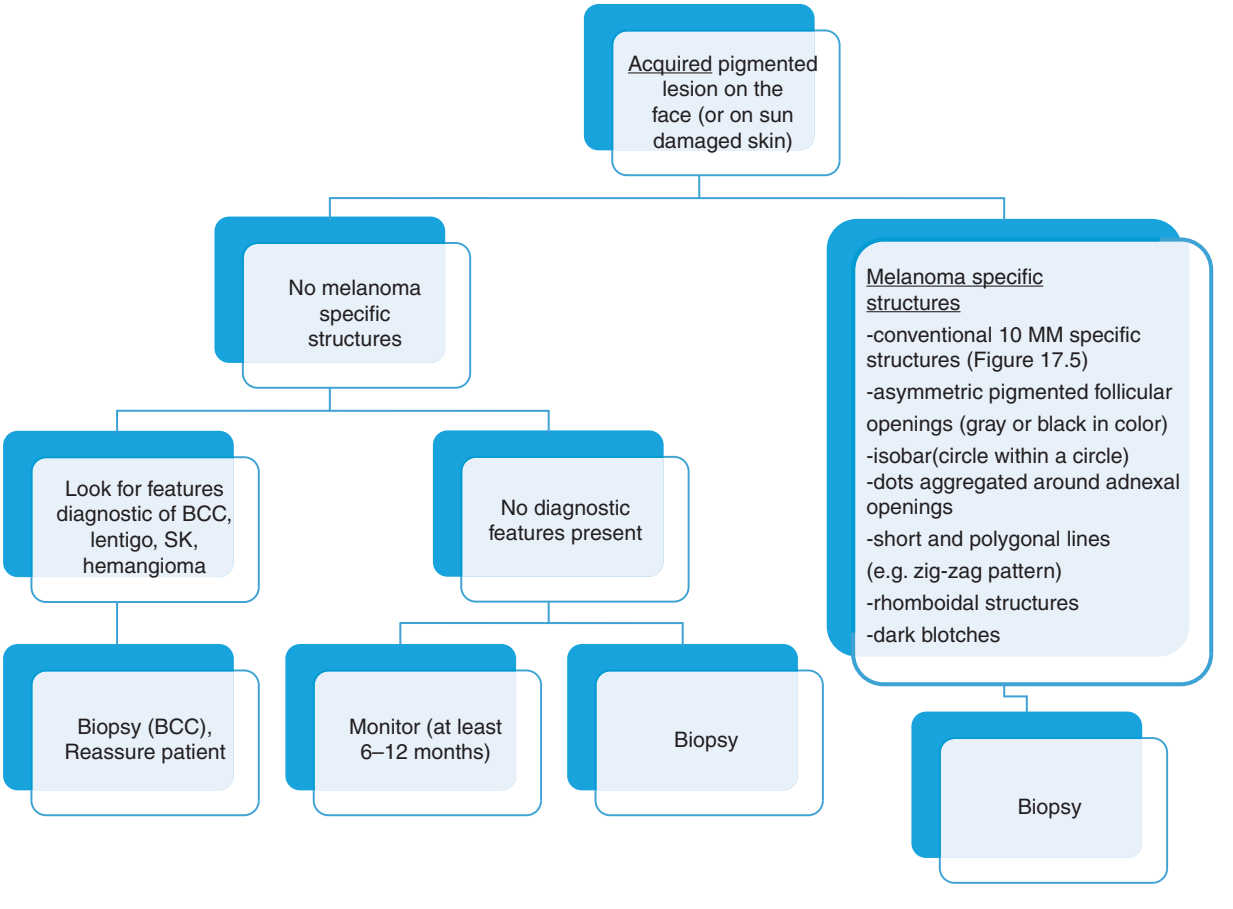
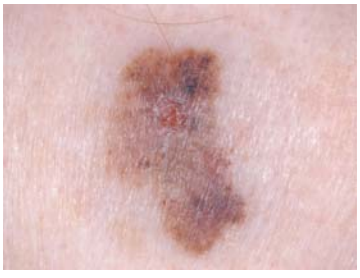
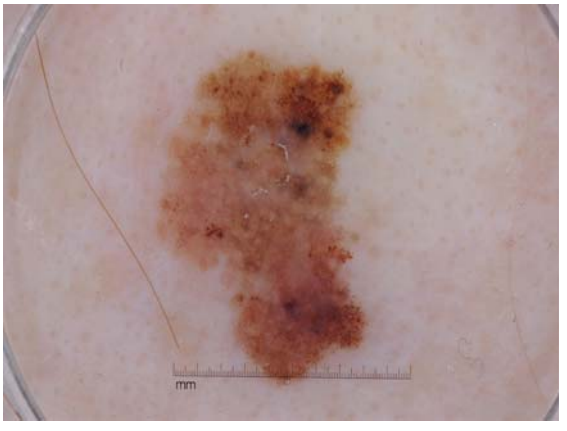


Figure 8d.21 This clinical decision algorithm is designed to assist clinicians in their management decision regarding pigmented lesions on the face or on other chronically sun-damaged skin. For details regarding this decision-making algorithm please refer to the text.



▲ **Figure 8d.22a** This is a superficial spreading melanoma on the forehead of this woman.



◀ **Figure 8d.22b** Dermoscopy reveals features commonly associated with superficial spreading melanoma, such as atypical network, streaks, atypical dots, and globules.

dermoscopy is that lentigo maligna often appears darker under dermoscopy then it does with the naked eye.

Key Points

The melanoma-specific structures seen in lentigo maligna melanoma on the face or other areas of chronic sun-damaged skin include the following:

- Asymmetric follicular openings or follicular openings that have a darker or grayer color as compared with the color or the rest of the surrounding lesion.
- Annular–granular pattern with polygonal lines and granularity.
- Lines creating rhomboidal structures or other polygonal shapes.
- Blotches with preserved follicular openings or blotches that obscure or obliterate follicular openings.

REFERENCES

Ahlgrimm-Siess, V., Massone, C., Scope, A., et al., 2009, Reflectance confocal microscopy of facial lentigo maligna and lentigo maligna melanoma: a preliminary study. *Br J Dermatol*, 161, 1307–16.

Cognetta, A., Stolz, W., Katz, B., Tullos, J. & Gossain, S., 2001, Dermatoscopy of lentigo maligna. *Dermatol Clin*, 19, 307–18.

Sahin, M., Ozturkcan, S., Ermertcan, A. & Gunes, A., 2004, A comparison of dermoscopic features among lentigo senilis/initial seborrheic keratosis, seborrheic keratosis, lentigo maligna and lentigo maligna melanoma on the face. *J Dermatol*, 31, 884–9.

Schiffner, R., Schiffner-Rohe, J., Vogt, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42(1 Pt 1), 25–32.

Stante, M., Giorgi, V., Stanganelli, I., Alfaioli, B. & Carli, P., 2005, Dermoscopy for early detection of facial lentigo maligna. *Br J Dermatol*, 152, 361–4.

8e Amelanotic and hypomelanotic melanoma

Juergen F. Kreusch, Scott W. Menzies, and Giuseppe Argenziano

Diagnosis of amelanotic melanoma is one of the greatest challenges in dermatology, even if supported by advanced techniques, such as dermoscopy. Identification of poorly pigmented melanoma, including amelanotic melanoma, is hampered by two circumstances. First, only few, if any, of the well-known features of melanoma are present, owing to lack of melanin. Second, most hypopigmented tumors do not raise suspicion for melanoma, especially in their early and small variants. Thus, amelanotic melanoma is frequently excised in advanced stages with misdiagnoses of, for example, intradermal nevus, fibroma, pyogenic granuloma, or wart.

Hypopigmentation in melanoma requires a more precise definition. There are tumors lacking any trace of melanin, even if viewed under the dermoscope. These tumors are truly "amelanotic melanoma." Secondly, there are "hypomelanotic" tumors that have some melanin pigmentation but lighter than conventional pigmented melanoma. One variety has faint brownish or other lightly colored melanin pigment that may occupy the entire lesion area (light-colored melanoma). Another has larger or smaller pigmented sections occupying less than 25% of the lesion with the remainder being amelanotic (partially pigmented melanoma). Finally, melanomas in advanced stages of regression are poorly pigmented or focally depigmented (regression). These tumors are not described in this chapter. Nevertheless, it should be mentioned that they can be distinguished reliably from amelanotic and hypomelanotic melanoma by dermoscopy via the presence of regression structures.

It is evident that tumors containing little or no melanin lack most of the established clinical features of melanoma based on pigmented structures. However, the less pigment a tumor contains, the better one can recognize its blood vessels by dermoscopy. In fact, aside from geometrical parameters, such as diameter, elevation, and outline, the vascular structures are frequently the only clue for amelanotic melanoma and dermoscopy is helpful for identifying these. Therefore, knowledge of tumoral vascular structures is essential for identifying these tumors.

Vascular structures are soft tissue and are thus easily compressible, and if compressed will not be visible. Use of contact fluids with low viscosity, such as alcohol, enhances this phenomenon, since fluid with low viscosity requires more pressure for complete contact, or else the liquid will flow off the area under observation. Furthermore, alcohol evaporates quickly. To view vessels it is recommended that ultrasound gel be used as a contact fluid. Owing to its high viscosity, the gel does not flow away. One may achieve good optical contact between the glass plate and the tumoral surface without pressure. The effect of compression can be controlled easily by raising and lowering the pressure of the glass plate upon the tumoral surface and observing the disappearance and re-filling of the vessels. This artifact will not occur with non-contact dermoscopic instruments that utilize polarized light for illumination since they do not directly contact the skin and therefore no compression of vessels due to direct pressure can occur.

VASCULAR PATTERNS OF NORMAL SKIN

To identify the different vascular structures in tumors one needs to first recognize the normally occurring vascular structures in normal skin (Kreusch, 2002). At all sites of the body where the architecture of the dermal–epidermal interface consists of dermal papillae and epidermal rete ridges (i.e., trunk, arms, and legs) one finds pinpoint-like vessels of 0.01–0.02 mm in diameter. The dots are regularly arranged; they represent the terminal capillaries within the dermal papillae.

In the skin surface crests of palms and soles the red dots are aligned along the ridges. Sometimes the upper dermal plexus is faintly visible as a coarse network of broader vessels below the small red dots. Owing to the dispersion of light on collagen fibers in the tissue, these vessels cannot be imaged sharply. They appear slightly blurred and their color is pink if compared with the crimson vessels located directly below the epidermis.

The nailfold capillaries are tiny loops. However, running parallel to the skin surface they are visible not as dots but as loops of up to 0.5–2 mm in length. Their characteristic differences and diagnostic importance in autoimmune diseases, such as lupus erythematosus or dermatomyositis have been extensively described (Beltrán et al., 2007). Only in rare instances do they have to be distinguished from vessels in paraungual tumors.

Facial skin usually has suffered from long-term UV-light exposure with consequent thinning of the epidermis. Thus, dermal papillae and rete ridges have disappeared. Small red dots are absent; vessels of the dermal plexus are visible dermoscopically as regularly branching tree-like structures, running parallel to the skin surface. The naked eye perceives telangiectasia of the cheeks as sharply demarcated lines. However, under the dermoscope they have similarities to vessels of the dermal plexus elsewhere, insofar as the regularly branching vessels of facial skin appear slightly blurred and of a pink hue. This may be very helpful for discriminating them from sharply demarcated and crimson tumoral vessels.

TUMORAL VASCULAR PATTERNS

Only a few papers dealing with the vascular architecture within melanoma have been published (Kreusch, 2002; Argenziano et al., 2004; Menzies et al., 2008). As for skin vessels the acquisition of knowledge of tumoral vessels should begin with viewing the normal skin and frequently inspecting the vascular structures within hypopigmented benign tumors, such as dermal nevi, so as to become familiar with "normal" patterns (Vázquez-López et al., 2004). The vascular structures within an amelanotic melanoma are distinctly different ("abnormal"). If using vascular patterns for differentiation of tumors, three aspects have to be observed: (*i*) The shape of the blood vessels; (*ii*) the arrangement of the blood vessels; and (*iii*) additional features (e.g., white halo).

There are only a few principal vascular structures in tumors: (*i*) Comma vessels (in intradermal nevi); (*ii*) dotted vessels (90% likelihood for melanocytic lesions, especially Spitz nevi); (*iii*) linear–irregular vessels (in melanoma and other skin malignancies); (*iv*) arborizing vessels [in basal cell carcinoma (BCC)]; (*v*) hairpin vessels (in keratinizing tumors, especially if surrounded by a whitish halo, and melanoma); and (*vi*) glomerular vessels (in Bowen's disease).

Morphology of vessels in melanoma undergoes time-dependent changes during tumor growth. Surprisingly, vessels in early stages of amelanotic melanoma appear more orderly arranged and homogenous in shape (almost exclusively dotted vessels) as compared with advanced tumors of large vertical diameter. In these advanced tumors the vessels are longer and coarser, they appear more irregular, and are quite variable.

Thin melanoma (<0.5 mm Breslow thickness) is supplied by point-like vessels in a quite regular arrangement across the entire tumoral area. Tumors of 0.5–2 mm thickness reveal vessels of point-like and of hairpin appearance, still, the arrangement of vessels is quite regular. Beyond 2 mm tumoral thickness the hairpin loops are more twisted and splintered, their arrangement is not as regular as in thin tumors. Hence, they were described as linear–irregular vessels. Melanoma of more than ~3 mm thickness develop a different structure of vascular supply. As vertical growth apparently cannot be maintained by further elongation of the capillary loops, vessels arising from the adjacent dermal plexus appear on the tumoral surface. These vessels resemble arborizing vessels of BCC; however, their winding and branching is less bizarre and irregular as compared with BCC.

The arrangement of vessels and additional features may give valuable information for the final diagnosis. In keratoacanthoma, vascularization is encountered exclusively at the periphery of the lesion, the center being filled with a yellowish keratotic plug. In warts, the vessels are scattered across the entire area of the wart. In keratinizing tumors, such as seborrheic keratoses, warts, keratoacanthoma, or squamous cell carcinoma, hairpin vessels are surrounded by a whitish halo, which frequently merges into a yellowish homogenous layer of keratin. The whitish halo represents the layer of vital keratinocytes surrounding the feeding vessels in their center. The white halo surrounding blood vessels is absent in melanocytic lesions that are supplied by vascular loops, as in melanoma and Spitz nevi.

DIAGNOSING AMELANOTIC MELANOMA

There are four main characteristics that should be taken into account when dealing with a possible amelanotic melanoma. First, a good proportion of amelanotic melanomas are nodular. Thus, in many instances, amelanotic melanoma is a clinically elevated tumor, firm on palpation, and referred by the patient to be growing in the last few months. These three characteristics can be summarized by the EFG (Elevation, Firmness, Growth) rule that could be used as a clinical guide when dealing with melanomas lacking the classical ABCD clinical criteria (Chamberlain et al., 2003).

Second, the true prevalence of amelanotic melanoma is quite low. In most cases melanomas lacking significant pigmentation are of the "hypomelanotic" type. By using dermoscopy, the residual pigmentation can be more easily seen as small areas of blue, to white-blue, to grayish areas involving small parts of the tumor. Sometimes residual pigment network or brown, gray-to-black dots/globules may also be seen as the residual epidermal component at the periphery of an amelanotic proliferating nodule.

Third, within the amelanotic area, vessels are easily visualized by the use of dermoscopy. In many instances, melanoma is typified by atypical, polymorphic vessels (defined as having two or more vessel morphologic types). Dotted vessels may be seen in combination with linear–irregular and/or hairpin–irregular vessels not surrounded by a whitish halo.

Last but not least, a good proportion of amelanotic and hypomelanotic melanomas show a typical pinkish background color, the so-called milky red areas. This dermoscopic feature is not specific for melanoma, being frequently seen also in BCC and pyogenic granuloma. However, milky red areas are almost never seen in intradermal nevi or seborrheic keratoses.

Recently, Menzies et al. published a large series of amelanotic and hypomelanotic melanomas to determine their predictive dermoscopy features (Menzies et al., 2008). One hundred and five melanomas (median Breslow thickness 0.76 mm), 170 benign melanocytic lesions, and 222 nonmelanocytic lesions lacking significant pigment (amelanotic, hypomelanotic, and partially pigmented) were scored for 99 dermoscopy features. Diagnostic models were derived and tested on independent randomly selected lesions. The most significant negative predictors of melanoma overall were multiple (>3) milia-like cysts, comma vessels with a regular distribution, comma vessels as the predominant vessel type, symmetrical pigmentation pattern, and irregular or multiple blue-gray globules. The most significant positive predictors were blue-white veil, scar-like depigmentation, multiple blue-gray dots, irregular-shaped depigmentation, irregular brown dots/globules, 5–6 colors, predominant central vessels, and peripheral light brown structureless areas occupying more than 10% of the surface area of the lesion. Of the vascular-related features the most predictive for melanoma were in order predominantly central vessels, hairpin vessels, milky red pink areas, greater than one shade of pink, combination of dotted and linear–irregular vessels, and linear irregular vessels as the predominant vessel type. A simple model distinguishing melanoma from all nonmelanoma gave a sensitivity of 70% and specificity of 56% in the test set (Table 8e.1). Importantly, it was shown to be relatively easier to distinguish all malignant amelanotic/hypomelanotic lesions from all benign lesions (rather than to attempt to discriminate melanoma from other malignant lesions, such as BCC). In this regard additional important features are large diameter vessels, arborizing vessels, ulceration, gray color, and any feature of a pigmented BCC. Using this data a model distinguishing all malignant lesions from benign lesions gave a 96% sensitivity and 37% specificity in the test set (Menzies et al., 2008).

Table 8e.1 Simple Dermoscopy Model for the Diagnosis of Melanoma Lacking Significant Pigment[a]

Negative feature (if present nonmelanoma)
>3 Milia-like cysts
Positive features (any one present, then melanoma)
Irregular sized or distributed brown dots/globules
Multiple blue/gray dots
Irregular-shaped depigmentation
Blue-white veil
>1 Shade of pink
Predominant central vessels
Dotted + linear irregular vessels

[a]70% of amelanotic/hypomelanotic melanoma are detected by this rule.

STRATEGIES FOR DETECTING AMELANOTIC MELANOMA

It is a life-saving diagnostic procedure if a dermatologist identifies amelanotic melanoma at an early stage of growth. While amelanotc melanomas often lack concerning clinical features, dermoscopy will usually reveal atypical vessels (Jaimes et al., 2011). Dermoscopy can raise the index of suspicion for almost all cases of amelanotic melanoma, especially early ones. However, we have to change our strategy in selecting lesions for dermoscopic examination. In addition to using dermoscopy on large and dark tumors, we need to also start using dermoscopy on small and nonpigmented lesions, which often escape our attention and are not examined any further. This results in a filter mechanism toward large and dark lesions. Small and hypopigmented tumors ("atypical melanoma") are neglected. "Atypical melanoma" frequently are not examined by dermoscopy and are not photographed nor excised. In most studies eye-catching melanoma with advanced thickness, mostly reddish or pink nodules, frequently ulcerated, are over-represented and the dermoscopic studies and their results are biased toward this type of tumors.

The recommendations for detecting amelanotic melanoma are as follows:

1. Do not restrict dermoscopy to only large and pigmented lesions.
2. Regressive melanoma present different dermoscopic features as compared with amelanotic melanoma.
3. When viewing a nonpigmented lesion make sure the instrument does not exert pressure onto the vessels causing them to blanch.
4. Lesions with loop-like vessels lacking a white halo must be considered suspicious for amelanotic melanoma.
5. Lesions with pinpoint vessels should be considered melanocytic, and hence melanoma needs to be excluded based on other dermoscopy features.
6. Remember that nodular lesions are particularly difficult to analyze—vessels of pyogenic granuloma are blurred and barely visible, lesions with vessels characteristic for BCC, dermal nevus, keratinizing tumors help to rule out the diagnosis of melanoma. The remaining lesions have to be dealt with carefully as potential melanomas cannot be ruled out.
7. A lesion "without features" must be re-examined or biopsied as melanoma needs to be ruled out in these lesions.

Key Points

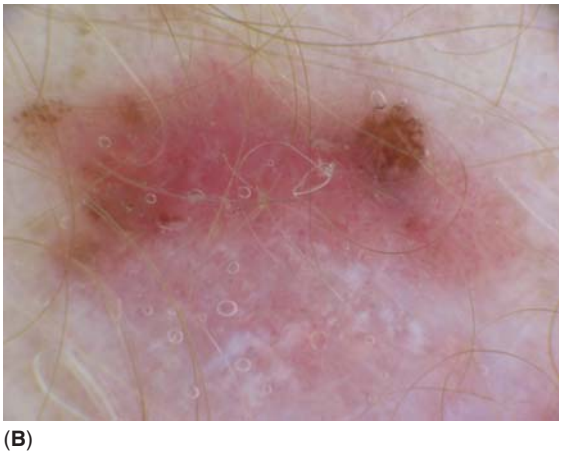
- There are only a few principal vascular structures in tumors:
  1. Comma vessels (in intradermal nevi);
  2. Dotted vessels (90% likelihood for melanocytic lesions, especially Spitz nevi and melanoma);
  3. Linear–irregular vessels (in melanoma and other skin malignancies);
  4. Arborizing vessels (in basal cell carcinoma);
  5. Hairpin vessels (in keratinizing tumors, especially if surrounded by a whitish halo; and melanoma, especially if present in a pink background.);
  6. Glomerular vessels (in Bowen's disease).
- Biopsy any EFG-positive lesion that cannot be recognized as clearly benign.
- Biopsy lesions with nonspecific pigment pattern that can be seen as structureless areas of brown-to-gray color involving part or the whole lesion.
- Biopsy lesions with both dotted and linear–irregular vessels, especially if those vascular structures cannot be recognized in other lesions within the same patient (comparative approach).
- Biopsy lesions exhibiting milky red areas (or >1 shade of pink) regardless of any other feature present within the lesion.
- Biopsy lesions with hairpin vessels or predominantly central vessels if you suspect a melanocytic lesion based on other dermoscopy features.
- Always biopsy lesions with features of BCC prior to treatment (arborizing vessels, large diameter vessels, ulceration, and any feature of pigmented BCC).

The following figures illustrate the diagnosis of amelanotic and hypomelanotic melanoma (Figs. 8e.1–8e.11).

▲ **Figure 8e.1a** Melanoma, clinical image.

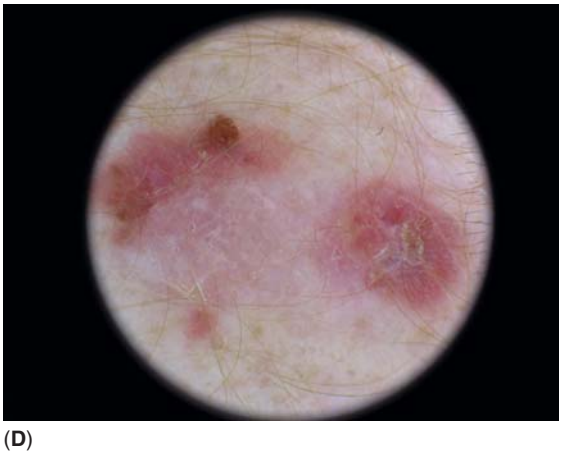
◀ **Figure 8e.1b** Partially pigmented melanoma with remnants of pigment network and an amelanotic nodular area typified by milky red color.

▲ **Figure 8e.2a** Melanoma, clinical image.



(**B**)

(**C**)



(**D**)

Figure 8e.2 (**B**) Partially pigmented, regressive melanoma, with remnants of brown network and globules. Milky red areas together with polymorphic vessels are clearly visible. The latter are typified by a combination of dotted vessels (**B, C**) and linear–irregular and hairpin vessels (Fig. 8e.6). A large white scar-like area of regression is also visible (**D**).

▲ **Figure 8e.3a** Melanoma, clinical image.

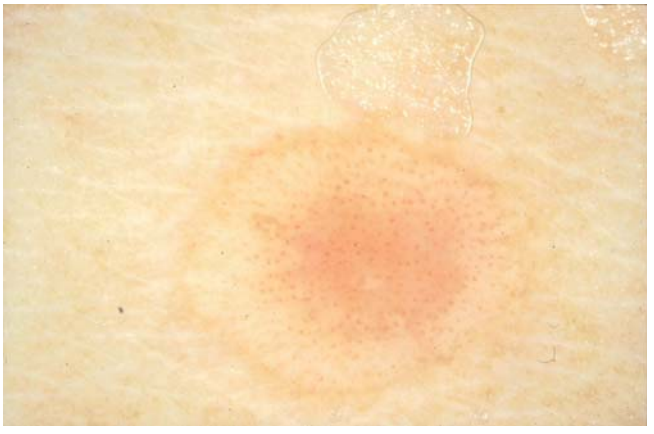
◀ **Figure 8e.3b** True amelanotic, ulcerated, nodular melanoma with linear–irregular and dotted vessels clearly visible over a milky red background color.

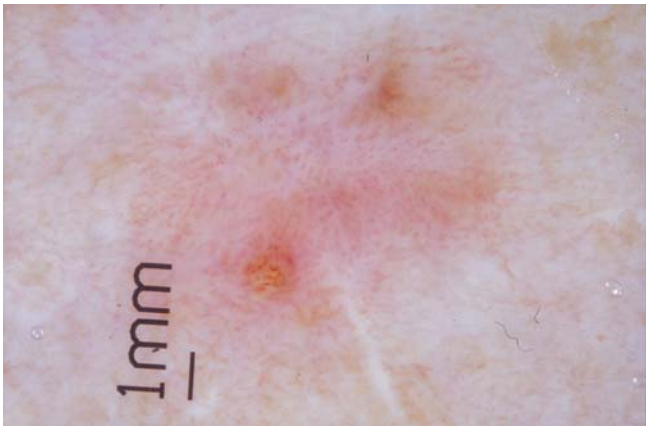
▲ **Figure 8e.4a** Melanoma, clinical image.

◀ **Figure 8e.4b** Amelanotic nodular melanoma typified by polymorphic vessels (combination of dotted, linear–irregular, and hairpin vessels) and milky red areas.

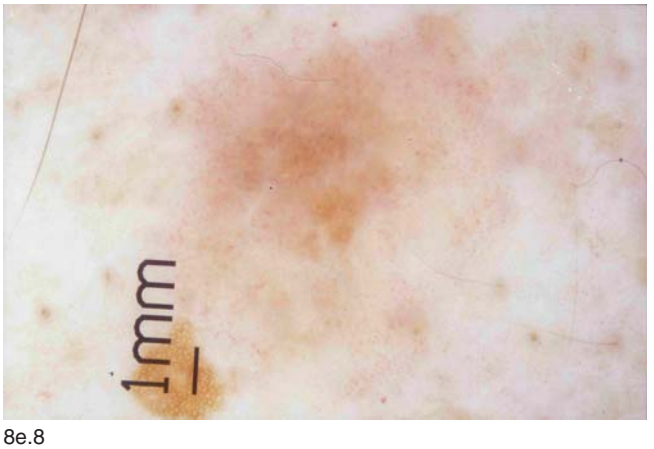
▲ **Figure 8e.5a** Melanoma, clinical image.

◀ **Figure 8e.5b** Hypomelanotic melanoma with linear–irregular and hairpin vessels over a milky red background color.

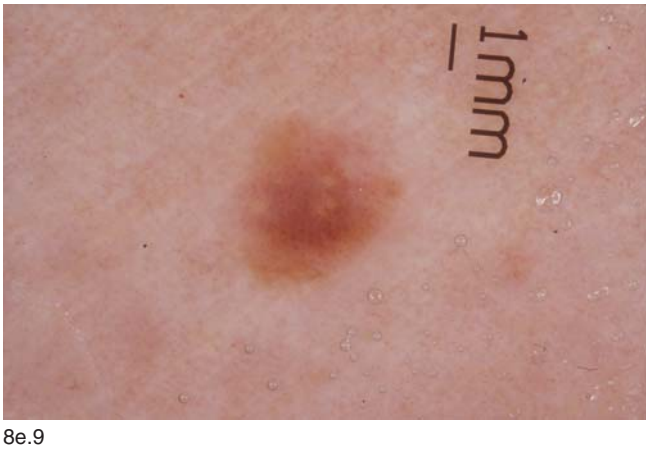

8e.6



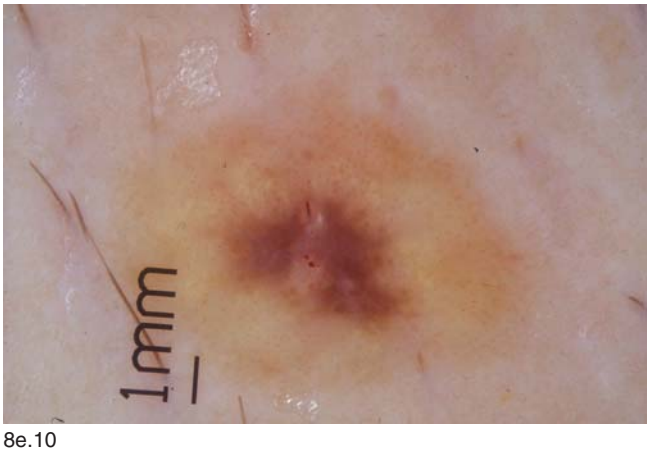
8e.7



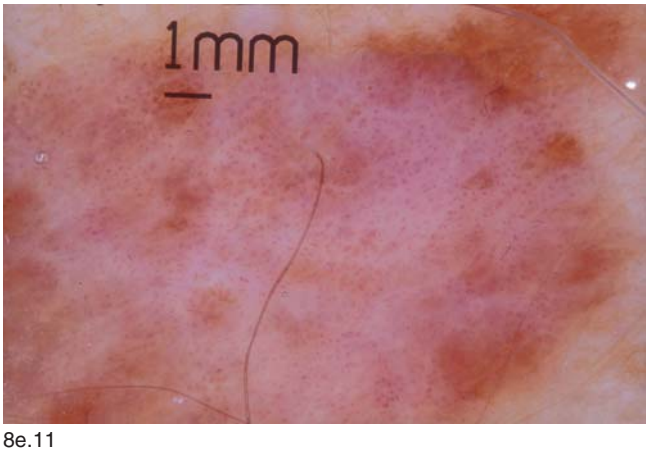
8e.8



8e.9



8e.10



8e.11

Figure 8e.6–8e.11 Dermoscopy examples of early melanomas showing dotted vessels and variable amount of brown color *source*: Courtesy of SurPrise e.K., Luebeck, Germany.

REFERENCES

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Beltrán, E., Toll, A., Pros, A., Carbonell, J. & Pujol, R.M., 2007, Assessment of nail-fold capillaroscopy by ×30 digital epiluminescence (dermoscopy) in patients with Raynaud phenomenon. *Br J Dermatol*, 156, 892–8.

Chamberlain, A.J., Fritschi, L. & Kelly, J.W., 2003, Nodular melanoma: patients' perceptions of presenting features and implications for earlier detection. *J Am Acad Dermatol*, 48, 694–701.

Jaimes, N., Braun RP., Thomas, L., Marghoob, AA., 2011, Clinical and dermoscopic characteristics of amelanotic melanomas that are not of the nodular subtype. *J Eur Acad Dermatol Venereol.*

Kreusch, J.F., 2002, Vascular patterns in skin tumors. *Clin Dermatol*, 20, 248–254.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Vázquez-López, F., Kreusch, J. & Marghoob, A.A., 2004, Dermoscopic semiology: further insights into vascular features by screening a large spectrum of nontumoral skin lesions. *Br J Dermatol*, 150, 226–31.

8f Equivocal lesions, false positive, and false negative

Susana Puig, Josep Malvehy, Ashfaq A. Marghoob, and Giuseppe Argenziano

A certain subset of cutaneous melanomas (CMs) lack sufficient dermoscopic features and criteria to be correctly diagnosed as melanoma (Argenziano et al., 2007; Puig-Butille et al., 2007). Moreover, the dermoscopic diagnosis of early CM can be difficult, especially in patients with multiple atypical nevi. Very early superficial spreading CM and nodular CM can be symmetric lesions that lack any melanoma-specific structures and do not have a multicomponent pattern. Further diagnostic difficulties may occur when CM mimics benign pigmented skin lesions (PSLs), such as seborrheic keratosis (Argenziano et al., 2003) or lacks pigmentation as in the case of amelanotic melanoma (Menzies et al., 2008). In addition, occasionally, some tumors may be misdiagnosed as melanoma. In an effort to improve the diagnostic accuracy of dermoscopy we described in this chapter both types of lesions—melanomas that are difficult to diagnose with dermoscopy and tumors that are misdiagnosed as melanoma with dermoscopy (Marghoob et al., 2009).

MELANOMAS MIMICKING OTHER TUMORS

The most important differential diagnosis of melanoma is the differentiation of melanoma from nevi, especially Clark nevi. Clark nevi are acquired nevi that are usually larger than 5 mm, have a macular component, and manifest some of the clinical criteria associated to melanoma, such as asymmetry, color variegation, and border irregularity.

Clark Nevus-Like Melanomas (Fig. 8f.1)

In our experience, over 50% of all melanomas removed were initially clinically diagnosed as probable Clark nevi. Most of these melanomas were diagnosed in patients with multiple atypical nevi or Clark nevi. In patients with numerous Clark nevi it is important to maximize both sensitivity and specificity, which translates into detecting early melanomas without the added morbidity associated with the removal of many benign nevi including Clark's nevi/dysplastic nevi. This can be achieved by digital monitoring and this explains why many of the melanomas in these patients were detected and biopsied because of changes noted on sequential digital followup (both short-term and long-term monitoring). Other dermoscopic features that led to the removal of these melanomas included the presence of regression structures and/or the presence of peripheral hyperpigmentation. It was also observed that some of these melanomas presented with uniform or central hyperpigmentation, multifocal hyper- and/or hypopigmentation, or central hypopigmentation.

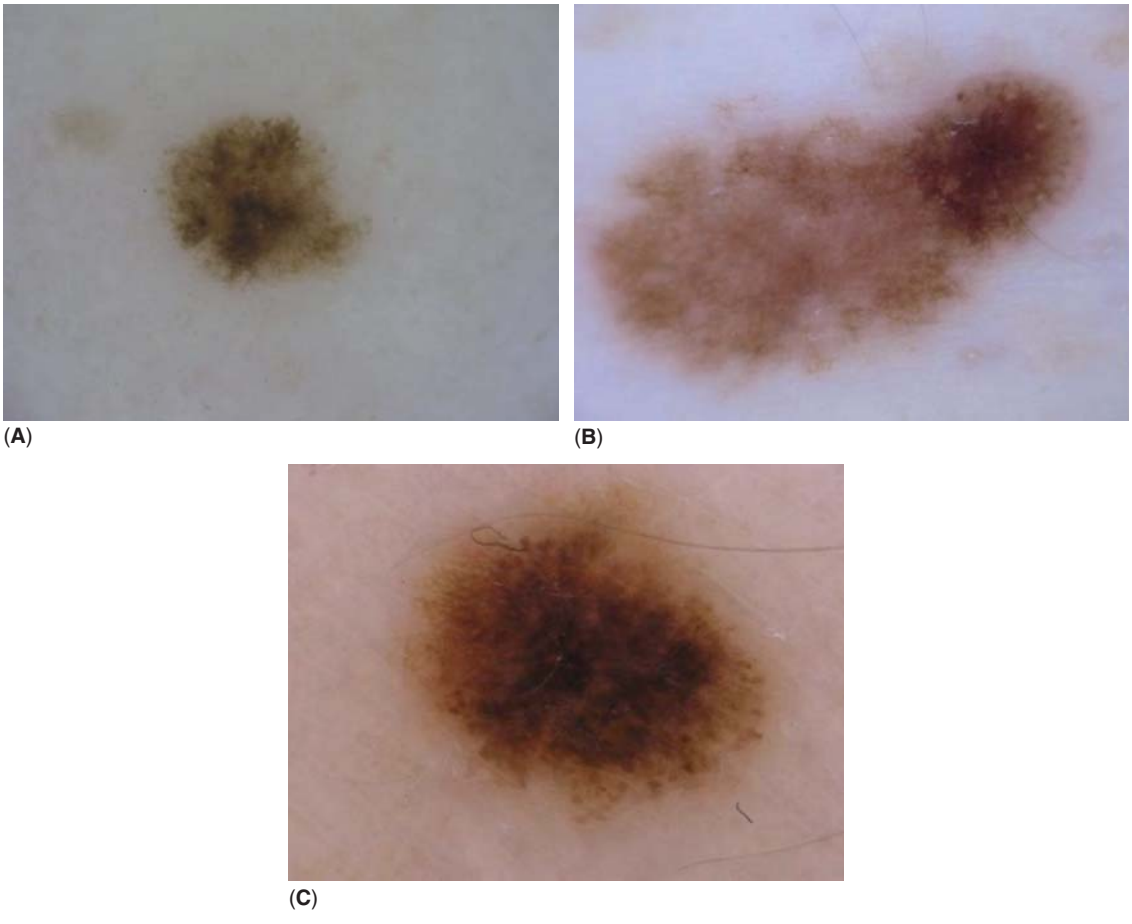


Figure 8f.1 Shown here are three melanomas that resemble Clark's nevi. (**A**) Under dermoscopy the lesion shows reticular pattern and multifocal hyperpigmentation. The diagnosis was melanoma. (**B**) Dermoscopy of another Clark nevus-like melanoma with peripheral hyperpigmentation that developed during digital followup. (**C**) This lesion shows a reticular pattern with a peripheral rim of globules that are irregularly distributed. The lesion was excised because enlargement of the lesion was detected by digital followup on the leg of this 50-year-old lady. The diagnosis was in situ melanoma.

In patients without many clinically atypical nevi, the main reason leading to the surgical removal of these subtle melanomas is that they often present as isolated lesions or as outlier lesions. Although they may display an equivocal dermoscopic appearance, they are often removed since in this type of patient scenario the main goal is to maximize diagnostic sensitivity for melanoma (Fig. 8f.2). Since these patients do not have many nevi, maximizing specificity is not so critical.

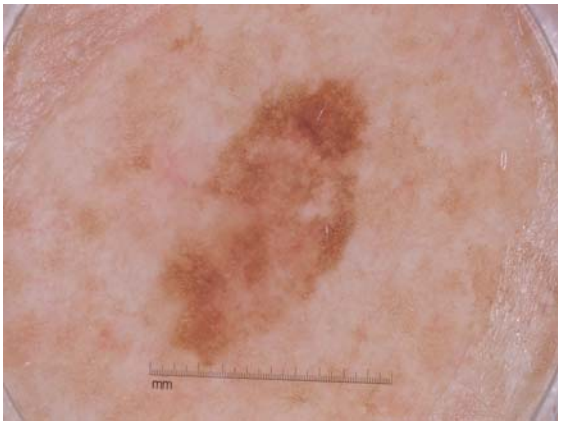
Congenital Nevus/Dermal Nevus-Like Melanoma (Fig. 8f. 3)

Focal melanomas arising in congenital nevi may be difficult to detect because the overall pattern manifest by such lesions may be consistent with a congenital nevus (Fig. 8f.3). Such melanomas are usually found based on a history of change. In addition, any congenital nevus displaying a melanoma-specific structure, such as atypical network, focal negative network, crystalline structures, streak, irregular blotches, blue-white veil, or regression structures should be viewed with caution (Fig. 8f.3).

Some melanomas may present as papillomatous lesions (Fig. 8f.4) and may even have comedo-like openings and milia-like cyst. Patient history of change or complaints of symptoms pertaining to the lesion usually bring such lesions to the clinician's attention. The clues to the diagnosis of such melanomas are the presence of any melanoma-specific structures, in particular, variable amounts of a bluish pigmentation (Fig. 8f.3), or atypical vessels (Fig. 8f.4). Lastly, it should be remembered that lesions that are

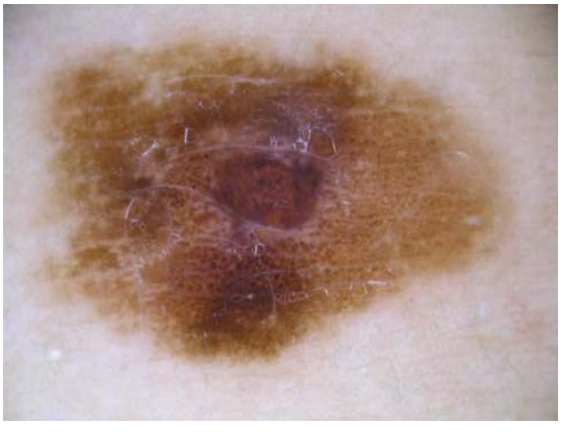
▲ **Figure 8f.2a** This patient has one large outlier lesion on her back.

◀ **Figure 8f.2b** Clinical close-up image of the lesion. This lesion was not present during her youth, and thus it was not a congenital nevus.



◀ **Figure 8f.2c** Dermoscopy reveals patches of network and tan structureless areas. This lesion was biopsied and was a melanoma in situ.

▲ **Figure 8f.2a** Congenital nevus-like melanoma. Clinical picture of a melanocytic lesion in the lumbar area of a 13-year-old girl. The lesion was present since early childhood.



◀ **Figure 8f.3b** Dermoscopy shows a globular pattern with a homogenous area in the center. The lesion exhibits several colors, including bluish pigmentation. This lesion proved to be a melanoma.

raised (nodular, palpable, or elevated) should never be subjected to digital followup. If melanoma enters the differential diagnosis for a raised lesion (Fig. 8f.4), then a biopsy should be performed.

Spitz/Reed Nevus-Like Melanoma (Fig. 8f.5)
The starburst pattern is characteristic of Spitz nevi. However, spitzoid lesions in adults are often challenging to diagnose histologically with approximately 50% of these lesions being diagnosed as melanomas by at least some pathologists. Thus, we are of the opinion that all spitzoid lesions in an adult should be removed since the pre-test probability of melanoma is greater in older persons.

Blue Nevus-Like Melanoma (Fig. 8f.6)
It is well known that homogenous blue pigmentation is a common pattern seen in blue nevi, malignant blue nevi, nodular melanoma/dermal melanoma, and cutaneous metastasis of melanoma. The history of recent changes and/or the history of a previous melanoma are the clues for the diagnosis. Dermoscopic clues to the correct diagnosis include differing shades of blue, pink color, crystalline structures, and atypical vessels.

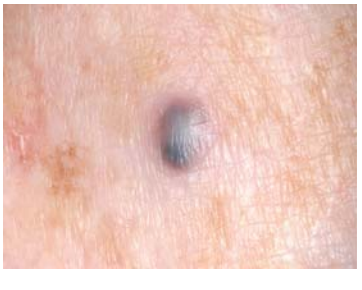
Angioma-Like Melanoma (Fig. 8f.7)
Some amelanotic melanomas (primary or metastatic) clinically and dermoscopically resembled hemangiomas (Figs. 8f.7 and 8f.8). Dermoscopically

▲ **Figure 8f.4a** Clinical image of a papillomatous pink melanoma.

◀ **Figure 8f.4b** Dermoscopy reveals atypical vessels.

▲ **Figure 8f.5a** This lesion was a new lesion that developed on the abdomen of a 28-year-old woman with the atypical mole syndrome.

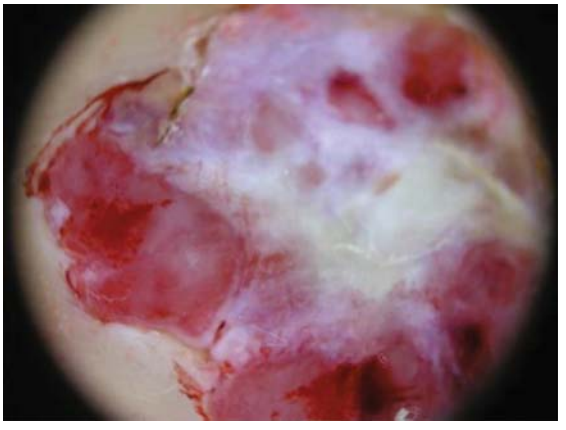
◀ **Figure 8f.5b** Dermoscopy reveals a starburst pattern with a central blue-white veil. This lesion proved to be an invasive melanoma on biopsy.



▲ **Figure 8f.6a** Clinical image of a blue nevus-like papule on the shoulder of this 80-year-old man. The lesion is new and developed over the past year.

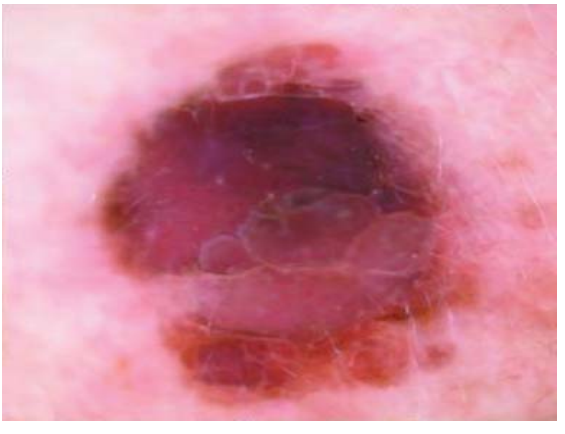
◀ **Figure 8f.6b** Dermoscopy reveals blue, tan, and pink colors. Few serpentine vessels are also visible. The lesion was biopsied and was consistent with a primary dermal melanoma.

▲ **Figure 8f.7a** Angioma-like melanomas. Clinical picture of a nonpigmented and ulcerated tumor on the sole.



◀ **Figure 8f.7b** Dermoscopy shows the absence of melanocytic criteria and a presence of a peripheral white collarette with red-whitish homogenous areas in the center. The pattern is indistinguishable from a pyogenic granuloma.

▲ **Figure 8f.7c** Clinical picture of a reddish fast growing tumor in the check of a lady.



◀ **Figure 8f.8d** Dermoscopy of the tumor showing false lacunas with red to purple ill-defined structures resembling lacunas and the presence of some linear vessels inside these structures in association with milky red areas.

▲ **Figure 8f.8a** Clinical image of a lesion that proved to be melanoma.

◀ **Figure 8f.8b** Dermoscopy reveals features that may be mistaken for a hemangioma. However, notice that the lesion does not have any classic lacunas separated by blue-white septa. It does have some irregular vessels within the red areas, which is not a feature seen in hemangiomas.

they can reveal red-to-purple ill-defined lacunar-like structures, serpentine vessels, and milky red areas (Fig. 8f.9).

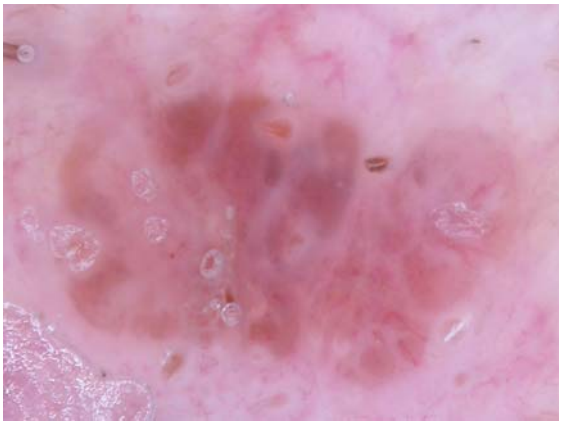
Besides melanomas mimicking hemangiomas, some fast-growing nonpigmented nodular melanomas may have a morphology resembling pyogenic granulomas. Pyogenic granulomas reveal a peripheral white collarette with red-whitish homogenous areas in the center, with fine linear irregular vessels.

One last word regarding lesions resembling pyogenic granulomas is warranted here. It is our opinion that any lesion clinically diagnosed as a pyogenic granuloma should be biopsied to confirm the clinical impression, especially in adults since the pre-test probability of melanoma is much greater in adults.

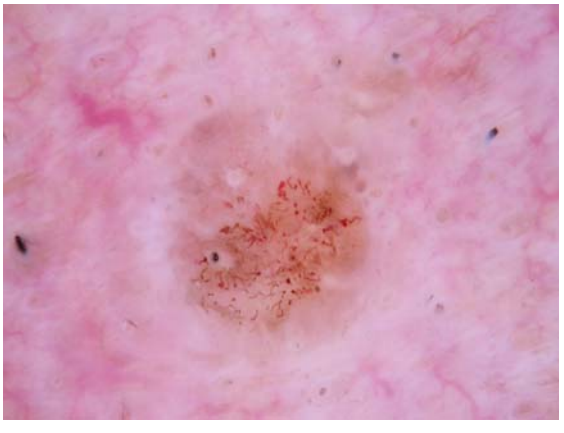
Basal Cell Carcinoma-Like Melanoma (Fig. 8f.10)

Melanomas may lack specific dermoscopic criteria of a melanocytic lesion (Fig. 8f.10) or may reveal features that mimic criteria commonly associated with basal cell carcinomas (BCCs), such as blue-gray nonaggregated globular structures (blue globules and ovoid nests), streaks (leaf-life areas) and arborizing vessels (Figs. 8f.11, 8f.12, 8f.13). For further details regarding the subtle differences between pigmented BCC and melanoma please see chapter 10 (exceptions to two-step rule). Lastly, it should be stressed that a melanoma that is clinically misdiagnosed as BCC will not have any bearing on the ultimate management decision, which is to biopsy the lesion; the histopathology will ultimately provide the clinician with the correct diagnosis of melanoma. Thus, although the clinician's ego may

▲ **Figure 8f.9a** This patient presented with two lesions on the cheek. The lesion on the left had clinical features of a hemangioma and the lesion on the right had clinical features of a basal cell carcinoma.



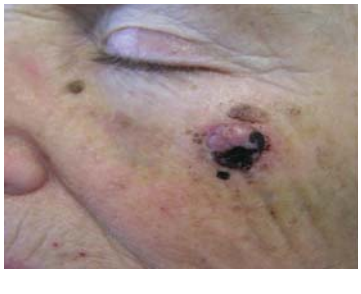
◀ **Figure 8f.9b** Dermoscopic features manifest by the lesion on the left could be mistaken for lacunas of a hemangioma. However, notice that the red blotches are not classic lacunas because they are not separated from each other by blue-white septae and they do not occupy the entire lesion. Also notice the irregular blood vessel in the lower right corner of the lesion. This lesion was biopsied and was consistent with a focus of metastatic melanoma.



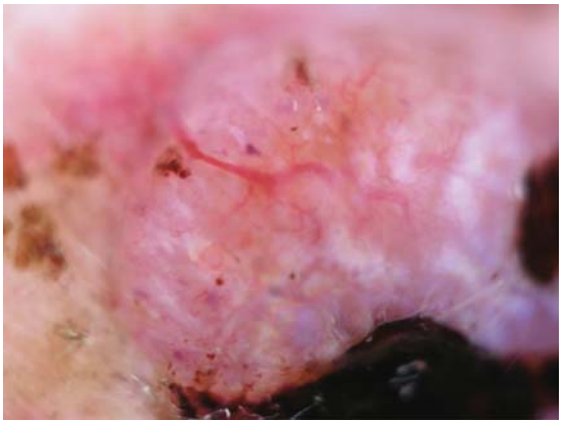
◀ **Figure 8f.9c** Dermoscopy of the lesion on the right reveals multiple serpentine and cork-screw vessels. This lesion was also a focus of metastatic melanoma.

▲ **Figure 8f.10a** BCC-like melanomas. Clinical picture of a nonpigmented, ulcerated, tumor on the trunk, in photo-damaged skin.

◀ **Figure 8f.10b** Dermoscopy of the lesion shows the absence of criteria for a melanocytic lesion and revealed the presence of ulceration. According to the algorithm of Menzies for the diagnosis of BCC the lesion could be misdiagnosed as a BCC. This lesion happens to be an amelanotic melanoma with linear–irregular vessels and ulceration.



▲ **Figure 8f.10c** Clinical picture of a nonpigmented tumor on the cheek of an elderly patient.

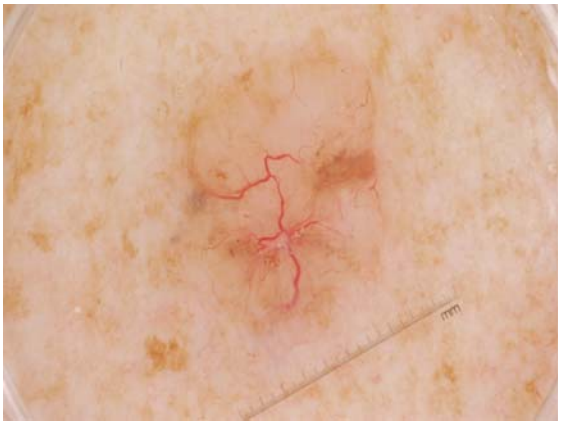


◀ **Figure 8f.10d** Dermoscopy of the lesion shows absence of criteria for melanocytic lesion and presence of arborizing vessels and ulceration. According to the algorithm of Menzies for the diagnosis of BCC the lesion could be misdiagnosed as BCC. This lesion was in fact an amelanotic melanoma with thick branched vessels and ulceration. *Abbreviation*: BCC, basal cell carcinoma.

▲ **Figure 8f.11a** Clinical image of a rapidly growing lesion on the cheek of an 18-year-old male patient.

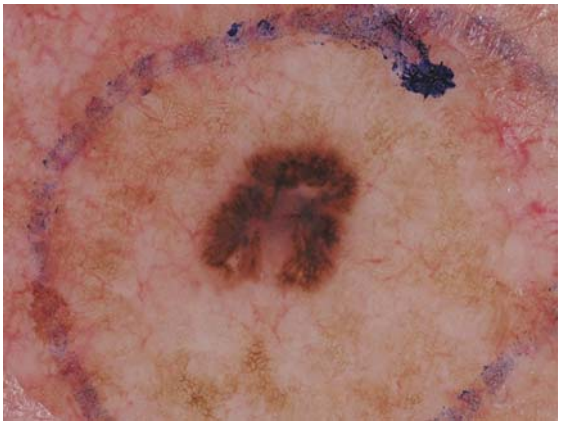
◀ **Figure 8f.11b** Dermoscopy reveals a few arborizing vessels and numerous serpentine vessels. This lesion was a nodular melanoma. One clue to the diagnosis is the presence of numerous serpentine vessels, which is not a common vascular structure seen in BCC. Another clue is that the entire lesion is pink; giving the appearance that all of the vessels are surrounded by a pink stroma. This pink color is even more pronounced when viewed with polarized dermoscopy. In BCC most of the vessels will usually be arborizing and they often occur in a background that is less pink and more whitish. The whitish color or shiny white areas are more conspicuous when viewed with polarized light (Fig. 8f.12). *Abbreviation*: BCC, basal cell carcinoma.

▲ **Figure 8f.12a** Clinical image of a basal cell carcinoma.



◀ **Figure 8f.12b** Dermoscopy shows predominantly arborizing vessels and a background color that is more whitish than pink.

▲ **Figure 8f.13a** Clinical image of a thin melanoma.



◀ **Figure 8f.13b** Dermoscopy reveals branched streaks and a central area that is relatively hypopigmented. Some of the peripheral branched streaks (atypical network) could be mistaken for leaf-like structures, especially those around 3 to 4 o'clock. The constellation of leaf-like structures and central hypopigmentation would lead an observer to the incorrect diagnosis of pigmented basal cell carcinoma. In fact, this lesion has an atypical network and a central blue-white veil, which are both melanoma-specific features. The biopsy of this lesion revealed melanoma.

have suffered somewhat, the patient's management and treatment would not have suffered at all.

Seborrheic Keratosis-Like Melanoma

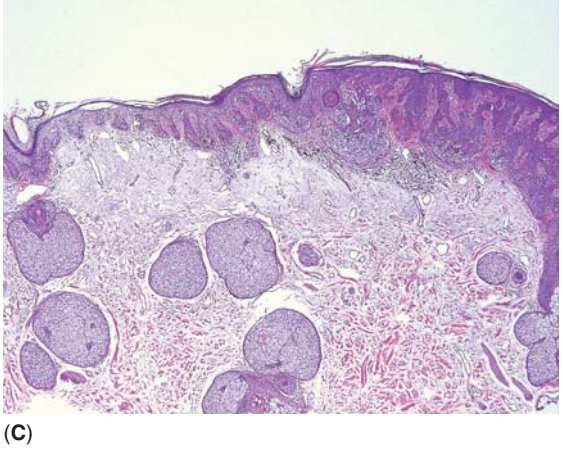
Some melanomas may show structures that are associated with the diagnosis of lentigo or seborrheic keratosis (SK), such as fingerprint-like structures, sulci filled with keratin, milia-like cysts, and comedo-like openings. These seborrheic keratosis-like melanomas often display variable nuances of a gray-blue coloration and atypical vessels, both of which should increase the index of suspicion that the lesion is a melanoma (Fig. 8f.14). We want the reader to be aware that these seborrheic keratosis-like melanomas are primary melanomas that simply happen to display a morphology that overlaps with seborrheic keratosis. This is in counter distinction to melanomas that on occasion develop within pre-existing seborrheic keratosis (Fig. 8f.15). In addition, some congenital nevi can have an SK like morphology. Melanomas arising in such SK-like congenital nevi may appear clinically as a typical SK.

Amelanotic (Includes Hypomelanotic) Melanoma

Amelanotic melanomas lack specific dermoscopic criteria of melanocytic or nonmelanocytic lesions. They present clinically as amelanotic plaques, macules, or nodules. They often appear as relatively symmetric lesions with a scaly surface (Figs. 8f.16 and 8f.17). These amelanotic melanomas come to the patient's or clinician's awareness because of change in its clinical morphology, symptoms or because they are outlier lesions (ugly duckling lesions). Dermoscopy of these amelanotic melanomas will

▲ **Figure 8f.14a** Clinical image of an irregularly pigmented lesion on the neck.

(**B**)



(**C**)

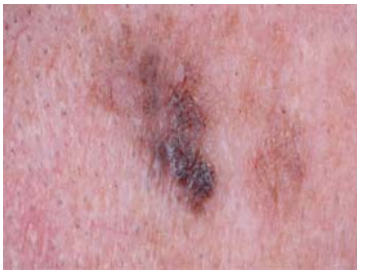
Figure 8f.14 (**B**) Dermoscopy reveals prominent comedo-like openings and milia-like cysts in the center of the lesion. In such cases both anchoring bias and search satisfaction bias may lead to the incorrect clinical diagnosis of seborrheic keratosis. Careful scrutiny of this lesion reveals the presence of network, which is visible at the far right side of the lesion. According to the first step in the two-step dermoscopy algorithm, the presence of network automatically classifies this lesion as a melanocytic tumor. In other words, the presence of network trumps the presence of comedo-like openings and milia-like cysts for the purpose of classifying lesions as melanocytic or nonmelanocytic tumors. Once correctly identified as a melanocytic tumor, the additional presence of a blue-white veil and irregular vessels, which can be seen on the bottom left corner of the lesion, helps to correctly diagnose this lesion as a melanoma. (**C**) Histopathology of the lesion revealed an invasive melanoma with seborrheic keratosis-like features. Note the comedo-like openings and milia-like cysts in the pathology image.

usually reveal the presence of atypical vascular structures, such as dotted vessels (Fig. 8f.18). Amelanotic lesions that have a combination of both dotted and serpentine (linear–irregular) vessels are classified as having a polymorphous vessel pattern (Fig. 8f.17). A polymorphous vessel pattern is highly suggestive of a diagnosis of melanoma. Another dermoscopic structure that can aid in the detection of amelanotic melanomas are the so-called crystalline structures (Fig. 8f.19). The crystalline structures consist of shiny white lines or areas and these structures can only be seen with polarized light dermoscopy. In a melanocytic neoplasm the presence of crystalline structures is highly indicative of a diagnosis of melanoma or Spitz nevus.

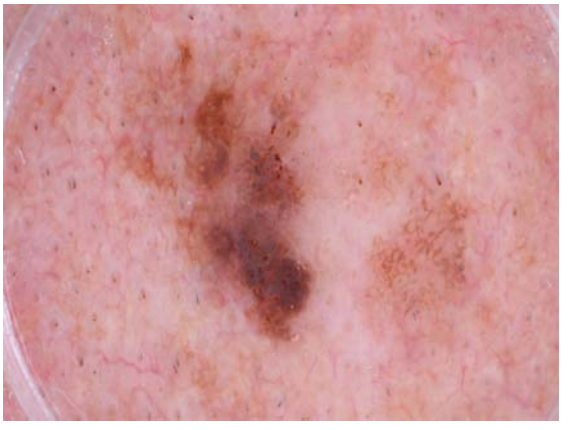
OTHER TUMORS MIMICKING MELANOMAS

Dermoscopy has improved our ability to detect cutaneous malignancy. Although some pigmented BCCs and some pigmented Bowen's disease lesions may be mistaken for melanoma using dermoscopy, this clinical error in diagnosis will have little to no bearing on management since a biopsy will be performed regardless (Figs. 8f.20 and 8f.21). As stated above, dermoscopy has improved our ability to detect melanoma (increased sensitivity) and has also improved our specificity by reducing the number of benign lesions being excised. The ratio of melanoma to benign lesions excised decreased with the use of dermoscopy from approximately 1/15 to 1/7 in the hands of experts using digital dermoscopy and followup. With that said, some benign lesions have a clinical and dermoscopic morphology that overlaps with melanoma, and thus a proportion of benign lesions will inevitably be excised so as not to miss a melanoma. Almost any benign skin growth can on occasion mimic a melanoma; however, some of the most common ones are Clark nevi (Fig. 8f.22), combined nevi (Fig. 8f.23), Spitz nevi (Figs. 8f.24 and 8f.25), congenital nevi (Fig. 8f.26), and seborrheic keratosis (Fig. 8f.27). In addition, due to the presence of vessels, crystalline structures or regression structures, irritated seborrheic keratosis (Fig. 8f.28) and lichen planus-like keratosis (Fig. 8f.29) can also be mistaken dermoscopically for melanoma. Many other benign growths, such hemangiomas, angiokeratomas, and dermatofibromas can on occasion mimic melanoma (Fig. 8f.30).

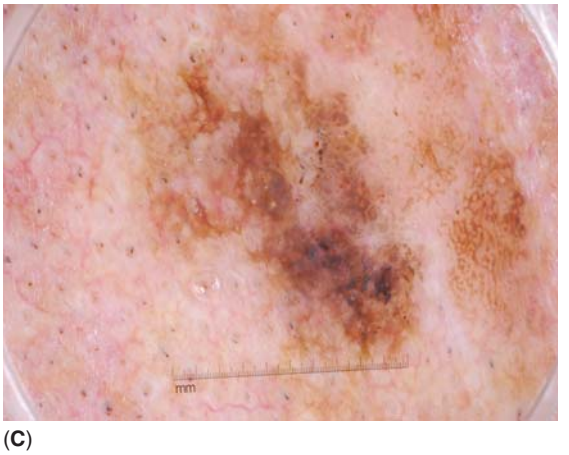
In conclusion, dermoscopy improves the accuracy in the diagnosis of melanoma and helps reduce the number of unnecessary excisions of benign lesions. However, it is important to be aware that melanomas can sometimes mimic benign lesions. Careful examination and maintaining a high index of suspicion will usually prompt the clinician to biopsy these lesions. In addition, many benign lesions can mimic melanoma leading the clinician to perform a biopsy. Thus, a certain proportion of benign lesions will have to be excised in order to maintain a high sensitivity for diagnosing melanoma.



▲ **Figure 8f.15a** Clinical image of an irregularly pigmented lesion on the cheek.



(**B**)



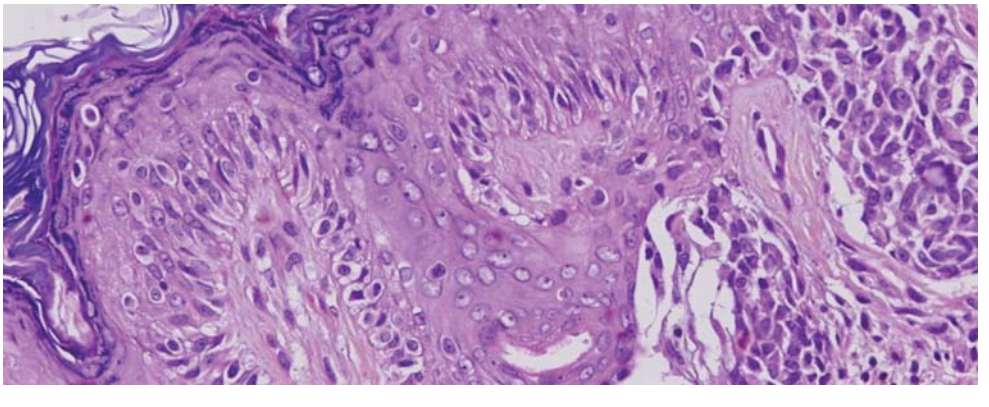
(**C**)

(**D**)

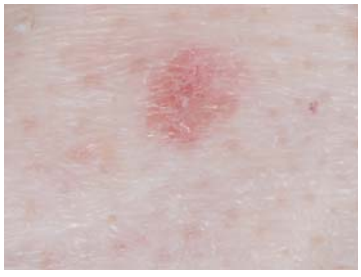
Figure 8f.15 (**B**) Dermoscopy of the lesion revealed gyri, sulci, crypts, and fingerprint-like structures—all features of a seborrheic keratosis. (**C**) One year later a focal change was observed in this lesion. The lesion developed a focus of course blue-gray granularity. (**D**) As can be seen in the histopathology image, this lesion showed a melanoma arising in association with a seborrheic keratosis.

▲ **Figure 8f.16a** Amelanotic melanoma. Nonpigmented macule on the limb of an albino patient.

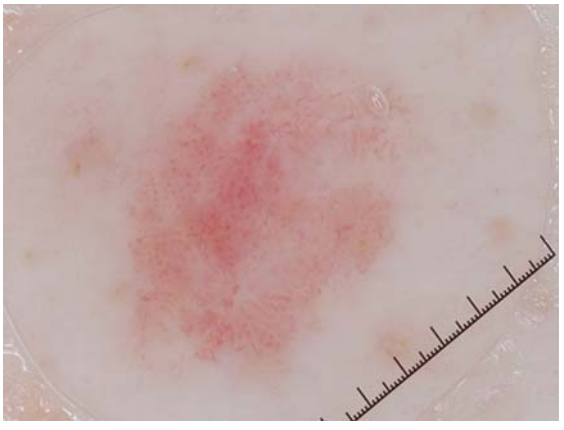
◀ **Figure 8f.16b** Under dermoscopy the lesion shows dotted vessels.



◀ **Figure 8f.16c** Pathology shows atypical proliferation of melanocytes with pagetoid spread and atypical nesting. The lesion was diagnosed as an in situ melanoma (H&E, ×30).



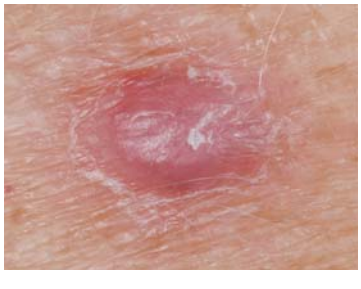
▲ **Figure 8f.17a** Clinical image of a pure amelanotic melanoma. The lesion is relatively symmetric, has regular borders, and a scaly surface.



◀ **Figure 8f.17b** Dermoscopy reveals a polymorphous vascular pattern, which should raise concern for melanoma. Histopathology confirmed that this lesion was a thin microinvasive melanoma. Melanomas that have no visible melanin pigment on clinical and dermoscopy examination are referred to as dermoscopically amelanotic melanoma.

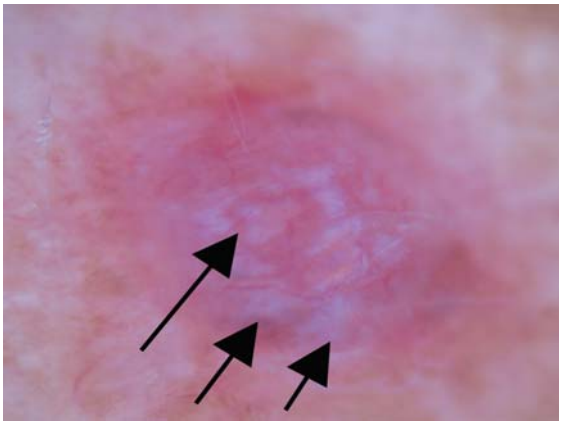
▲ **Figure 8f.18a** Clinical image of a relatively symmetric macule with a slightly scaly surface.

◀ **Figure 8f.18b** Dermoscopy reveals a slight tan color and numerous dotted vessels. Histopathology confirmed this to be a microinvasive melanoma. Clinically amelanotic melanomas that have some visible pigment under dermoscopy are referred to as hypomelanotic melanomas.

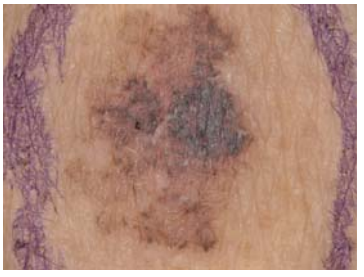


▲ **Figure 8f.19a** Clinical image of a 5 mm pink symmetric papule with slight scale.

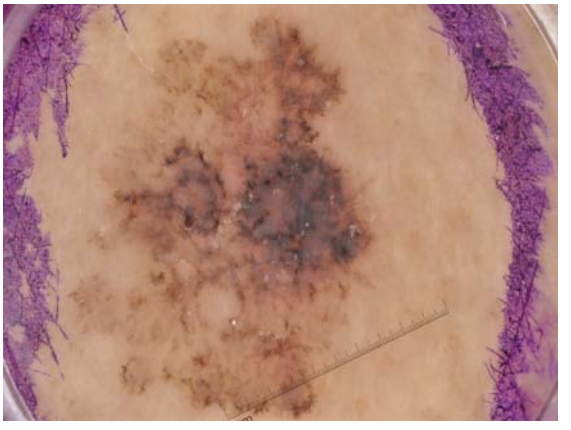
◀ **Figure 8f.19b** Nonpolarized dermoscopy reveals a few serpentine vessels.



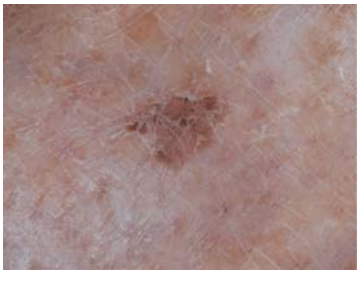
◀ **Figure 8f.19c** Polarized dermoscopy reveals shiny white areas, which are called crystalline structures. The crystalline structures are only visible with polarized light dermoscopy and they are highlighted by the arrows in the image provided.



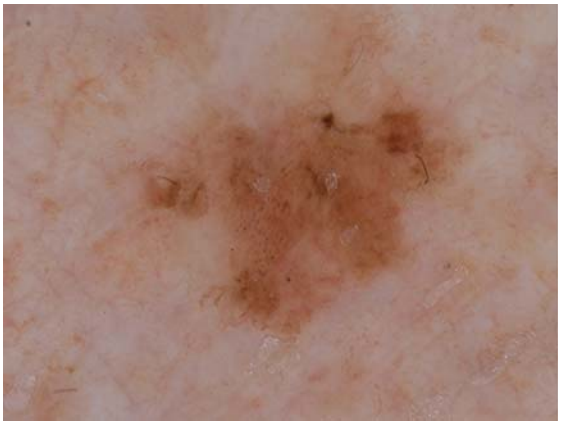
▲ **Figure 8f.20a** Clinical image of an irregularly pigmented lesion that has clinical characteristics of melanoma.



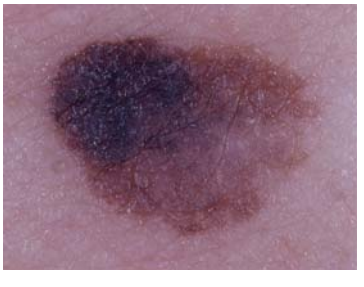
◀ **Figure 8f.20b** Dermoscopy reveals streak-like areas, blue-white veil, shallow ulceration, and spoke-wheel-like structures. Spoke-wheel-like structures are 100% specific for the diagnosis of BCC. The streak like structures in this lesion are not streaks as seen in melanocytic lesions but instead represent leaf like structures. This lesion is a BCC. *Abbreviation*: BCC, basal cell carcinoma.



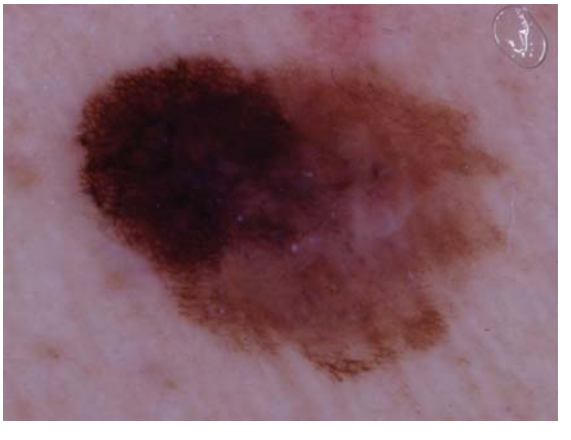
▲ **Figure 8f.21a** Clinical image of pigmented Bowen's disease. The lesion is slightly scaly.



◀ **Figure 8f.21b** Dermoscopy shows areas with structureless brown pigment. In addition, one focal area at the periphery reveals multiple brown dots aligned linearly, which is a specific feature present in some cases of pigmented Bowen's disease lesions. However, since structureless brown color and peripheral dots can also be seen in melanoma, it is easy to see how these lesions could be diagnosed clinically as melanoma.

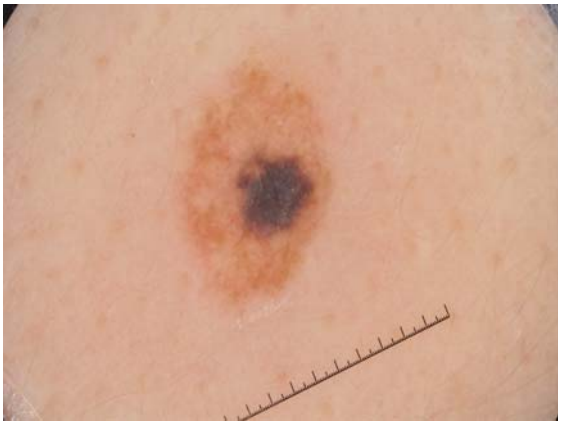


▲ **Figure 8f.22a** Clinical image of a Clark nevus.



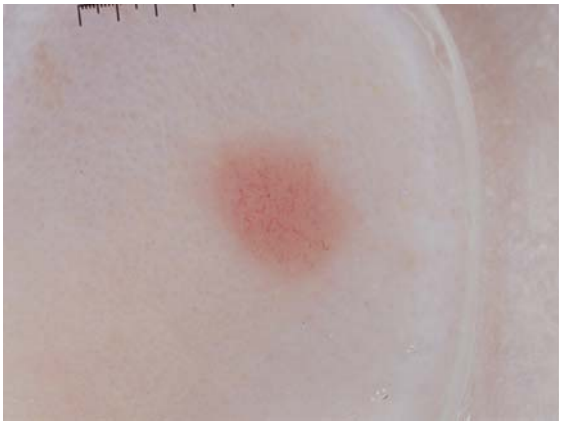
◀ **Figure 8f.22b** Dermoscopy reveals a melanocytic neoplasm with atypical network, blotch, and a blue-white veil. This lesion looks like a melanoma but after excision and through step sectioning this lesion was confirmed to be a moderately atypical Clark nevus.

▲ **Figure 8f.23a** Clinical image of a combined nevus.



◀ **Figure 8f.23b** Combined nevi usually consist of a Clark nevus together with a blue nevus. The blue nevus component usually appears as a blotch with a blue-white veil as can be seen in this image. It is easy to see how these lesions can be confused for melanoma.

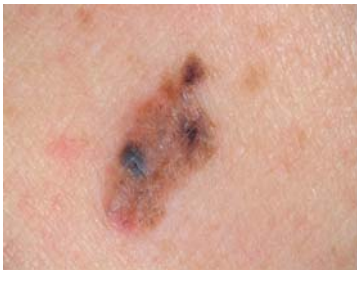
▲ **Figure 8f.24a** Pink papule on the nose of a 3-year-old girl.



◀ **Figure 8f.24b** Dermoscopy reveals a polymorphous vascular pattern. This pattern can also be seen in melanoma. This lesion was a Spitz nevus.

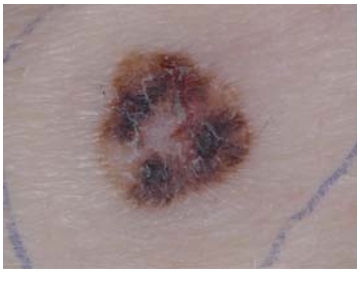
▲ **Figure 8f.25a** Darkly pigmented lesion on the arm of a 2-year-old girl.

◀ **Figure 8f.25b** Dermoscopy reveals streaks and crystalline structures, which are structures that are commonly seen in both Spitz nevi and melanoma. This lesion was a Spitz/Reeds nevus. The presence of crystalline structures indicates that the image was captured with a polarized dermoscope because this structure is visible only with polarized light.

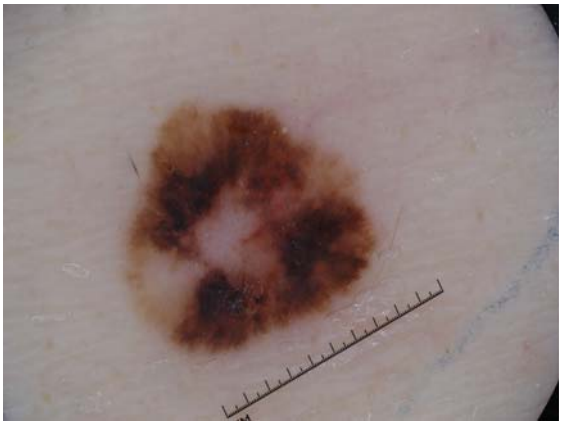


▲ **Figure 8f.26a** Clinical image of a small congenital nevus.

◀ **Figure 8f.26b** Dermoscopy reveals an asymmetric multicomponent pattern. This lesion clearly looks clinically like a melanoma; however, after excisional biopsy and thorough step sectioning the diagnosis rendered was a congenital melanocytic nevus without atypia.

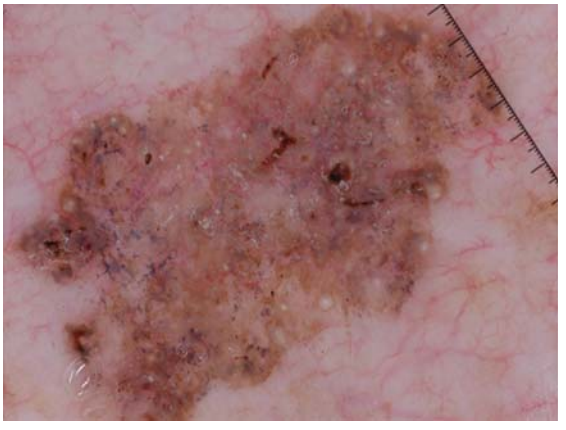


▲ **Figure 8f.27a** Clinical image of an irregularly pigmented lesion on the thigh.



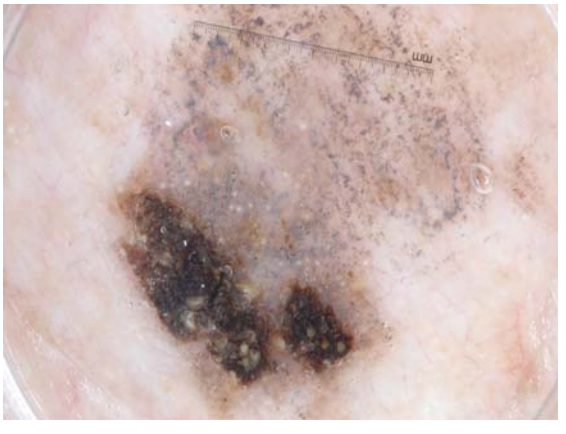
◀ **Figure 8f.27b** Dermoscopy reveals a lesion with multiple colors and streak-like structures at the periphery. This lesion was biopsied and after thorough step sectioning confirmed to be a seborrheic keratosis.

▲ **Figure 8f.28a** Clinical image of an irritated seborrheic keratosis.



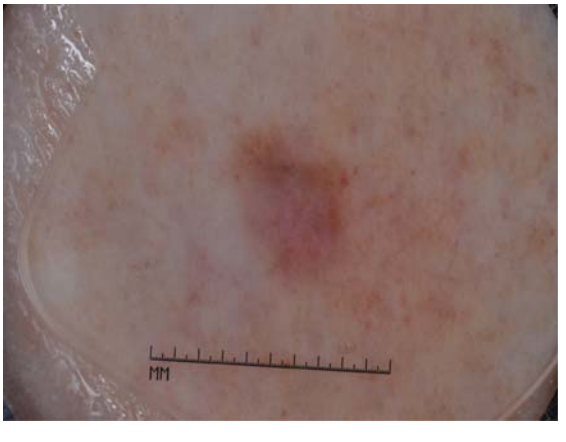
◀ **Figure 8f.28b** Dermoscopy reveals pigment and regression structures consisting of peppering. Although the lesion also has milia-like cysts and comedo-like opening, it is easy to see why melanoma is in the differential diagnosis. Biopsy of this lesion confirmed this to be an irritated seborrheic keratosis.

▲ **Figure 8f.29a** This lesion has the clinical appearance of a melanoma.



◀ **Figure 8f.29b** Dermoscopy reveals that over 50% of the lesion has regression structures consisting of peppering. The presence of extensive regression structures raises the concern for melanoma. Histopathology of this lesion revealed a lichen planus-like keratosis.

▲ **Figure 8f.30a** Clinical image of a firm papule on the leg.



◀ **Figure 8f.30b** Dermoscopy reveals a milky red area and tan pigment. This pattern can be seen in melanoma and in dermatofibroma. This lesion was biopsied and the histopathology confirmed this lesion to be a dermatofibroma.

REFERENCES

Argenziano, G., Rossiello, L., Scalvenzi, M., et al., 2003, Melanoma simulating seborrheic keratosis: a major dermoscopy pitfall. *Arch Dermatol*, 139, 389–91.

Argenziano, G., Zalaudek, I., Ferrara, G., et al., 2007, Dermoscopy features of melanoma incognito: indications for biopsy. *J Am Acad Dermatol*, 56, 508–13.

Marghoob, A.A., Changchien, L., DeFazio, J., et al., 2009, The most common challenges in melanoma diagnosis and how to avoid them. *Australas J Dermatol*, 50, 1–13; quiz 14–5.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Puig-Butille, S., Argenziano, G., Zalaudek, I., et al., 2007, Melanomas that failed dermoscopic detection: a combined clinicodermoscopic approach for not missing melanoma. *Dermatol Surg*, 33, 1262–73.

8g Desmoplastic melanoma and metastatic melanoma

Steven Q. Wang, Natalia Jaimes-López, and Ashfaq A. Marghoob

Desmoplastic melanoma (DM) is a rare variant of melanoma characterized by the association of invasive spindle-shaped melanoma cells within a prominent fibrotic stroma. It comprises less than 4% of all melanomas and has an overall incidence rate of 2.0 per million, with 69% of the cases presenting in patients older than 60 years, with a peak at 80 years of age (Conley et al., 1971; Busam, 2005; Quinn et al.,1998; Feng et al., 2011).

DM represents an important diagnostic pitfall for clinicians and pathologists because these tumors can mimic fibrotic lesions, such as scars and dermatofibromas; benign lesions, such as congenital nevi and epidermal inclusion cysts; and malignant tumors, such as basal cell carcinoma and lentigo maligna (LM)(Wharton et al., 1999). This may explain why the initial clinical suspicion for melanoma is often low and diagnosis is often delayed (Wharton et al., 1999; Smithers et al., 1990).

Clinically, DM tends to develop on chronically sun-exposed skin of the head and neck in white males (Feng et al., 2011; Wharton et al., 1999; Chen et al., 2008); however, it can also be found on the extremities, trunk, and mucosae (Feng et al., 2011; Kilpatrick et al., 1996). DM has been reported to present as a slow-growing, firm, amelanotic or hypomelanotic papule, nodule or plaque (Wharton et al., 1999), which may develop de novo or in association with a LM (Busam, 2011).

Although the average Breslow thickness, at the time of initial diagnosis, of these tumors is relatively deep and the local recurrence rate is high; the incidence of nodal metastasis is lower than for other forms of cutaneous melanoma of comparable Breslow thickness. Systemic metastases are uncommon but if they do occur they preferentially metastasize to the lungs (Lens et al., 2005). Overall, the 5-year survival rate has been reported to be of 91% if it is localized to the skin, 76% if regional nodes are involved and 42% if it has metastasized to distant sites (Feng et al., 2011). However, the survival rate is greatly influenced by the histologic type of DM; those lesions that are purely desmoplastic (>90% desmoplasia in the invasive component) have a much better survival rate than those that are mixed (<90% desmoplasia in the invasive component).

Dermoscopic features of DM have only been described in a few cases (Debarbieux et al., 2008). Reasons for a dearth of information regarding the clinical and dermoscopic morphology of DM includes the uncommon occurrence of this melanoma variant, the nonspecific clinical presentation and the broad clinical differential diagnoses, which often includes benign entities. As a consequence, many clinicians do not capture clinical or dermoscopic images of lesions that prove to be DM on histopathology.

Dermoscopic features that have been described and seen in DM include (Figs. 8g.1–8g.7).

1. Regression structures, including white scar-like areas and peppering (Debarbieux et al., 2008). The white scar-like area can be found in conjunction with peripheral network, resembling that of dermatofibroma. With polarized light dermoscopy the scar-like area will reveal crystalline structures.
2. Vascular structures, including serpentine vessels and/or milky red areas (Debarbieux et al., 2008). In addition, cork-screw vessels and prominent dotted vessels may also be observed.
3. DM presenting in association with a LM will manifest features commonly seen in LM together with focal firm areas manifesting scar-like areas, crystalline structures, blue-white veil, and/or irregular vessels (Debarbieux et al., 2008).

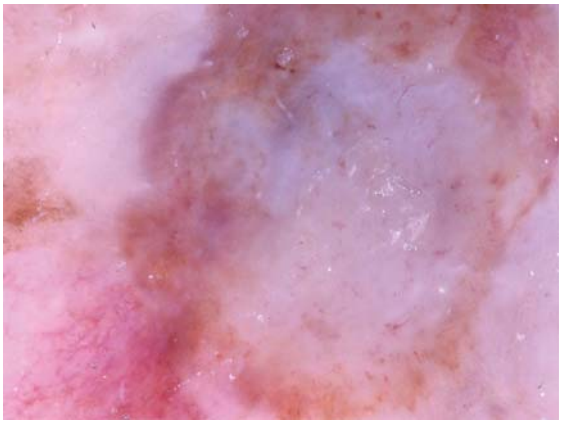
Overall, the clinical and dermoscopic clues for DM are few. As a result, a high index of suspicion is needed to diagnose DM, and the differential diagnosis of DM should be entertained when encountering any of the following clinical scenarios:

1. Amelanotic or hypomelanotic new or changing firm lesion on sun-damaged skin.
2. Lesion with a scar-like appearance that is indurated or firm on palpation, without a history of trauma or prior surgery at the site.
3. Lesion that reveals peppering and/or atypical vascular structures, and is firm on palpation.
4. Suspected LM that has a focal firm area on palpation.
5. Lack of clinical and dermoscopic correlation.
6. Lesion manifesting any of the dermoscopic features mentioned above.

METASTATIC MELANOMA

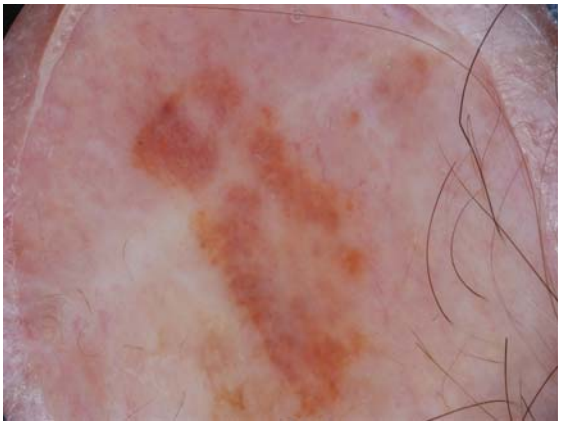
According to the American Joint Committee on Cancer (AJCC) melanoma staging, metastases from melanoma can be categorized into regional and distant metastases. Regional metastatic melanoma comprises nodal and intralymphatic metastases (i.e., satellites and intransit metastases) and these patients are categorized as having stage III disease (Balch et al., 2009). On the other hand, patients with distant metastatic disease are categorized as having stage IV disease and carrying with it a worse prognosis as compared with stage III disease (Balch et al., 2009).

▲ **Figure 8g.1a** Clinical image of an amelanotic firm scar-like area on the chest of an 85-year-old man. The patient was not aware of any trauma to account for this lesion.

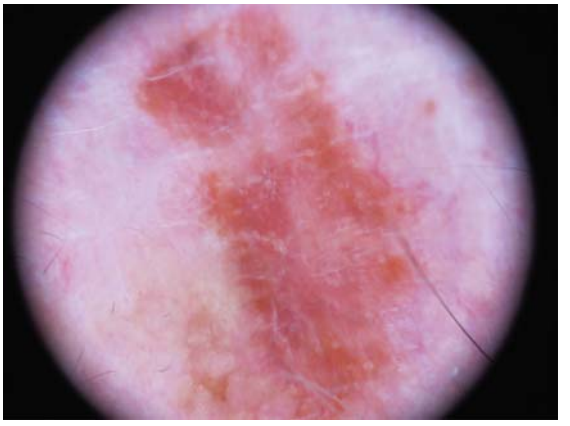


◀ **Figure 8g.1b** Dermoscopy reveals tan pigment at the periphery with a central scar-like area. This particular pattern can be seen in dermatofibroma; however, the distribution of pigment, size of lesion, its location and the atypical vessels seen within the scar-like area are highly unusual for DF. Near the center of the scar-like area is a cork-screw vessel; there are also numerous hairpin and serpentine vessels. This lesion was excised and was a 5.6 mm desmoplastic melanoma.

▲ **Figure 8g.2a** Clinical image of a firm tan plaque on the forehead.

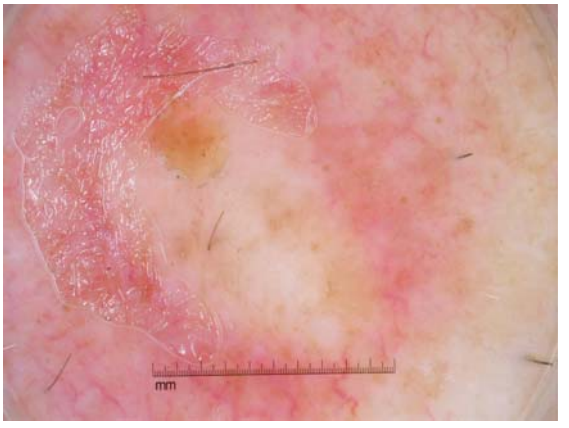


◀ **Figure 8g.2b** Nonpolarized dermoscopy reveals nondescript tan color and areas with a pink hue.



◀ **Figure 8g.2c** Polarized dermoscopy reveals numerous crystalline structures. Biopsy of this lesion was consistent with desmoplastic melanoma.

▲ **Figure 8g.3a** Clinical image of a firm cystic nodule. The serous crust is the site of a biopsy.



◀ **Figure 8g.3b** Dermoscopy reveals a scar-like area with a few dotted vessels. Cysts may display arborizing vessels (Fig. 8g.4) coursing over their surface but they will never have dotted vessels on their surface. Thus, the presence of a cystic nodule with dotted vessels is highly unusual. The biopsy of this lesion was consistent with desmoplastic melanoma.

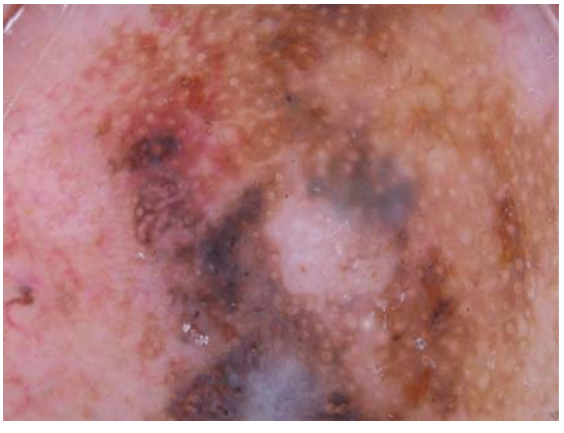
▲ **Figure 8g.4a** Clinical image of a cyst on the back.

◀ **Figure 8g.4b** Dermoscopy of this cyst reveals a punctum and numerous arborizing vessels coursing over the surface of this cyst. Desmoplastic melanomas with a cystic appearance will not have a punctum and if vessels are seen they will have a different morphology, including dotted, hairpin, cork-screw, and polymorphous.

▲ **Figure 8g.5a** Clinical image of a thick, ulcerated, amelanotic, desmoplastic melanoma on the forehand.

◀ **Figure 8g.5b** Dermoscopy reveals a large ulcer with surrounding polymorphous vessels. This was a desmoplastic melanoma.

▲ **Figure 8g.6a** Clinical image of a LM on the ear. On clinical examination there was a firm area noted on palpation.



◀ **Figure 8g.6b** Dermoscopy reveals classic features of LM (see chapter 8d, "Lentigo maligna melanoma"). The area that is firm on palpation reveals a white scar-like area and another focus of a firm area with a blue-white veil. These areas reveal a polymorphous vascular pattern. This lesion was excised and was a lentigo maligna melanoma with a desmoplastic component.

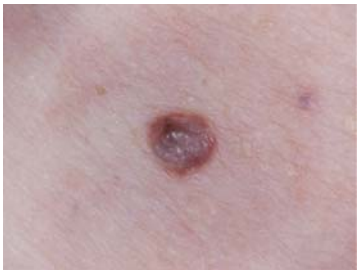
▲ **Figure 8g.7a** Clinical image of a tan patch on the arm of this 80-year-old woman. A focal firm bluish area was noted at the peripheral edge of this tan patch.

◀ **Figure 8g.7b** Nonpolarized dermoscopy reveals a relatively structureless patchy tan area with few brown dots. The focal firm area has a blue-white veil. With polarized dermoscopy (image not shown) this nodule had crystalline structures.

Clinically, cutaneous melanoma metastases, whether regional or distant, have a similar morphology. They can present as pigmented or amelanotic nonspecific papules or nodules without any other clinically distinctive features. Some may not be clinically conspicuous until after found by clinical palpation of the skin. They can present as solitary lesions or as multiple aggregated or disseminated lesions.

Dermoscopy can assist in correctly identifying some of these cutaneous metastatic melanoma foci due to the atypical features and structures visualized, such as irregular vessels, crystalline structures, and irregular pigment distribution (Schulz, 2000; Bono et al., 2004; Minagawa et al., 2009; Assmann et al., 2000).

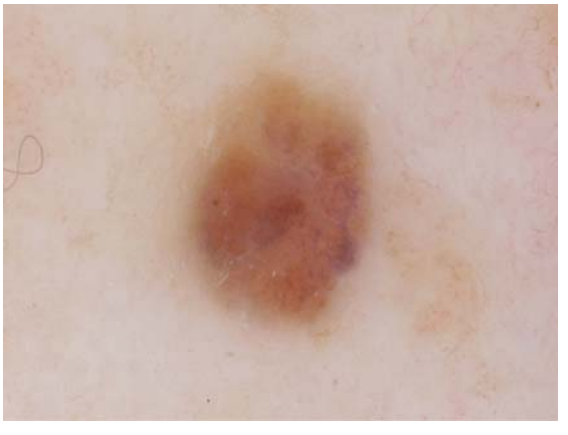
1. Pigmented variants of cutaneous melanoma metastases often present as nonspecific pigmented lesions with brown, reddish-brown, blue, gray-blue, and/or black colors throughout the entire lesion, but the colors tend to be distributed in an asymmetric fashion (Figs. 8g.8–8g.10). There tend to be differing hues of these various colors, including hues of pink within each lesion. These lesions are often classified as melanocytic lesions via the two-step dermoscopy algorithm by default since they lack any defining structures for a melanocytic or for one of the nonmelanocytic lesions. According to the two-step dermoscopy algorithm all featureless lesions need to be evaluated with a rule out diagnosis of melanoma. Since these lesions are raised and palpable the only management option is to biopsy them since monitoring is not advocated for raised lesions.
2. Both pigmented and amelanotic variants of cutaneous melanoma metastases often manifest vascular structures as the only



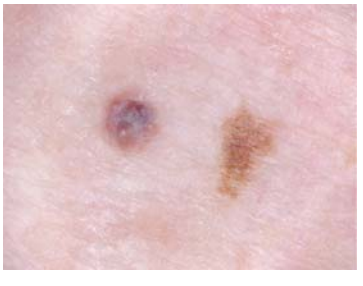
▲ **Figure 8g.8a** Clinical image of a pigmented cutaneous melanoma metastatic focus.

◀ **Figure 8g.8b** Dermoscopy reveals a homogenous reddish-brown homogenous papule with a subtle whitish veil and a few milky red globules.

▲ **Figure 8g.9a** Clinical image of a pigmented cutaneous melanoma metastatic focus.



◀ **Figure 8g.9b** Colors seen with dermoscopy include brown, bluish-gray, and pink. The lesion is relatively structureless except for a few irregular vessels and focal blue white veil.



▲ **Figure 8g.10a** Clinical image of a pigmented cutaneous metastatic focus.

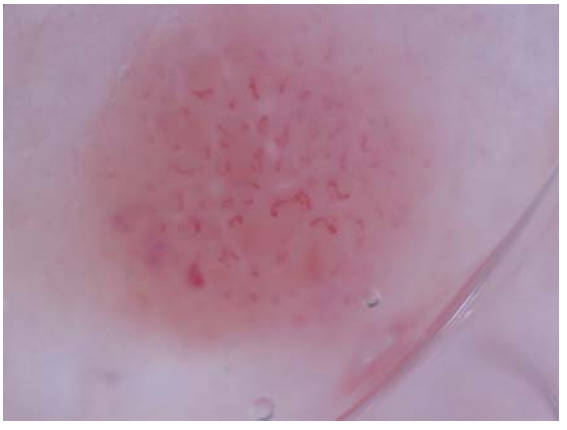
◀ **Figure 8g.10b** Dermoscopy reveals a lesion with different colors, including tan, reddish, and blue-white. The lesion is relatively structureless except for a few vessels.

clue to diagnosis and they can also reveal crystalline structures when viewed with polarized dermoscopy (Figs. 8f.8 and 8f.9 in chapter 8F) (Figs. 8g.11–8g.18).

a. The most frequent vascular morphologies observed under dermoscopy are corkscrew-like or tortuous vessels, glomerular vessels, irregular hairpin vessels, milky red globules, and arborizing vessels that are thick and have few branches compared with those seen in basal cell carcinoma (Figs. 8g.11–8g.18). The presence of crystalline structures in these metastatic foci is quite commonly seen with polarized dermoscopy.

b. Lacunae-like structures, also known as "saccular pattern" (Schulz, 2000; Bono et al., 2004) can also be observed in melanoma metastases. When presenting with this pattern they can mimic angioma-like lesions (see –Figs. 8f.8 and 8f.9 in chapter 8f, "equivocal lesions") (Schulz, 2000). Unlike the typical lacunae seen in angiomas, which are well-defined, homogenous in color, and separated by septae, in melanoma metastases they have a red-to-purple ill-defined appearance and vessels may be seen inside the lacunae-like structures. Vessels within lacunae are never seen in hemangiomas.

▲ **Figure 8g.11a** Clinical image of an amelanotic cutaneous melanoma metastatic focus.

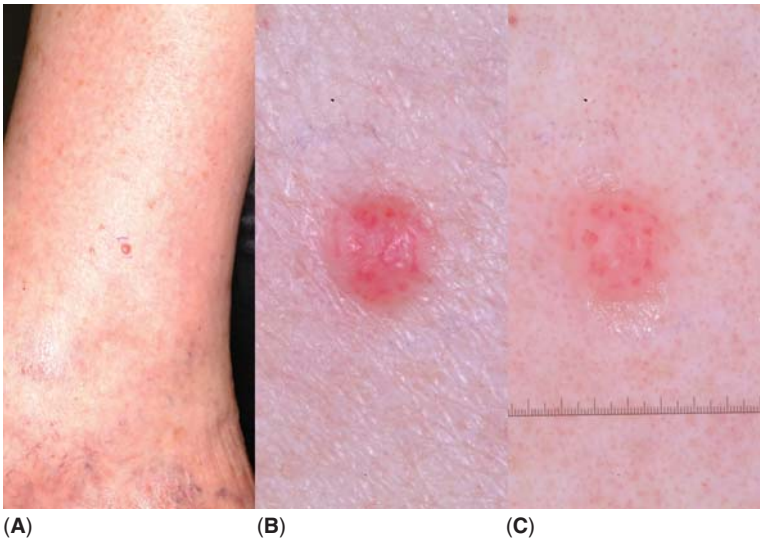


◀ **Figure 8g.11b** Nonpolarized dermoscopy reveals numerous atypical tortuous blood vessels.

◀ **Figure 8g.11c** Polarized dermoscopy of this metastatic focus reveals numerous crystalline structures.

▲ **Figure 8g.12a** Clinical image of a few amelanotic cutaneous melanoma metastatic lesions.

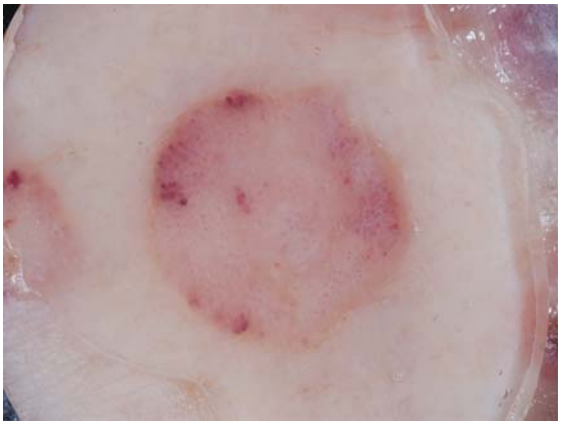
◀ **Figure 8g.12b** Dermoscopy of each papule reveals atypical vessels, many of which are tortuous.



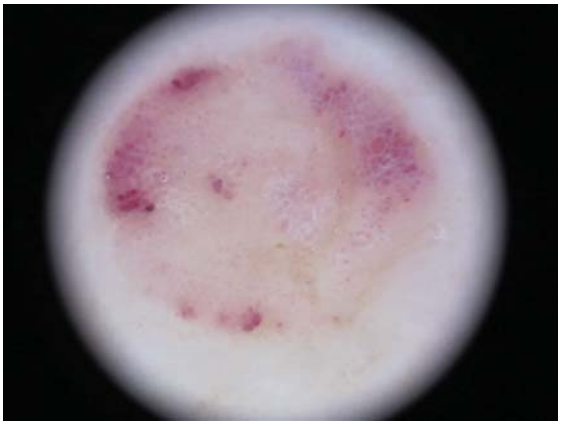
(**A**) (**B**) (**C**)

Figure 8g.13 (A) reveals a few skin colored papules on the ankle of this patient who had a melanoma excised from her sole. (B) is teh clinical close up image of the larger papule. With dermoscopy (C) this amelanotic melanoma metastatic focus reveals tortuous vessels.

▲ **Figure 8g.14a** Clinical image of an amelanotic melanoma metastatic focus.



◀ **Figure 8g.14b** Nonpolarized dermoscopy reveals numerous milky red globules and polymorphous vessels.



◀ **Figure 8g.14c** Polarized dermoscopy reveals the same structures as mentioned in **B** but in addition also reveals crystalline structures.

▲ **Figure 8g.15a** Clinical image of metastatic melanoma.

◀ **Figure 8g.15b** Dermoscopy reveals numerous serpentine vessels.

▲ **Figure 8g.16a** Clinical image of metastatic melanoma.

◀ **Figure 8g.16b** Dermoscopy reveals one thick arborizing vessel and in addition, there is a polymorphous vascular pattern at the periphery.

▲ **Figure 8g.17a** Clinical image of a melanoma metastatic focus.

◀ **Figure 8g.17b** Notice the polymorphous vascular pattern with dermoscopy.

▲ **Figure 8g.18a** Clinical image of a tan papule.

◀ **Figure 8g.18b** Dermoscopy reveals a tan color and a polymorphous vascular pattern. This lesion was a focus of metastatic melanoma.

REFERENCES

Assmann, A., Farthmann, B., Burkhardt, O., et al., 2000, Cerebriform nodular amelanotic metastases of malignant melanoma: a challenge in differential diagnosis of a rare variant. *Br J Dermatol*, 142, 533–6.

Balch, C.M., Gershenwald, J.E., Soong, S.J., et al., 2009, Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*, 27, 6199–206.

Bono, R., Giampetruzzi, A.R., Concolino, F., et al., 2004, Dermoscopic patterns of cutaneous melanoma metastases. *Melanoma Res*, 14, 367–73.

Busam, K.J., 2005, Cutaneous desmoplastic melanoma *Adv Anat Pathol.*, 12, 92–102.

Busam, K.J., 2011, Desmoplastic melanoma. *Clin Lab Med*, 31, 321–30.

Chen, J.Y., Hruby, G., Scolyer, R.A., et al., 2008, Desmoplastic neurotropic melanoma: a clinicopathologic analysis of 128 cases. *Cancer*, 113, 2770–8.

Conley, J., Lattes, R. & Orr, W., 1971, Desmoplastic malignant melanoma (a rare variant of spindle cell melanoma). *Cancer*, 28, 914–36.

Debarbieux, S., Ronger-Salve, S., Dalle, S., Balme, B. & Thomas, L., 2008, Dermoscopy of desmoplastic melanoma: report of six cases. *Br J Dermatol*, 159, 360–3.

Feng, Z., Wu, X., Chen, V., Velie, E. & Zhang, Z., 2011, Incidence and survival of desmoplastic melanoma in the United States, 1992–2007. *J Cutan Pathol*, 38, 616–24.

Kilpatrick, S.E., White, W.L., Browne, J.D., 1996, Desmoplastic malignant melanoma of the oral mucosa. An underrecognized diagnostic pitfall. *Cancer*, 78, 383–9.

Lens, M.B., Newton-Bishop, J.A. & Boon, A.P., 2005, Desmoplastic malignant melanoma: a systematic review. *Br J Dermatol*, 152, 673–8.

Minagawa, A., Koga, H., Sakaizawa, K., Sano, K. & Saida, T., 2009, Dermoscopic and histopathological findings of polymorphous vessels in amelanotic cutaneous metastasis of pigmented cutaneous melanoma. *Br J Dermatol*, 160, 1134–6.

Quinn, M.J., Crotty, K.A., Thompson, J.F., et al., 1998, Desmoplastic and desmoplastic neurotropic melanoma: experience with 280 patients. *Cancer*, 83, 1128–35.

Schulz, H., 2000, Epiluminescence microscopy features of cutaneous malignant melanoma metastases. *Melanoma Res*, 10, 273–80.

Smithers, B.M., McLeod, G.R. & Little, J.H., 1990, Desmoplastic, neural transforming and neurotropic melanoma: a review of 45 cases. *Aust NZ J Surg*, 60, 967–72.

Wharton, J.M., Carlson, J.A. & Mihm, M.C., Jr., 1999, Desmoplastic malignant melanoma: diagnosis of early clinical lesions. *Hum Pathol*, 30, 537–42.

9 Special locations

9a Palms and soles

Josep Malvehy and Susana Puig

Pigmented lesions located on the palms and soles often display a parallel-pigment pattern when viewed with dermoscopy. This is due to the unique anatomy of volar skin and it is this anatomy that is responsible for our dermatoglyphics or fingerprints (Saida et al., 2002; Saida et al., 2004; Saida & Koga, 2007). In this chapter we provide a review of the dermoscopy criteria of melanocytic lesions and subcorneal hemorrhage on volar skin (palms/soles).

ANATOMY OF THE SKIN OF PALMS AND SOLES AND DERMOSCOPIC CORRELATION

The unique anatomy of volar skin is responsible for why the pigment in melanocytic lesions is arranged in parallel lines (Fig. 9a.1) (Saida et al., 2002; Saida et al., 2004; Saida & Koga, 2007). To better understand the dermoscopic structures visualized on volar skin requires an understanding of the histologic anatomy of volar skin that accounts for these observations:

1. A thick stratum corneum helps explain why melanin pigment located in the upper dermis appears bluish in color under dermoscopy (Fig. 9a.2). This is due to the physics of light; an effect known as the Tyndall effect. This accounts for why most compound nevi appear brown in color on nonvolar skin, while they often exhibit a bluish color on the palms and soles (Fig. 9a.2).
2. Furrows (sulcus superficialis) and ridges (crista superficialis) are created by the rete ridges known as the crista limitans and the crista intermedia (Fig. 9a.1). The crista limitans is associated with the furrow and the crista intermedia is associated with the ridge. The eccrine duct passes through the center of the crista intermedia rete ridge and opens on the surface of the ridge. For reasons that have not yet been fully elucidated, nevi tend to be localized to the rete ridges of the crista limitans or preferentially transfer their pigment to keratinocytes associated with the furrow (Fig. 9a.3). In contrast, melanoma cells tend to cluster around the rete ridges of the crista intermedia (Fig. 9a.4). It is this preferential localization of benign and malignant melanocytes or pigment that is responsible for the parallel-pigment pattern commonly seen in volar skin lesions. At times it may be difficult to differentiate the furrows from the ridges. Clues to help differentiate ridges from furrows include the observations that ridges are wider than the furrows and that the eccrine ducts open on the surface of the ridge. However, sometimes even this knowledge is insufficient at helping discriminate between the ridges and the furrows. One technique that can help facilitate the identification of the furrows and ridges is the ink test; the details of which are described in Figure 9a.5.

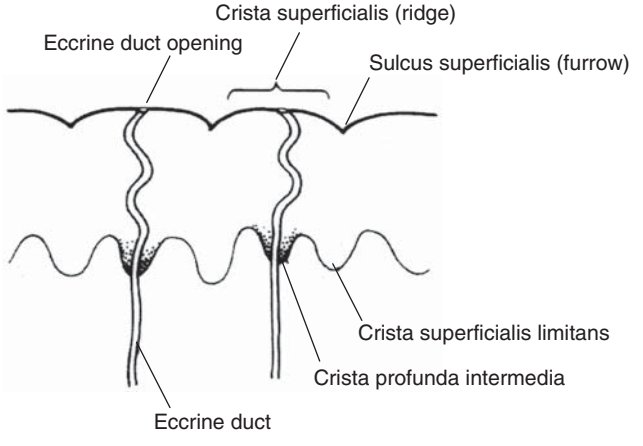
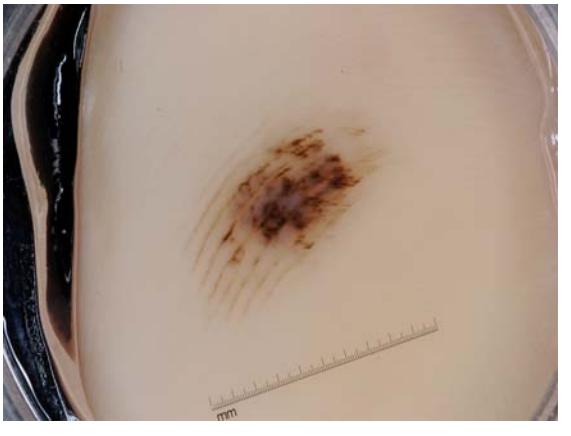


Figure 9a.1 Schematic diagram of the anatomy of volar skin.

▲ **Figure 9a.2a** Clinical image.



◀ **Figure 9a.2b** Dermoscopy reveals a predominant parallel-furrow pattern. The center of this compound nevus has a bluish hue. This blue hue is due to the Tyndall effect.

3. The characteristic eccrine gland with its ductal openings, which are located in the center of the ridge, can be seen easily with dermoscopy. These eccrine openings appear as regularly spaced small white dots on the ridges.
4. Absence of follicular openings.
5. The demarcation line delineating glabrous (non–hair bearing) from nonglabrous (hair bearing) skin is named "Wallace line" after H. J. Wallace from *St. Thomas Hospital* in *London.* Lesions located below the Wallace line (i.e., palms and soles) will show the criteria of acral volar skin, such as the parallel pattern (Fig. 9a.6). Lesions located above the Wallace line will show dermoscopy criteria of nonglabrous skin, such as the reticular pattern. Melanocytic lesions located at the junction of Wallace line often appear atypical since they will manifest a multicomponent pattern with dermoscopic features of both glabrous and nonglabrous skin (Fig. 9a.7).

DERMOSCOPY OF MELANOCYTIC TUMORS ON PALMS AND SOLES

On the palms and soles, pigmented lesions may pose a diagnostic challenge. It has been suggested by some that melanocytic lesions on palms and soles should be excised because they have an increased risk for being melanoma. However, evidence-based medicine does not support this view, and thus benign melanocytic tumors (i.e., nevi) on volar skin do not need to be considered differently in terms of risk to melanoma then nevi on any other anatomical site. The quintessential dermoscopic feature of benign melanocytic tumors on volar skin is that the pigment in nevi is predominantly localized to the furrows (Fig. 9a.8). In contrast, in melanoma the pigment is predominantly localized on the ridges (Fig. 9a.4) or is present diffusely across both ridges and furrows (i.e., without preferential localization to the crista intermedia or limitans) resulting in homogenous pigmented areas that encompass both ridges and furrows (Fig. 9a.9).

BENIGN DERMOSCOPY PATTERNS ON PALMS AND SOLES

The classic dermoscopic patterns (Fig. 9a.10) associated with nevi include the *parallel-furrow pattern (palms and soles), lattice-like pattern (palms and soles), and fine fibrillar or filamentous pattern on the sole (N.B. a fibrillar pattern on the palms should always raise suspicion for melanoma)* (Saida et al., 2002; Saida et al., 2004; Saida & Koga, 2007; Saida et al., 2011b; Saida et al., 2011a). *Other benign patterns include the globular pattern, homogenous pattern, and reticular pattern.* Small benign pigmented melanocytic lesions can exhibit a combination of globules and lines in the *globule-streak pattern.* Finally, benign nevi traversing Wallace line need to be evaluated differently. The portion of the lesion that is above the Wallace line needs to be evaluated by criteria defined for nonglabrous skin, such as network, streaks, and globules. The portion of the lesion situated below Wallace line needs to be evaluated via criteria defined for volar skin as described in this chapter and chapter 8b, "Acrolentiginous melanoma" (Figs. 9a.6 and 9a.7).

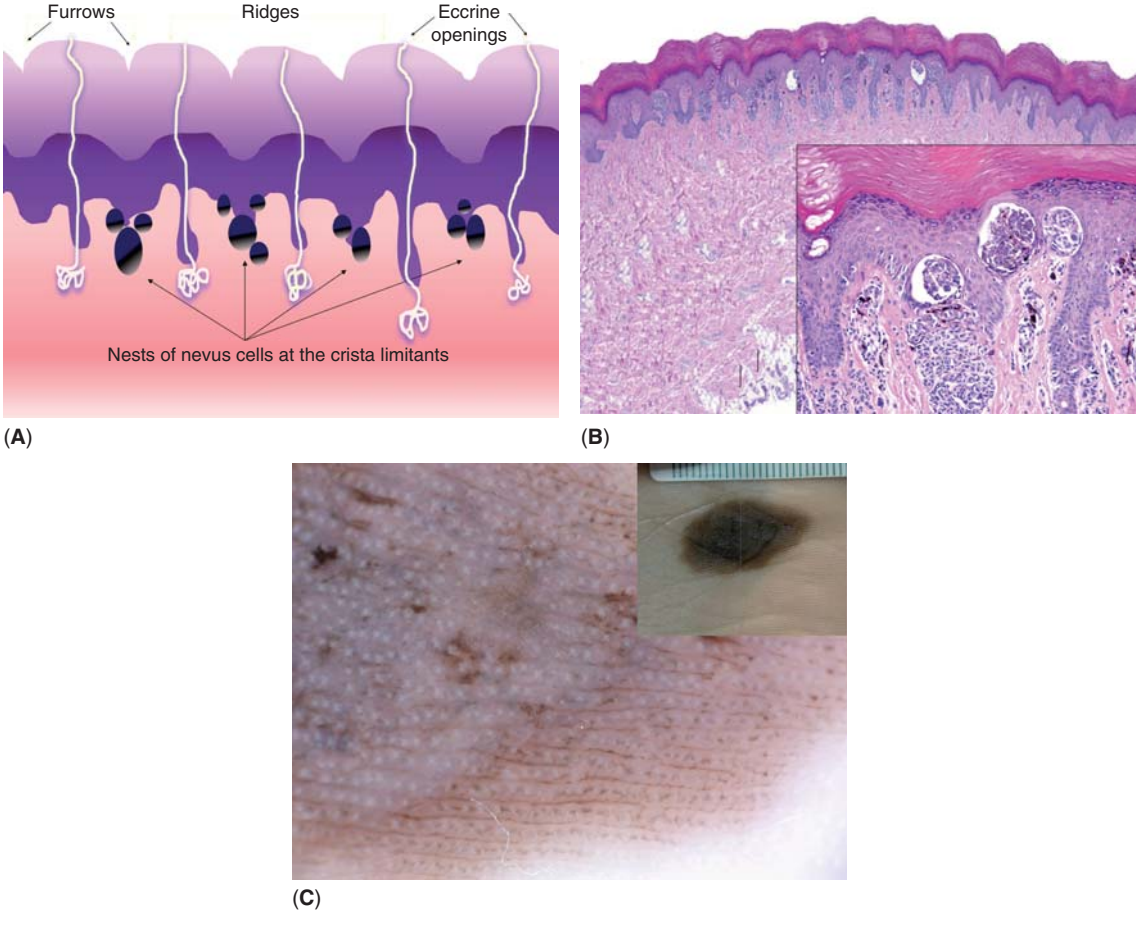


Figure 9a.3 (**A**) Schematic depiction of a melanocytic nevus on volar skin. The nevus cells tend to localize around the crista limitans, which corresponds to the furrows. (**B**) Histopathologic correlation of the parallel-furrow pattern in a congenital nevus with nests of melanocytic cells located predominantly along the dermoepidermal junction near to the crista limitans (furrows). (**C**) Dermoscopy of a congenital nevus reveals a typical parallel-furrow at the periphery. White dots aligned on the ridge correspond to the openings of the eccrine ducts.

The Classic Benign Patterns

Parallel-furrow pattern (Figs. 9a.8 and 9a.11) consists of linear pigmentation that is predominantly localized to the furrows. Histology of this pattern reveals melanocytes that are preferentially located around the crista limitans with melanin columns arranged vertically in the epidermis and stratum corneum (Fig. 9a.3). There are four parallel-furrow pattern subtypes (Fig. 9a.12), which consist of the single line variant, the double line variant, the single dotted line variant, and the double dotted line variant (Figs. 9a.13–9a.16). These patterns are common on the palms and on the skin of the sole between the arch of the foot and the weightbearing parts of the foot.

The lattice-like pattern is similar to the parallel-furrow pattern with the addition of parallel-pigment bands that cross over the ridges from one furrow to the next like the rungs of a ladder. This pattern can be seen on the palms and is the most common pattern on the arch area of the sole (Figs. 9a.17 and 9a.18) (Altamura et al., 2006; Malvehy & Puig-Butille, 2004; Miyazaki et al., 2005; Saida et al., 2004).

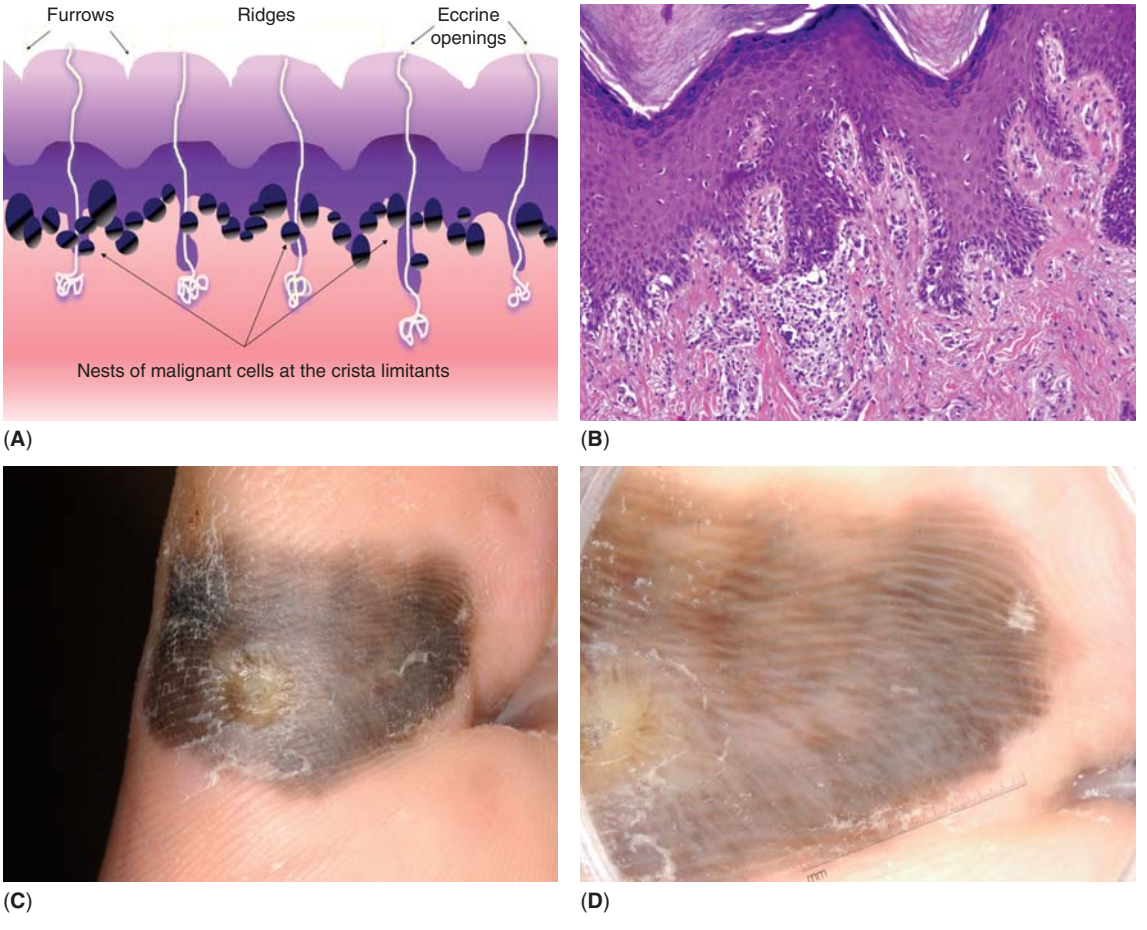
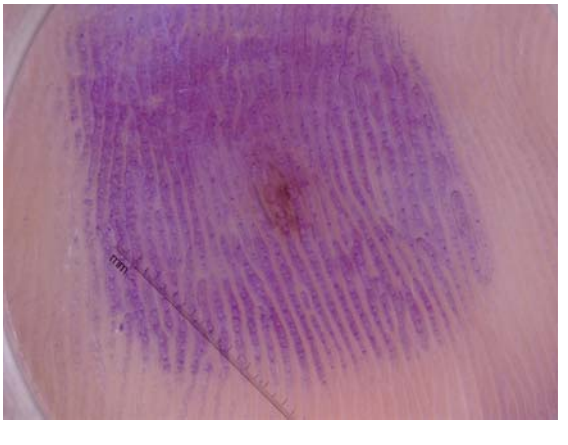


Figure 9a.4 (**A**) Schematic depiction of an acrolentiginous melanoma on volar skin. The melanoma cells tend to localize around the crista intermedia but can also be found along the crista limitans. When the pigment is predominantly located around the crista intermedia the pattern manifest in dermoscopy is a parallel-ridge pattern. (**B**) Histopathologic correlation of an ALM with invasion of the ridges. (**C**) Clinical image of an ALM. (**D**) Dermoscopic view of an ALM revealing a parallel-ridge pattern. *Abbreviation*: ALM, acrolentiginous melanoma.

▲ **Figure 9a.5a** The ink test to help find the ridges and furrows: use a felt tip marker and paint the skin and then wipe off the excess ink with an alcohol swab.



◀ **Figure 9a.5b** The ink will help outline and highlight the ridges and eccrine duct openings making it easy to conclude whether the lesion's pigment is located on the ridges or in the furrows when viewed with dermoscopy.

▲ **Figure 9a.6a** Benign compound nevus on the lateral area of the foot.

◀ **Figure 9a.6b** Dermoscopic examination shows a transition pattern with parallel-furrow pattern (volar skin) and globules (*center*) with remnants of pigment network in nonvolar skin (*left side of lesion*).

▲ **Figure 9a.7a** This nevus is located on the toe and it is traversing Wallace line. The Wallace line separates the volar skin from the nonglabrous skin of the hands and feet.

◀ **Figure 9a.7b** Dermoscopy of this nevus reveals two distinct patterns. The portion on volar skin reveals a parallel pattern and the portion on the nonglabrous skin reveals a network pattern.

▲ **Figure 9a.8a** Clinical image of a nevus on the sole.

◀ **Figure 9a.8b** Dermoscopy reveals a parallel-furrow pattern. Notice that the nonpigmented ridges are wider than the pigmented furrows. Also notice that the white dots, corresponding to eccrine duct openings, are visible on the ridge.

▲ **Figure 9a.9a** Melanoma located on the ball of the foot.

◀ **Figure 9a.9b** Dermoscopy shows diffuse pigmentation involving both the furrows and ridges.

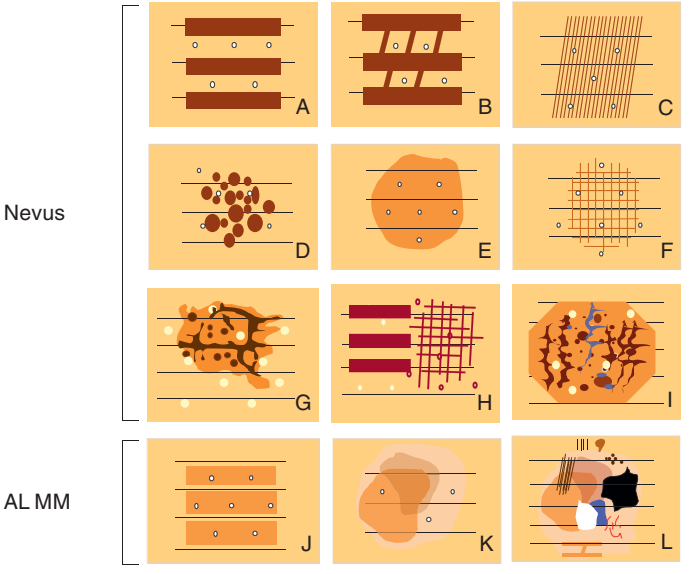


Figure 9a.10 Schematic representation of the major patterns encountered in melanocytic lesions on volar skin. The classic benign patterns are (**A**) parallel-furrow pattern with parallel black lines, which represent the furrows of the volar skin markings and small white dots corresponding to the eccrine duct openings. (**B**) Lattice pattern with pigmentation following the furrows plus linear bands of pigment crossing from one furrow to the next similar to rungs of a ladder. (**C**) Fibrillar pattern with parallel fine streaks crossing the dermoglyphics in a tangential direction. Other benign patterns include (**D**) globular pattern in which the globules are not associated with a parallel pattern. (**E**) Homogenous diffuse pigment pattern with light brown homogenous pigmentation with an amorphous appearance. (**F**) Reticular pattern with well-defined pigment network that is not associated with the skin markings. The nontypical benign patterns (**G** and **I**) do not conform to a classic benign nor to a classic malignant pattern. (**G**) Is a nevus with globules and serration. The schematic shown in panel (**H**) is called the "transition pattern" since this pattern is frequently seen in nevi that cross over Wallace line. In such cases the nonglabrous skin will reveal structures, such as network and the portion of the lesion on volar skin will reveal a parallel pattern. The malignant patterns are (**J**) parallel-ridge pattern with more prominent pigment on the ridges then on the furrows, (**K**) homogenous diffuse irregular-pigmented pattern (usually >7 mm to 1 cm in diameter) with pigmented blotches of various shades of brown (as well as other colors, such as bluish and pink colors) observed throughout the entire lesion or in focal areas of a lesion, and (**L**) the multicomponent pattern, which often reveals an abrupt edge, diffuse pigmentation, peripheral irregular globules and dots, multiple colors, atypical streaks in combination with localized areas exhibiting benign patterns (fibrillar, parallel-furrow, or lattice-like).

Figure 9a.11 Stereotypical parallel-furrow pattern in a compound nevus.

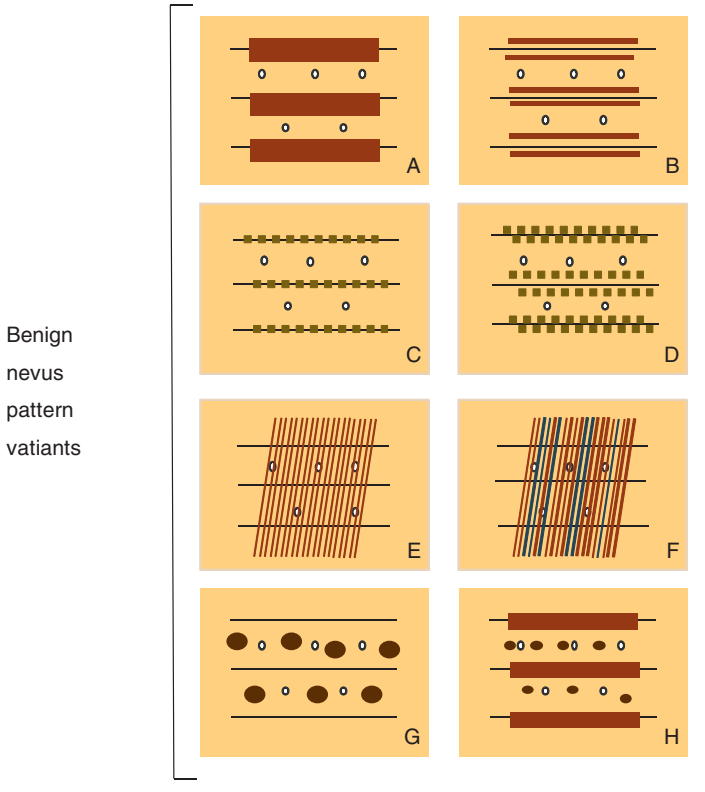


Figure 9a.12 Subtypes of benign patterns seen on volar skin. (**A**) Classic parallel-furrow pattern, (**B**) double-line-furrow pattern, (**C**) single-dotted-line parallel-furrow pattern, (**D**) double-dotted-line parallel-furrow pattern, (**E**) fine typical fibrillar pattern on sole is a benign pattern, (**F**) atypical fibrillar pattern on sole is considered suspect (N.B.: both typical and atypical fibrillar patterns on the palms should be considered suspicious), (**G**) crista dotted pattern is commonly seen in congenital nevi, and (**F**) parallel-furrow pattern together with dots/globules on the ridges is known as the "peas in a pod" pattern. This pattern is commonly seen in congenital nevi.

Figure 9a.13 Parallel-furrow pattern with linear pigmentation within the furrow. Diagnosis: melanocytic nevus.

The fibrillar pattern consists of dense fibrillar pigmentation composed of multiple thin parallel lines that cross both the furrows and ridges. The lines have a transverse orientation in relation to the furrows and ridges. This pattern results from the effects of intermittent/constant horizontal pressure being applied to the stratum corneum. This horizontal pressure results in the stratum corneum growing in a slanted direction (in the direction of the lateral pressure), thereby also causing the melanin columns in the stratum corneum to be slanted and giving a fibrillar appearance. This pattern

▲ **Figure 9a.14a** Clinical image of a benign acral nevus, with a double parallel-line-furrow pattern.

◀ **Figure 9a.14b** Dermoscopic image.

Figure 9a.15 Parallel-furrow pattern, single-dotted-line variant, with dotted pigmentation within the furrow. Diagnosis: melanocytic nevus.

Figure 9a.16 Parallel-furrow pattern, double-dotted variant with dotted pigmentation along both sides of the furrow in a parallel fashion. Diagnosis: melanocytic nevus.

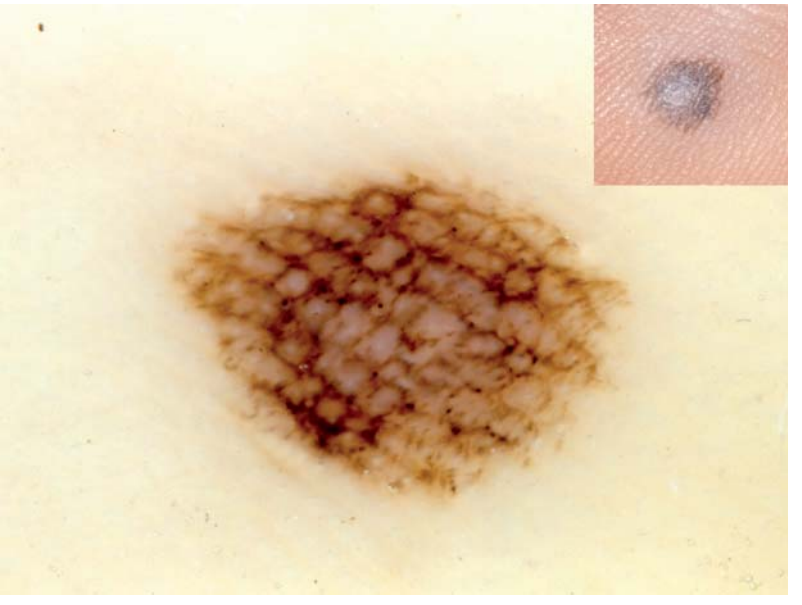


Figure 9a.17 Classic lattice pattern in this benign acral nevus.

▲ **Figure 9a.18a** Classic lattice pattern.

◀ **Figure 9a.18b** Notice the eccrine duct openings on the surface of the ridges.

is commonly seen on the weightbearing parts of the sole. The benign fibrillar pattern on the sole presents as a fine brown fibrillar pattern (typical fibrillar pattern) in which the lines show little variation in thickness and color (Figs. 9a.19–9a.21). There is a malignant variant of the fibrillar pattern (atypical fibrillar pattern) in which the lines present with varying thicknesses and colors (Fig. 9a.22) (Altamura et al., 2006; Bowling, 2007; Malvehy & Puig-Butille, 2004; Maumi et al., 2009; Miyazaki et al., 2005; Palleschi & Torchia, 2007; Palleschi et al., 2006). These atypical lines tend to be thicker and grayer in color as compared with their benign counterpart. Given the mechanism behind the creation of the fibrillar pattern it should be intuitively obvious as to why this pattern is not seen on the palms. In fact, any fibrillar pattern on the palms should be viewed with suspicion (Fig. 9a.23).

Other Benign Patterns

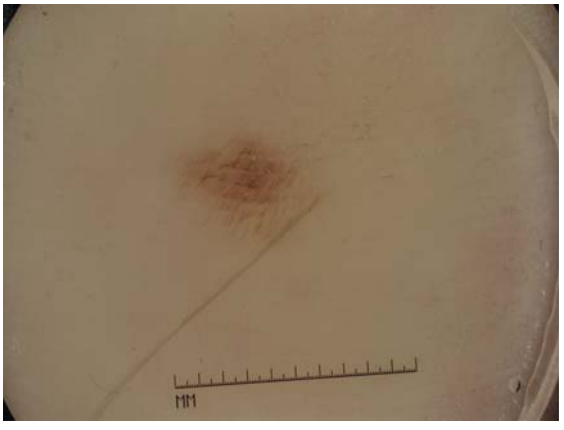
The reticular pattern can be seen on the arch of the foot. Although nevi on the arch of the foot usually have a lattice-like pattern, some can have a reticular pattern (Fig. 9a.24) (Malvehy & Puig-Butille, 2004; Miyazaki et al., 2005).

The globular pattern, corresponding to nests of nevomelanocytes, which can be small or large, can be seen on the palms and soles. Most of these lesions are presumed to be congenital nevi (Fig. 9a.25).

The homogenous pattern (Fig. 9a.26) consists of a uniformly tan-to-brown area that involves both furrows and ridges and is devoid

Figure 9a.19 Fibrillar pattern in a benign melanocytic nevus on the sole. This lesions is located in the area of high friction pressure on the sole.

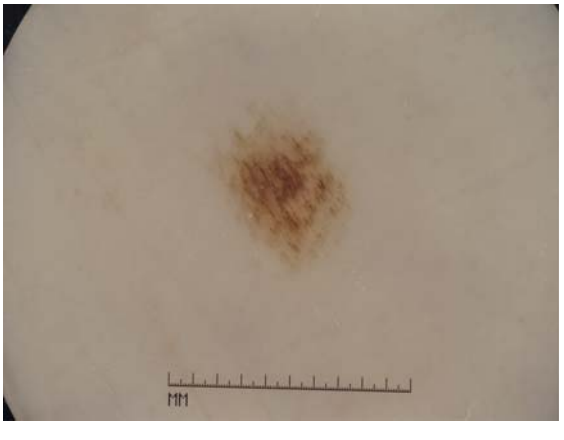
▲ **Figure 9a.20a** Clinical image.



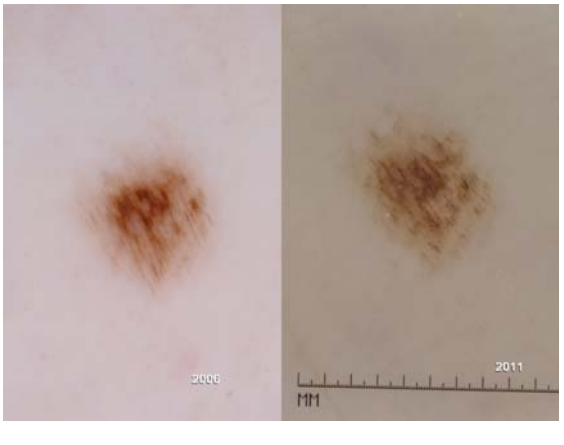
◀ **Figure 9a.20b** Dermoscopic image. Typical fine fibrillar pattern on the weight bearing area of the sole.

Figure 9a.21 Fibrillar pattern with numerous thin lines crossing the furrow in a slanted direction. Diagnosis: melanocytic nevus.

▲ **Figure 9a.22a** Clinical image of a lesion with an atypical fibrillar pattern.



◀ **Figure 9a.22b** Dermoscopic image of a lesion with an atypical fibrillar pattern.



◀ **Figure 9a.22c** This lesion was biopsied due to the atypical fibrillar pattern and because it had changed on digital monitoring. The pathology diagnosis was that of an atypical and highly unusual melanocytic lesion with borderline features for melanoma.

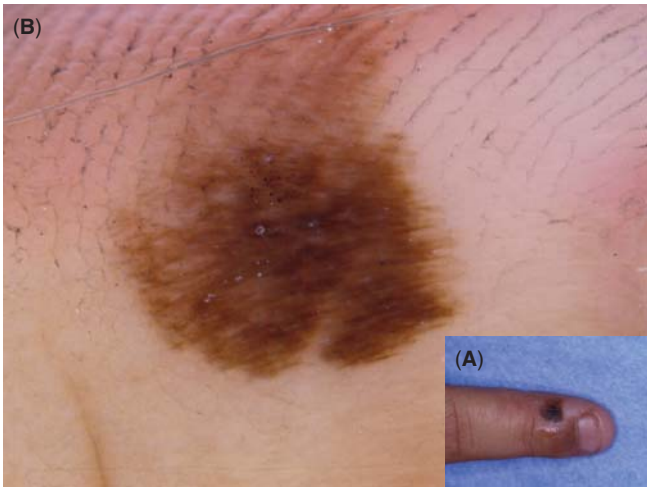


Figure 9a.23 (**A**) Clinical image of an ALM on the volar aspect of the finger. (**B**) Dermoscopy reveals a fibrillar pattern. N.B. Any lesion with a fibrillar pattern, regardless of whether it is a typical or an atypical fibrillar pattern, on the hands should be viewed with suspicion toward ALM. *Abbreviation*: ALM, acrolentiginous melanoma.

of any other structures or patterns. Lesions with a parallel pattern on volar skin may transform over time into a homogenous pattern. The homogenous-patterned nevi have been observed to fade away over time. The disappearance of such acral nevi has been observed during digital followup of benign neoplasms of soles and palms. It is surmised that these lesions disappear via transepidermal elimination of melanocytes.

The *peas in a pod pattern* consist of a parallel-furrow pattern in addition to the presence of globules on the ridges (Fig. 9a.27). This is a common pattern seen in congenital nevi on volar skin.

The nontypical patterns (Fig. 9a.10G, I) do not have any of the aforementioned benign patterns and also do not have any acrolentiginous melanoma (ALM)-specific patterns (see below) (Figs. 9a.28–9a.31). Lastly, as already discussed above, the transition pattern (Fig. 9a.10H) is seen in lesions that cross over Wallace line (Fig. 9a.7).

Malignant Dermoscopy Pattern for Acral Skin

The dermoscopic patterns considered specific for *ALM* are the parallel-ridge pattern and the multicomponent pigmentation pattern (chap. 8b). Of these two patterns the *parallel-ridge pattern* is the most specific dermoscopic pattern in acral melanoma in situ or early invasive acral melanoma (Fig. 9a.4). This is a distinct dermoscopic pattern that consists of a tan to dark brown

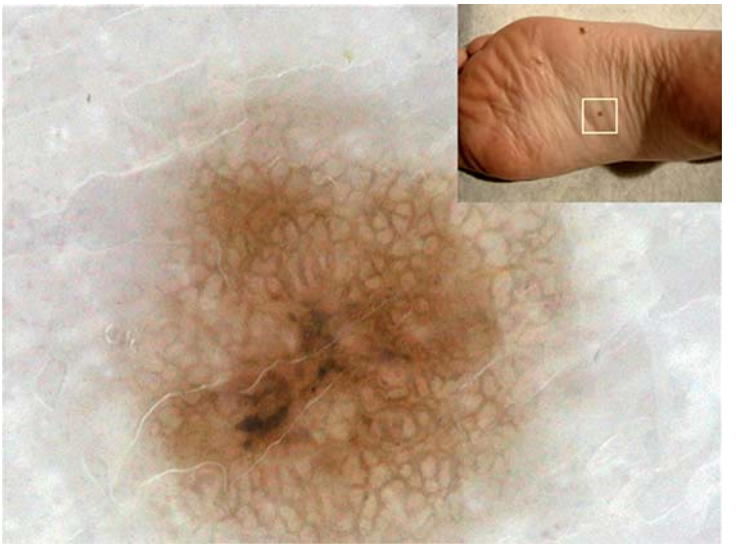


Figure 9a.24 Reticulated pattern on the arch of the sole.

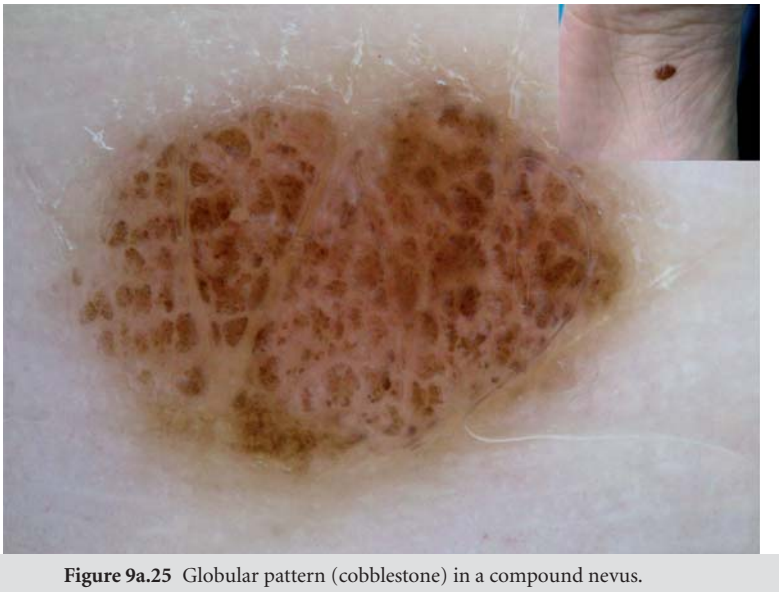


Figure 9a.25 Globular pattern (cobblestone) in a compound nevus.

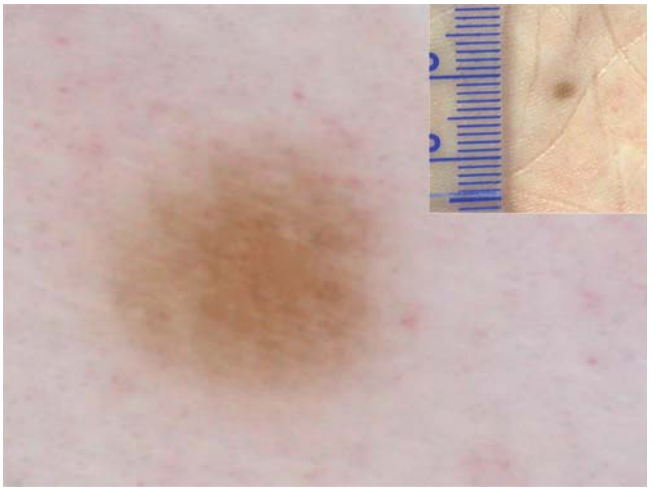
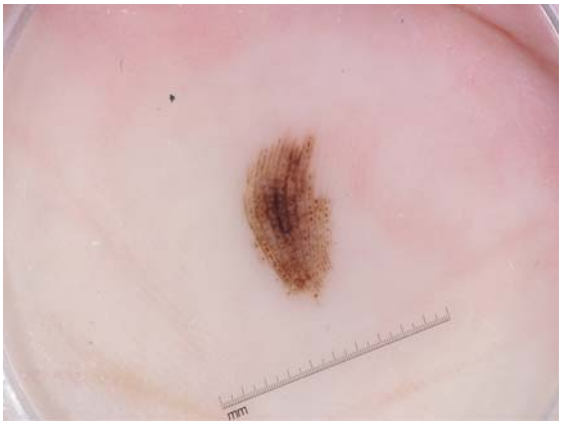


Figure 9a.26 Homogenous pattern.

▲ **Figure 9a.27a** Congenital nevus on the palm.



◀ **Figure 9a.27b** Dermoscopy shows a "peas in a pod" pattern, which consists of a parallel-furrow pattern together with dots/globules on the ridges (Fig. 9a.12H). Sometimes the globules on the ridges will be visible but the pigment in the furrows will not be present. This is considered a variant of the same pattern and is called the "crista dotted pattern" (Fig. 9a.12G).

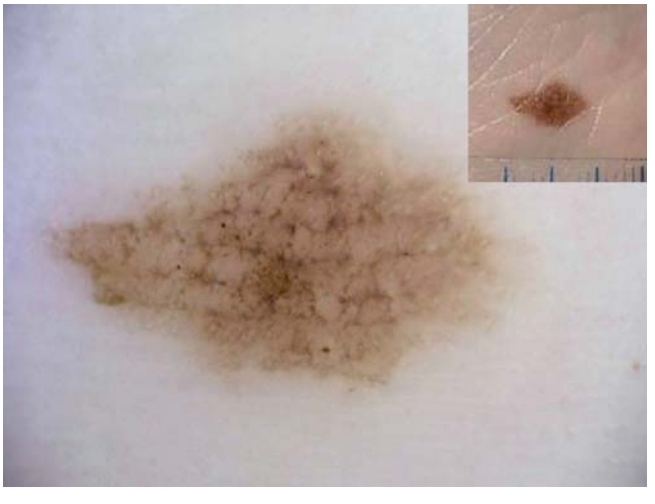
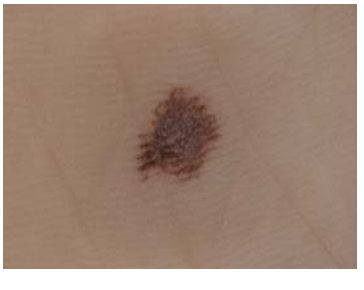


Figure 9a.28 Nontypical pattern in a benign nevus on the sole in a patient with dysplastic nevus syndrome.



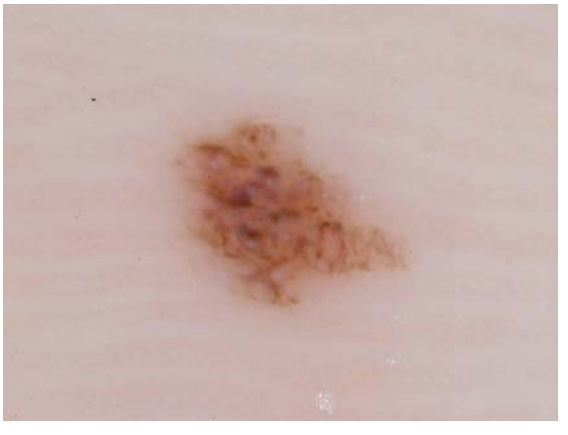
▲ **Figure 9a.29a** Clinical image of a nontypical pattern nevi.

◀ **Figure 9a.29b** Dermoscopic image of a nontypical pattern nevus.

▲ **Figure 9a.30a** Clinical image of a nontypical pattern nevi.

◀ **Figure 9a.30b** Dermoscopic image of a nontypical pattern nevus.

▲ **Figure 9a.31a** Clinical image of a nontypical pattern nevi.



◀ **Figure 9a.31b** Dermoscopic image of a nontypical pattern nevus.

▲ **Figure 9a.32a** Clinical image of an area of trauma on the foot.

◀ **Figure 9a.32b** Dermoscopy reveals a parallel-ridge pattern. Paring down the stratum corneum will help confirm that the pigment is due to subcorneal hemorrhage.

pigmentation on the ridges with relative hypopigmentation of the furrows. This pattern is normally present in the macular portions of melanomas in volar location. Some banal dermatologic entities can display a parallel-ridge pattern, including ethnic pigmentation in black skin, acral macules in Peutz–Jeghers syndrome, macules in Laugier–Hunziker syndrome and subcorneal hemorrhage (see also chap. 8b for details regarding the parallel-ridge pattern as well as other melanoma-specific patterns and structures).

SUBCORNEAL HEMORRHAGE

The presence of subcorneal blood may present with a parallel-ridge pattern, thereby mimicking melanoma (Figs. 9a.32 and 9a.33). In such cases the pigment, which can be reddish, bluish, purple, black, brownish, or rust colored, depending on the oxidative state of the hemoglobin, is deposited along the ridges. In subcorneal hemorrhage the pigmentation ends abruptly at the edge of the lesion, whereas in melanoma it tends to fade toward the periphery. The history of abrupt onset after sustaining trauma helps in differentiating subcorneal hemorrhage from ALM. In addition, subcorneal blood can be scraped off with a scalpel and in melanoma the pigment cannot be scraped off (see chap. 8b).

DERMOSCOPIC FINDINGS OF COMMON NONMELANOCYTIC ACRAL LESIONS

Dermoscopy can help identify skin infections, such as warts (Fig. 9a.34), tinea nigra (Fig. 9a.35), and scabies (Fig. 9a.36). Also dermoscopy can be useful in identifying palmar pits in patients with basal cell nevus syndrome (Gorlin syndrome) (Fig. 9a.37).

▲ **Figure 9a.33a** Clinical image of subcorneal blood.

◀ **Figure 9a.33b** Dermoscopy reveals a pattern known as "pebbles on the ridge." The pebbles correspond to pockets of congealed blood and they are located on the ridges.

Figure 9a.34 Typical dermoscopic image of a wart with dots corresponding to hemorrhage.

▲ **Figure 9a.35a** Clinical image of tinea nigra.

◀ **Figure 9a.35b** Dermoscopy reveals fine brown wispy strands that do not follow any particular pattern or anatomic structure, such as furrows or ridges. *Source*: Image courtesy of Dr. W. Stolz.

Figure 9a.36 Dermoscopic image of scabies (see chapter 11 for details).

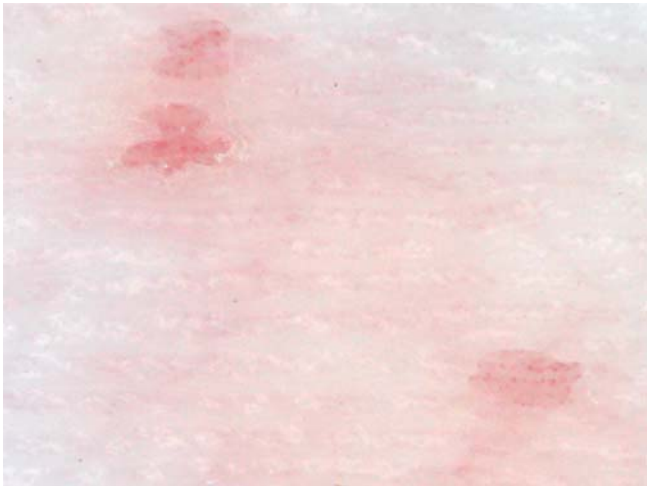
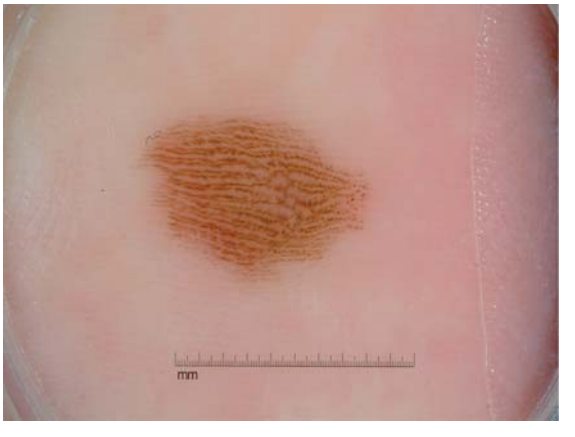


Figure 9a.37 Pits on the palm of a patient with Gorlin–Goltz syndrome. Notice the geographic border of the lesion and the presence of dotted vessels within the pits.

▲ **Figure 9a.38a** Clinical image of a nevus on the sole.



◀ **Figure 9a.38b** Dermoscopy of this lesion reveals a double-line-furrow pattern on the left side and a double-dotted-line-furrow pattern on the right side. Although this nevus has more than one pattern, it is still considered benign since it is only manifesting variations of the different classic benign patterns.

▲ **Figure 9a.39a** Clinical image of a volar nevus.

◀ **Figure 9a.39b** Under dermoscopy a portion of this lesion has a fibrillar pattern and another portion has a dotted-furrow pattern. Because both of these patterns are benign the entire lesion is considered to be a benign nevus.

CONCLUSION

An algorithm to assist in the decision-making process when evaluating volar melanocytic lesions can be found in chapter 8b (Fig. 8b.21). Lastly, we want to mention that it is quite common to encounter nevi on volar skin that manifest more than one benign pattern (Figs. 9a.38 and 9a.39). Lesions manifesting more than one of the classic benign patterns are classified as benign lesions in the algorithm shown in Figure 8a.21 (chapter 8b).

Key Points

1. The peculiar anatomy of volar skin results in the ridges and furrows that characterize the skin of the palms and soles.
2. Pigment in nevi tends to follow the furrows resulting in the parallel-furrow pattern. Pigment in melanomas tends to be more prominent on the ridges resulting in the parallel-ridge pattern seen in ALM.
3. Parallel-furrow, lattice-like, and typical (fine) fibrillar pattern are the most frequent patterns seen in benign nevi on volar skin.
4. Parallel-ridge pattern is the most characteristic finding in the in situ ALMs.

REFERENCES

Altamura, D., Altobelli, E., Micantonio, T., et al., 2006, Dermoscopic patterns of acral melanocytic nevi and melanomas in a white population in central Italy. *Arch Dermatol*, 142, 1123–8.

Bowling, J., 2007, Fibrillar pattern of an acquired plantar acral melanocytic naevus: correspondence between epiluminescence light microscopy and transverse section histology. *Clin Exp Dermatol*, 32, 103.

Malvehy, J. & Puig-Butille, S., 2004, Dermoscopic patterns of benign volar melanocytic lesions in patients with atypical mole syndrome. *Arch Dermatol*, 140, 538–44.

Maumi, Y., Kimoto, M., Kobayashi, K., et al., 2009, Oblique view dermoscopy changes regular fibrillar pattern into parallel furrow pattern. *Dermatology*, 218, 385–6.

Miyazaki, A., Saida, T., Koga, H., et al., 2005, Anatomical and histopathological correlates of the dermoscopic patterns seen in melanocytic nevi on the sole: a retrospective study. *J Am Acad Dermatol*, 53, 230–6.

Palleschi, G. & Torchia, D., 2007, Fibrillar pattern of acral melanocytic naevi may be a dermatoscopic, but not a histological artifact. *Clin Exp Dermatol*, 32, 324.

Palleschi, G.M., Cipollini, E.M., Torchia, D., Torre, E. & Urso, C., 2006, Fibrillar pattern of a plantar acquired melanocytic naevus: correspondence between epiluminescence microscopy and transverse section histology. *Clin Exp Dermatol*, 31, 449–51.

Saida, T. & Koga, H., 2007, Dermoscopic patterns of acral melanocytic nevi: their variations, changes, and significance. *Arch Dermatol*, 143, 1423–6.

Saida, T., Koga, H. & Uhara, H., 2011a, Key points in dermoscopic differentiation between early acral melanoma and acral nevus. *J Dermatol*, 38, 25–34.

Saida, T., Koga, H., Goto, Y. & Uhara, H., 2011b, Characteristic distribution of melanin columns in the cornified layer of acquired acral nevus: an important clue for histopathologic differentiation from early acral melanoma. *Am J Dermatopathol*, 33, 468–73.

Saida, T., Miyazaki, A., Oguchi, S., et al., 2004, Significance of dermoscopic patterns in detecting malignant melanoma on acral volar skin: results of a multicenter study in Japan. *Arch Dermatol*, 140, 1233–8.

Saida, T., Oguchi, S. & Miyazaki, A., 2002, Dermoscopy for acral pigmented skin lesions. *Clin Dermatol*, 20, 279–85.

9b Nails

Ralph P. Braun and Luc Thomas

INTRODUCTION

Longitudinal pigmentation of the nail is a common presenting problem in general dermatology. The differential diagnosis varies from subungual hematoma to fungal infection to a melanocytic lesion (i.e., lentigo, nevus, and melanoma) among others. Dermatologists are often unsure regarding their clinical diagnosis and lack confidence in managing this condition. Furthermore, many physicians are also reluctant to perform biopsies of the nail matrix because the procedure is painful and can result in permanent nail dystrophy. To complicate matters, when a decision to biopsy is finally rendered, it is not uncommon for inadequate biopsy specimens (e.g., biopsy specimen of the nail plate instead of the nail matrix) to be submitted to the pathologist. This in turn compromises the ability of the pathologist to render an accurate diagnosis. Fortunately, the use of noninvasive techniques, such as dermoscopy, can assist clinicians in correctly evaluating and diagnosing nail pigmentation. This in turn will reduce the number of unnecessary surgeries while helping physicians determine the most appropriate biopsy technique and site of biopsy if it were deemed necessary to biopsy.

PERSONAL HISTORY

The physician should try and elicit a history as to whether the pigment was present since birth or is acquired. Furthermore, the history of its duration, history of what made the patient first become aware of it, and whether the patient has observed any change in the nail lesion may provide clues for the correct diagnosis. Many patients find it difficult to verbally describe what the nail looked like and how it had changed over time. To overcome this problem we have found it useful to allow the patient to draw their impression of what the lesion initially looked like and to draw the perceived change on a simple schematic drawing of a nail.

Specific questions pertaining to athletic activities, recent trauma, physical exertion, such as long hiking trips, or the use of blood thinners, such as aspirin and warfarin, may help in differentiating subungual hemorrhage from other causes of nail pigment. Obtaining a thorough history of any medications the patient is ingesting, may help identify drugs that may contribute to abnormal nail pigmentation.

CLINICAL EXAMINATION

A complete examination must include the inspection of all 20 nails, periungual skin, and the oral mucosa because the examination of the oral (and genital mucosa) can aid in correctly identifying Peutz–Jeghers syndrome or the Laugier–Hunziker syndrome.

The clinician should record the diameter of the pigmentation at both the distal and proximal end of the nail. In addition, the color (or colors) and whether the lesion has an overall homogenous or heterogenous appearance should be recorded.

DERMOSCOPY EXAMINATION

For the examination of the nail apparatus we recommend the use of a gel, such as ultrasound gel or a hand sanitizer (Purell), as immersion medium. This is required because its decreased viscosity permits it to stay on the nail plate and fill any concavities without rolling off. For the evaluation of the pigmentation and to appreciate the thin lines within the nail band, it is useful to vary the focus of the device during the examination. The following criteria can be evaluated by dermoscopy.

DERMOSCOPY OF THE FREE EDGE OF THE NAIL

Apart from the examination of the nail plate, perionychium, and hyponychium, dermoscopy can also be used to examine the free edge of the nail plate (Fig. 9b.1) (Braun et al., 2006). Examination of the free edge of the nail plate can help determine whether the origin of the pigmentation is from the proximal or distal nail matrix. As a result of the natural growth of the nail, pigment produced in the proximal nail matrix will be incorporated into the upper portion of the nail plate and pigment produced in the distal nail matrix will appear in the lower part of the nail plate. Thus, when examining the free edge of the nail plate particular attention should be placed on determining whether the pigment is located in the upper or lower portion of the nail plate. This information, in turn, will help isolate which part of the matrix needs to be biopsied. If in doubt regarding the origin of the pigment, one can always obtain a nail clipping and stain it with Fontana–Masson stain. This will help determine the location of melanin within the nail plate, which in turn will help determine whether the pigment originated in the proximal or distal nail matrix.

DIFFERENTIAL DIAGNOSIS OF NAIL PIGMENTATION

The first and most important task necessary to diagnose the cause of nail pigmentation is to differentiate whether the pigment is of melanocytic or

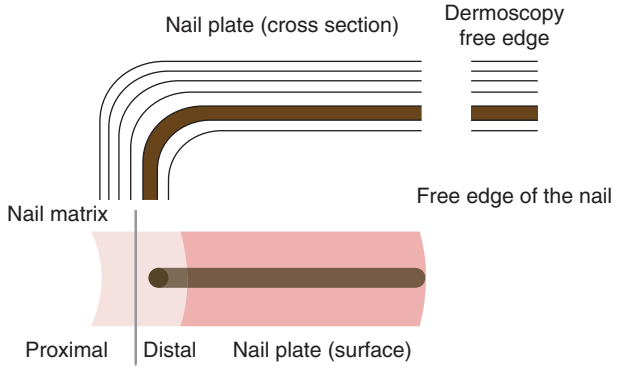


Figure 9b.1 Schematic drawing of free edge dermoscopy. As a result of the natural growth of the nail, pigment produced in the proximal nail matrix will be incorporated into the upper portion of the nail plate and pigment produced in the distal nail matrix will appear in the lower part of the nail plate. The schematic shown here is that of a lesion located in the distal nail matrix.

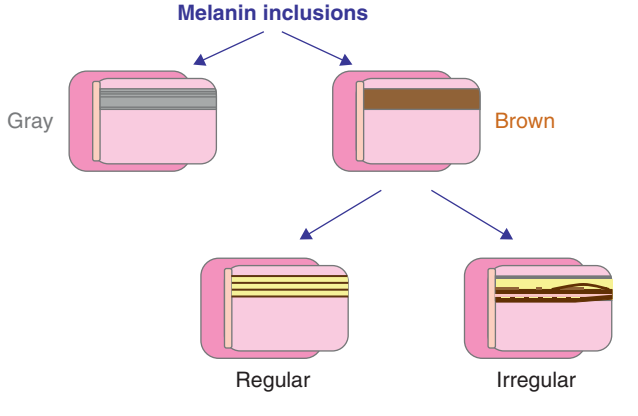


Figure 9b.2 Diagnostic algorithm for nail pigmentations of melanocytic origin: In the first step one has to determine if a nail pigmentation is of gray or brown color. In a lesion with brown color we need to determine if the brown bands are regular (nevus) or irregular (melanoma).

nonmelanocytic origin (Fig. 9b.2). In most cases this task can be accomplished by clinical inspection and examination with dermoscopy. In nonmelanocytic lesions, such as fungal infections or subungual hematoma, the pigment tends to be distributed diffusely (homogenously). In melanocytic lesions, the melanin is found in cellular inclusions, which can be easily identified as small granules of less than 0.1 mm in diameter under dermoscopy. Thus, if such granules are detected under dermoscopy, the lesion should be considered to be of melanocytic origin (Braun et al., 2007).

NAIL PIGMENT OF NONMELANOCYTIC ORIGIN

Exogenous Pigmentation

There are multiple causes that can lead to exogenous nail pigment. Among the most frequent causes are contact with chemical agents, topical application of therapeutic agents, such as silver nitrate or ethacridinlactat, tobacco, and cosmetics, such as henna and hair dyes.

Subungual Hematoma

Subungual hematoma usually appears as a reddish to reddish-black pigment depending on the age of the bleed. Dermoscopically, one is usually able to identify small reddish to reddish-black globules along the proximal and lateral margins of the pigment (Fig. 9b.3). The distal part will often have streaks of pigment (Fig. 9b.4). The pigment is homogenous and no melanin granules can be observed. The hematoma will progressively grow out distally as the nail plate grows. It is important to remember that a subungual hematoma can on rare occasions be caused by an episode of hemorrhage or caused by neovascularization within a tumor and, thus, the presence of subungual blood should not be used to rule out the diagnosis of melanoma. Hence, any subungual hemorrhage that does not grow out with the nail or that recurs at the same place requires special attention and further examination, including radiograph of the distal phalange to exclude exostosis. If the diagnosis cannot be determined by radiologic studies, then the lesion should be biopsied.

Fungal or Bacterial Infection

Nails infected with *Trichophyton rubrum* (var. *nigricans*) or with dermatiaceous fungi such as *Scytalidium dimidiatum* are pigmented (Fig. 9b.5). Although difficult to treat, the pigmentation will fade slowly after successful treatment.

NAIL PIGMENTATION OF MELANOCYTIC ORIGIN

As mentioned earlier, a nail pigmentation of melanocytic origin will reveal tiny melanin granules in the nail plate under dermoscopy. Once the nail pigmentation has been identified to be of melanocytic origin, one has to evaluate if the pigmentation is of gray or brown color.

Gray-Pigmented Band (Multiple Thin Homogenous Grayish Lines)

This pattern is usually a result of epithelial hyperpigmentation without accompanying melanocytic hyperplasia, such as seen in a lentigo Figure 9b.6, drug-induced pigmentation (Fig. 9b.7), and ethnic pigmentation (Fig. 9b.8). Some authors prefer to use the term "melanotic macule of the nail" for this entity.

Histopathology of these entities shows a normal number of melanin-containing melanocytes, which is approximately 6.5 cells/mm of the basal layer length.

Drug- and Radiation-Induced Nail Pigmentation

On clinical examination, drug- and radiation-induced longitudinal melanonychia can be seen as horizontal or longitudinal bands or as diffuse nail darkening. It may affect the nails of the hands and feet and it can involve one or more digits. Hyperpigmentation of the nail can also be associated with hyperpigmentation of the skin. Dermoscopically homogenous grayish bands composed of gray lines can be observed (Fig. 9b.7) and has been reported to occur during or after treatment with some drugs, chemotherapy, or radiation therapy. This type of nail pigmentation is more commonly seen in individuals with phototypes IV, V, and VI skin than in individuals with fair skin. It usually appears one to two months after starting the

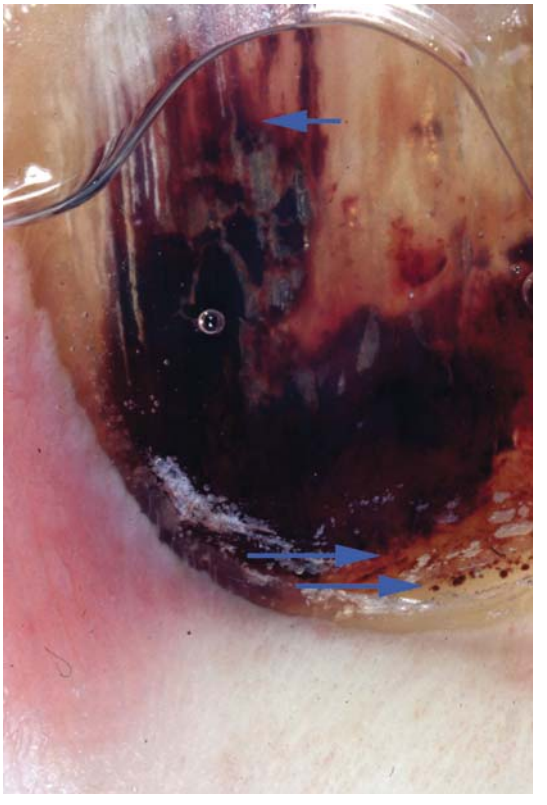


Figure 9b.3 Subungual hemorrhage in an adult's first toenail (recent lesion). Dermoscopy shows a characteristic purple coloration of the pigmentation with an elongated parallel linear pattern at the distal edge (*short arrow*) and a well-demarcated round proximal edge with characteristic features of blood spots (*long arrows*).

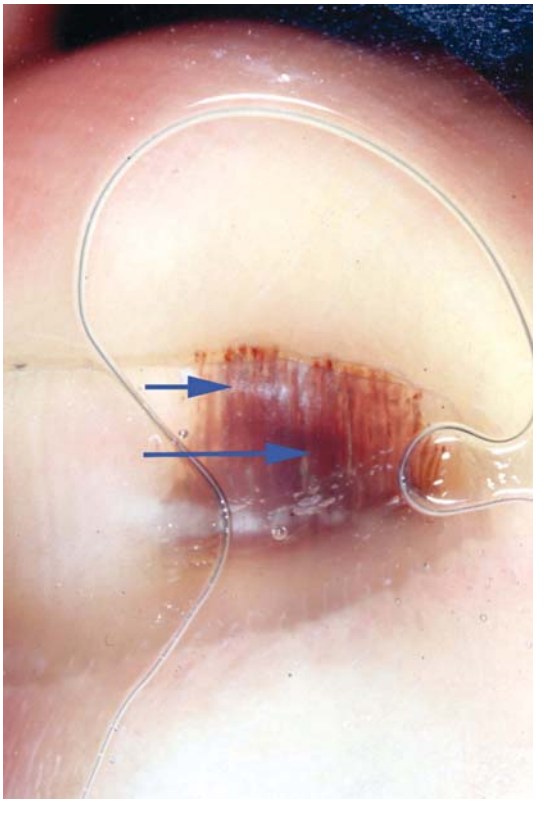


Figure 9b.4 Subungual hemorrhage in a child's toenail (old lesion). Note the elongated parallel linear pattern of the distal edge of the pigmentation (*short arrow*) and the purple-brown coloration of the proximal blood spot (*long arrow*).

offending agent. For example, it is estimated that 67% of patients receiving AZT for the treatment of HIV infection will develop this form of nail pigmentation. AZT-induced nail pigmentation usually develops between eight weeks and one year after starting therapy. After the treatment is completed, the pigmentation will progressively fade over several months but it may never completely disappear.

Endocrine Nail Pigmentation
This is a common feature of Addison's disease (diffuse pigmentation and/or longitudinal melanonychia (LM)). It may also be seen in Cushing's syndrome, after adrenalectomy, hyperthyroidism, acromegaly, and during pregnancy. The clinical and dermoscopy findings are very similar to drug- and radiation-induced longitudinal melanonychia. Endocrine longitudinal melanonychia may affect multiple digits. In Addison's disease, longitudinal melanonychia is typically associated with cutaneous and mucosal hyperpigmentation.

Nail Pigmentations Associated with HIV Infection
In patients who are HIV positive, nail pigmentation unrelated to AZT treatment has been described. The nail pigmentation usually affects multiple nails and is associated with pigmented macules of the palms, soles, and mucous membranes. In most reported cases the patients died within months after the pigmentation appeared.

Nail Pigmentations Associated with Inflammatory Nail Disorders
This type of nail pigmentation occasionally develops in nails affected by lichen planus, onychomycosis, chronic radiodermatitis, pustular psoriasis, or Hallopeau's disease. The pigmentation can be subtle at the beginning and become clearly clinically evident as the inflammatory process progresses. It is usually associated with nail scarring and abnormalities of the surface of the nail plate. The clinical and dermoscopy aspect of this entity is not specific.

Laugier–Hunziker Syndrome
Laugier–Hunziker syndrome is an acquired disorder of the pigment system. The characteristic findings include longitudinal melanonychia, and macular pigmentation of the lips, mouth, and anogenital area. The nail pigmentation may appear either as a single or double band with a diameter between 1 and 2 mm or as homogenous pigmentation of the lateral nail plate (Fig. 9b.9). Although the entire nail can become hyperpigmented, this is rather rare. This form of pigmentation can be associated with a pseudo-Hutchinson's sign.

Nail Pigmentation as a Result of Nonmelanocytic Nail Tumors
In rare cases nonmelanocytic nail tumors can activate melanocytes resulting in the formation of a longitudinal-pigmented nail band. This entity is most commonly seen in association with Bowen's disease. Any longitudinal melanonychia in the presence of a nonmelanocytic tumor requires biopsy.

Nutritional Nail Pigmentation
Pigmentation of the nails and the skin can be seen in vitamin B12 or folate deficiency. The pigmentation tends to have a bluish-black color. The pigmentation on the skin is accentuated over the knuckles and the distal phalanges. Usually the diagnosis is made based on laboratory examination. This type of nail pigmentation is completely reversible after vitamin B12 or folate administration.

Traumatic Nail Pigmentation
Repeated trauma, such as nail biting may induce nail pigmentation. This is predominantly seen after repeated minor trauma, such as picking, chewing,

▲ **Figure 9b.5a** Clinical picture of a pigmented band on a nail.

◀ **Figure 9b.5b** Dermoscopy shows a homogenous pigmentation without identifiable melanin granules in the nail plate. This image is consistent with a nail pigmentation of nonmelanocytic origin. In this case the pigmentation was due to onychomycosis.

▲ **Figure 9b.6a** Clinical image of a grayish longitudinal nail pigmentation.

◀ **Figure 9b.6b** Dermoscopy shows a homogenous grayish band in an ungula lentigo.

breaking, or rubbing of the proximal nailfold (frictional nail pigmentation). This entity is usually associated with visible abnormalities of the surface of the nail plate as a result of the repetitive nail matrix injuries.

Frictional longitudinal melanonychia is mainly seen on the toes and is often associated with foot deformities, unsatisfactory footwear, or both. This type of nail pigmentation may gradually fade once the repetitive trauma has subsided.

Ethnic Nail Pigmentation

Ethnic or racial nail pigmentations are physiologic longitudinal pigmentations of the nail or nails observed in dark-skinned individuals with skin type V and VI. They can present as single or more often multiple bands involving one or more digits (Fig. 9b.8).

Systemic Lupus Erythematosus and Scleroderma

Longitudinal melanonychia has been reported in rare cases of systemic lupus erythematosus and scleroderma.

BROWN-PIGMENTED BAND

The brown-pigmented band is usually composed of multiple thin brown lines. These lines can be regular or irregular and are caused by melanocytic hyperplasia or melanocytic proliferation as seen in a nevus or melanoma.

The term "melanocyte hyperplasia" should be reserved only for cases in which there is an increased number of melanin-containing melanocytes (>6.5 cells/mm of basal membrane length) within the basal and suprabasal layer. It is important to remember that the architecture of the nail matrix together with the dendritic morphology and the suprabasal location of the nail matrix melanocytes can histologically simulate an in situ melanoma. Therefore, it is often difficult to differentiate between melanocytic hyperplasia and in situ melanoma based on a partial biopsy specimen (i.e., punch biopsy specimen) of the nail matrix. Whenever possible

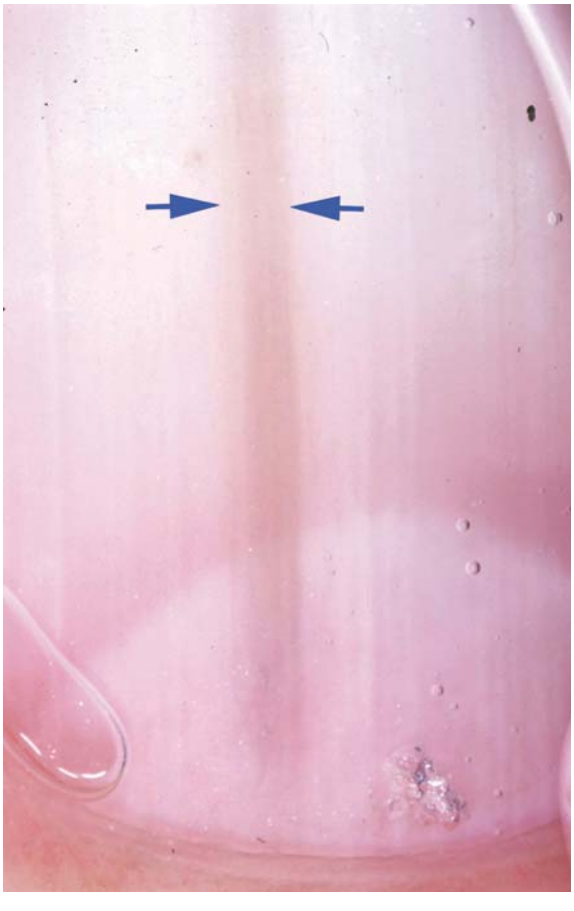


Figure 9b.7 Hydroxyurea-induced pigmentation of an adult's fingernail. The dermoscopic pattern is very similar to that of lentigo with grayish coloration of the background and thin gray lines (*between the two short arrows*).

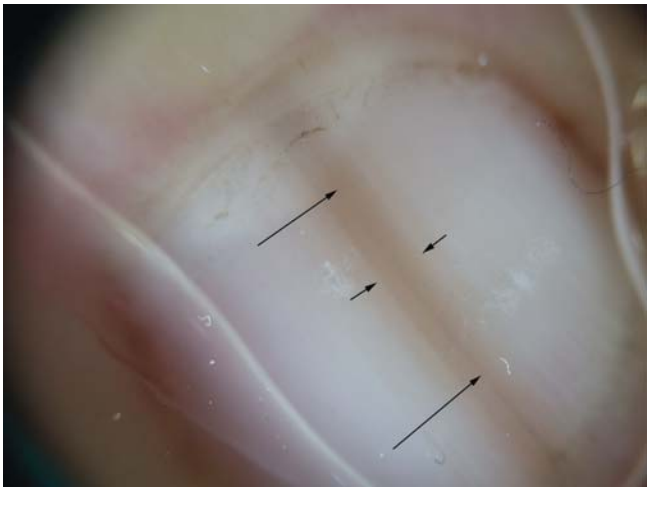
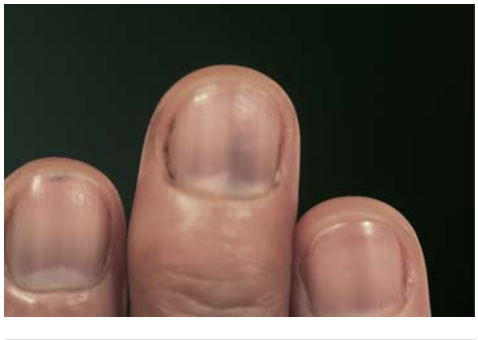


Figure 9b.8 Ethnic pigmentation of the toenail plate in a phototype V (*North African*) adult. Dermoscopy shows grayish coloration of the background (between the two *short arrows*) and thin superimposed gray lines (*long arrows*).



▲ **Figure 9b.9a** Clinical image of a patient with Laugier–Hunziker syndrome showing multiple grayish-pigmented bands.

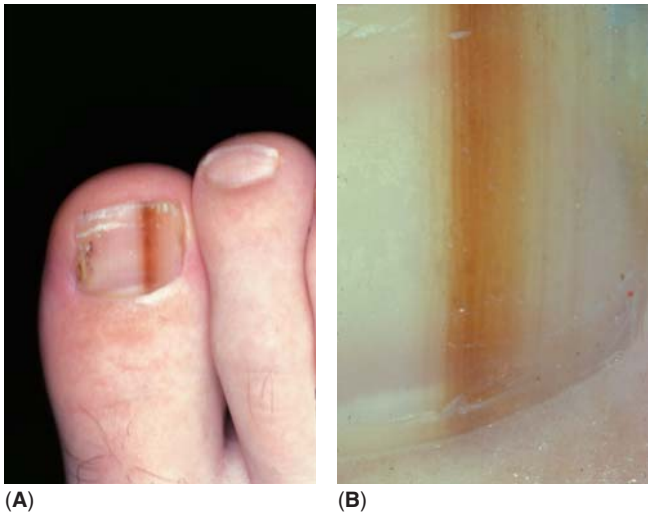
◀ **Figure 9b.9b** Dermoscopy shows multiple grayish bands in the nail plate. This finding is consistent with Laugier–Hunziker syndrome.

it is preferable to perform a complete longitudinal excision of the nail matrix associated with the band and submit it to the pathologist.

The following two main patterns can be observed.

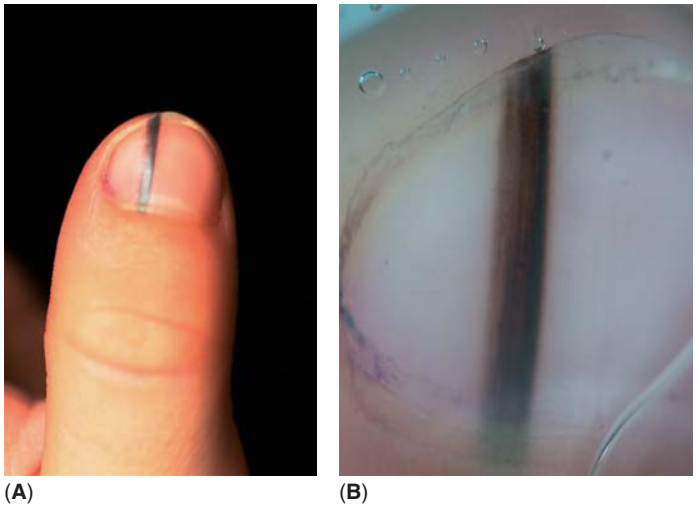
Regular Pattern: Brown Longitudinal Parallel Lines with Regular Spacing and Thickness

This pattern is usually associated with a brown homogenous color of the background band. The color of the individual lines within the band can vary from light brown (Fig. 9b.10) to dark brown to black (Fig. 9b.11). However, within any given band, the lines will be composed of similar shades of brown throughout the lesion. The spacing between the lines is regular and the thickness of the lines is relatively uniform throughout the band. The lines comprising the band are oriented parallel to each other. This is the typical aspect of nevi of the nail matrix. They can be acquired or congenital and can be seen in children and young adults. They can be heavily pigmented and simulate melanoma.



(**A**) (**B**)

Figure 9b.10 (**A**) Clinical image of a light colored nevus of the nail matrix. (**B**) Dermoscopy shows small melanin inclusions in the nail plate and brown longitudinal parallel lines with regular spacing and thickness.



(**A**) (**B**)

Figure 9b.11 (**A**) Clinical image of a dark nevus of the nail matrix. (**B**) Dermoscopy shows brown longitudinal parallel lines with regular spacing and thickness. The pigmentation can be observed through the translucent cuticule. This is a pseudo-Hutchinson sign and has to be distinguished from true Hutchinson sign, which corresponds to a true pigmentation of the cuticule or the periungual skin.

A pseudo-Hutchinson sign in which one can see the nail matrix pigment through a translucent cuticula is very common in nevi of the nail matrix (Fig. 9b.11). Histopathology shows nests of melanocytes at the dermoepidermal junction. Junctional nevi are more frequently found than compound nevi. In general, nail matrix nevi occur more often on fingernails than on toenails.

Irregular Pattern: The Band Comprises Multiple Longitudinal Brown to Black Lines with Irregular Spacing and Thickness and Disruption of Parallelism

This pattern is also associated with a brown pigmentation of the background nail band. However, the color of the individual lines varies from white to light brown to dark brown to gray to black (Fig. 9b.12). Irregular lines tend to have different degrees of pigmentation, varying thicknesses, and spacing. In some areas they might end abruptly and in others their parallelism is disrupted (Figs. 9b.13–9b.17). Blood spots can also be found in association with an irregular pattern (melanoma) and, thus, their presence does not automatically suggest the diagnosis of a subungual hemorrhage.

The irregular pattern is the predominant pigmentation pattern in melanoma of the nail matrix. Nail matrix melanoma has the same incidence across all races. However, they are the most frequent melanoma subtype in black and Asian populations. It usually affects middle-aged or elderly individuals. Nail matrix melanoma affects both fingernails and toenails and is most frequently found on the index finger, the thumb, the large toe, or all of them. Approximately 50% of patients with nail melanoma recollect preceding trauma. In melanomas that are growing rapidly the lines within the band are not parallel and the diameter of the entire band is wider at the proximal end. In advanced stages of dystrophy of the nail plate or even loss of the nail plate can be observed. This is a direct result of the progressive destruction of the nail matrix by the expanding tumor. Pigmentation of the nailfold cuticle and the surrounding skin, known as Hutchinson's sign, can frequently be observed.

The prognosis of nail matrix melanoma is generally worse than for melanoma in other sites. This may, in great part, be because of delays in diagnosis. We have the impression that nail matrix melanoma will lend itself well to sentinel node biopsy; however, there is currently no literature available addressing this issue.

WHICH LESIONS SHOULD BE BIOPSIED?

Any lesion with an irregular dermoscopy pattern should be biopsied.

Independent from the morphology seen under dermoscopy the following situations should alert the physician to the possibility of malignancy:

1. Isolated pigmented band on a single digit that develops during the fourth to sixth decade of life. Although melanoma can be seen in children it is a very rare event.
2. Nail pigmentation that develops abruptly in a previously normal nail plate.
3. Pigmentation that suddenly becomes darker or larger or when the pigment becomes blurred near the nail matrix.
4. Acquired pigmentation of the thumb, index finger, or large toe.
5. Pigment that develops after a history of digital trauma and in which subungual hematoma has been ruled out.
6. Any acquired lesion in patients with a personal history of melanoma.
7. If the pigmentation is associated with nail dystrophy, including partial nail destruction or absence of the nail plate.
8. If pigmentation of the periungual skin (including lateral nail folds) is found to be present (Hutchinson's sign). This includes pigment of the cuticle or hyponychium.

Besides the eight points mentioned, we are of the opinion that dermoscopy can greatly assist in the diagnosis and management decisions regarding nail pigmentations.

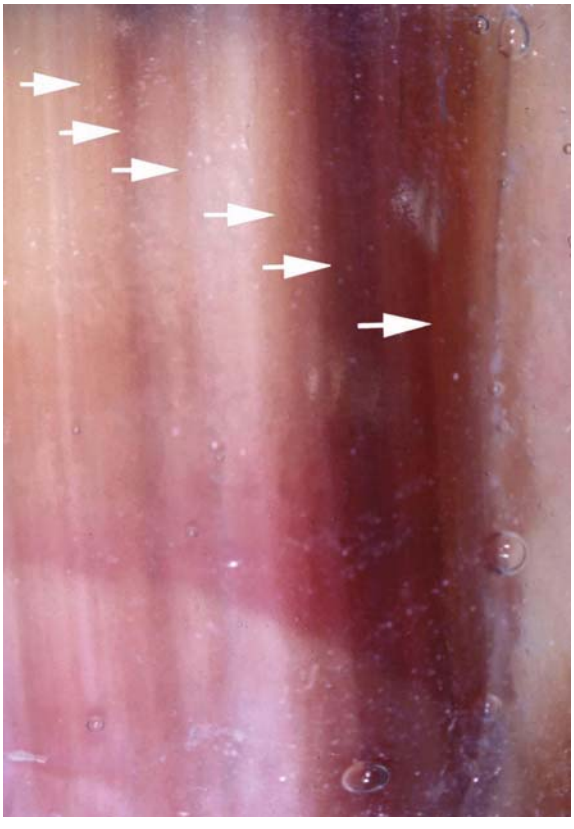


Figure 9b.12 Nail apparatus melanoma, acrolentiginous melanoma–type, Clark level III, 0.65 mm thickness in the big toenail. Dermoscopy shows brown coloration of the background and irregularly spaced, pigmented, and thick brown longitudinal lines (*arrows*).

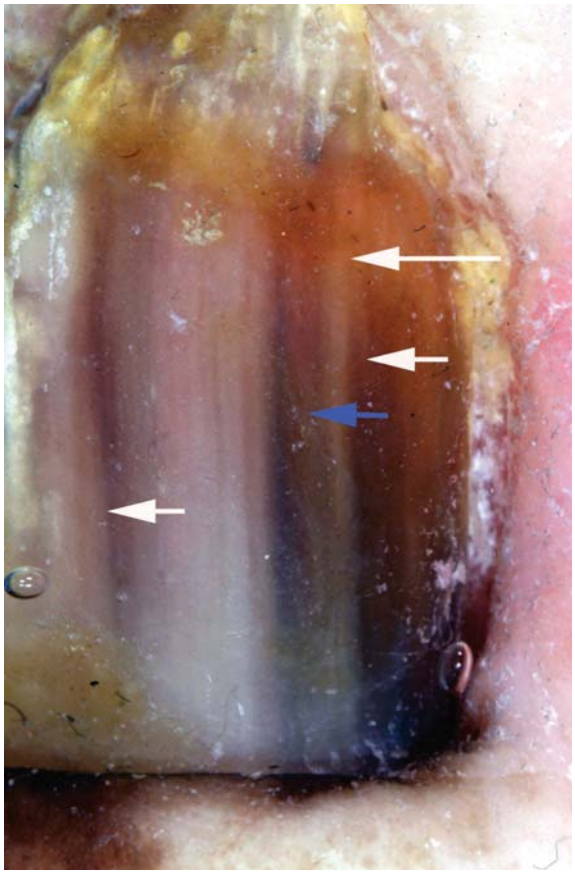


Figure 9b.13 Nail apparatus melanoma in a 72-year-old phototype IV male patient on the first left toenail. Note the irregular pattern of the brown lines (different thickness, color and spacing; *white arrows*) and an area of parallelism disruption (*blue arrow*).

(**A**)

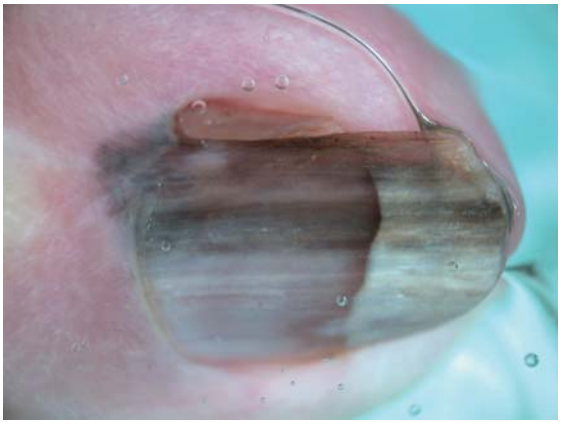
(**B**)

Figure 9b.14 (**A**) Clinical image of an in situ melanoma of the nail matrix. (**B**) Dermoscopy shows multiple brown bands of irregular spacing thickness and disruption of parallelism. This case also shows granular melanin inclusions in the nail plate.

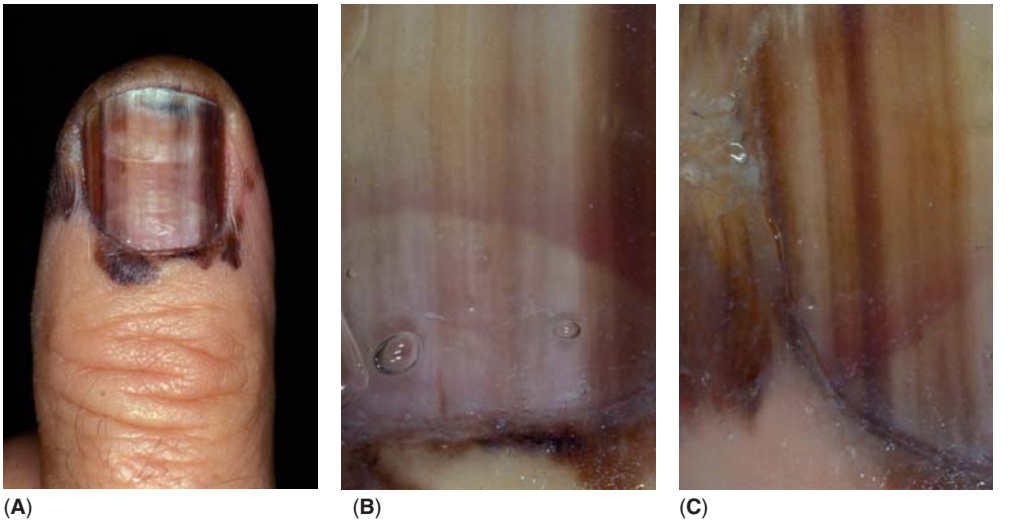
▲ **Figure 9b.15a** Clinical image of an in situ melanoma.

◀ **Figure 9b.15b** Dermoscopic image of an in situ melanoma.

▲ **Figure 9b.16a** Clinical image of an invasive melanoma of the nail matrix.



◀ **Figure 9b.16b** Dermoscopy shows irregular brown bands as well as a Hutchinson sign (pigmentation of the periungual skin).



(**A**) (**B**) (**C**)

Figure 9b.17 (**A**) Clinical image of an advanced melanoma of the nail matrix with extensive pigmentation of the periungual skin. (**B**) and (**C**) Dermoscopy shows irregular brown bands (Breslow 1.2 mm).

REFERENCES

Abimelec, P., 2009, Tips and tricks in nail surgery. *Semin Cutan Med Surg*, 28, 55–60.

Braun, R.P., Baran, R., Le Gal, F.A., et al., 2007, Diagnosis and management of nail pigmentations. *J Am Acad Dermatol*, 56, 835–47.

Braun, R.P., Baran, R., Saurat, J.H. & Thomas, L., 2006, Surgical Pearl: dermoscopy of the free edge of the nail to determine the level of nail plate pigmentation and the location of its probable origin in the proximal or distal nail matrix. *J Am Acad Dermatol*, 55, 512–13.

Gewirtzman, A., Saurat, J. & Braun, R.P., 2003, An evaluation of dermoscopy fluids and application techniques. *Br J Dermatol*, 149, 59–63.

Ronger, S., Touzet, S., Ligeron, C., et al., 2002, Dermoscopic examination of nail pigmentation. *Arch Dermatol*, 138, 1327–33.

Thomas, L. & Dalle, S., 2007, Dermoscopy provides useful information for the management of melanonychia striata. *Dermatol Ther*, 20, 3–10.

9c Face

Nancy H. Kim, Margaret C. Oliviero, Ralph P. Braun, Ashfaq A. Marghoob, and Harold S. Rabinovitz

Dermoscopy of facial lesions can be challenging because facial lesions often manifest different dermoscopic criteria than the same lesions found on different anatomic parts of the body. A pseudonetwork pattern rather than a true pigment network characterizes pigmented facial lesions. This pattern is created when adnexal openings, devoid of any pigment, are interspersed within a pigmented lesion that is located on skin that has blunted or absent rete ridges (Fig. 9c.1). The rete ridges on facial skin are attenuated due to the inherent anatomy of facial skin and due to epidermal thinning resulting from a lifetime of solar exposure (Magnus, 1981; Walter et al., 1990; Carey & Hogan 1990; Foley et al., 1993; Stolz et al., 2002) (Fig. 9c.2). It stands to reason that since pigment in the rete ridges produces the characteristic reticular network pattern on dermoscopy, melanocytic facial lesions will not normally reveal a typical network pattern. To complicate matters, many pigmented lesions, including both melanocytic and nonmelanocytic, may reveal a pseudonetwork pattern, and thus the presence of a pseudonetwork cannot be used to differentiate melanocytic from nonmelanocytic lesions. This pseudonetwork can be seen in melanocytic nevi, solar lentigines, early seborrheic keratosis (SK), pigmented actinic keratoses, and melanoma (Figs. 9c.34–9c.38). However, on rare occasions a melanocytic neoplasm on the face may reveal network and/or streaks as commonly seen in melanocytic lesions on nonglabrous skin. This is presumably due to the presence of preserved undulating rete ridges. Lastly, it is important to be aware that the reticular pattern can present as lines forming a network or as lines that do not form a clear network. The lines that do not form a clear network are also referred to as "fingerprint-like structures." As mentioned above, it is rare to see a reticular pattern consisting of a network on facial skin; however, it is quite common to see a reticular pattern consisting of fine thin lines on facial skin. These fine thin lines may correspond to pigment along the rete ridges or to ridges on the surface of the skin as commonly seen in SK and solar lentigines. Based on the aforementioned information, there are two distinct patterns commonly seen on facial skin: annular (also known as pseudonetwork) and reticular (also known as fingerprinting). Both the annular and reticular patterns can be seen in flat lesions. The annular pattern is characterized by small circles, which correspond to follicular and other adnexal openings. These circles are surrounded by varying amounts of pigment (Figs. 9c.3, 9c.4). This pattern can be seen in solar lentigines and melanocytic neoplasms that have a junctional component. The reticular pattern is characterized by fine thin lines and is most commonly seen in solar lentigines (Fig. 9c.5).

One of the most important roles for dermoscopy of facial lesions remains the early diagnosis of melanoma in situ on sun-damaged skin. The diagnosis of melanoma in situ on sun-damaged skin is made difficult by the fact that there are a number of lesions, which can mimic melanoma, including SK, lichen planus-like keratosis (LPLK), and pigmented basal cell carcinoma (BCC). Knowing the basic rules of facial dermoscopy can aid in the differentiation between melanoma simulators and melanoma (Fig. 9c.1, flow diagram).

NONMELANOCYTIC FACIAL LESIONS

The dermoscopic criteria for facial nonmelanocytic lesions are in general the same as the criteria for nonfacial lesions. BCCs, squamous cell carcinomas, and sebaceous hyperplasia are very common facial lesions and their features are outlined below. This is also true for SK, lentigines, LPLK, actinic keratosis and pigmented BCC; however, since these lesions can mimic melanoma they are discussed in the next section together with melanocytic lesions.

1. BCC (Figs. 9c.6–9c.8):
   a. Absence of a pigmented network
   b. Leaf-like structures (pigmented BCC)
   c. Multiple nonaggregated blue-gray dots or blue globular structures (pigmented BCC)
   d. Large blue to blue-gray ovoid nests (pigmented BCC)
   e. Spoke-wheel-like areas or concentric globular structures (pigmented BCC)
   f. Arborizing (serpentine or serpentine branched) telangiectasias
   g. Ulceration
   h. Pink-white to white shiny areas
2. Squamous cell carcinoma (Figs. 9c.9 and 9c.10):
   a. Dotted or glomerular vessels
   b. Scaling associated with these lesions often makes it difficult to visualize the underlying dermoscopic structures.
3. Sebaceous hyperplasia (Fig. 9c.11):
   a. Yellow to yellow-white lobular structures resembling popcorn.
   b. Linear winding or serpentine vessels at the periphery of the lesion that radiate toward the center of the lesion but do not cross the center of the lesion. These vessels are known as "wreath vessels" or "crown vessels."

DERMOSCOPY OF PIGMENTED NONMELANOCYTIC AND MELANOCYTIC FACIAL LESIONS

The annular pattern is characterized by small hypopigmented circles and follicular openings surrounded by varying amounts of pigment (Figs. 9c.3, 9c.4). Benign lesions tend to have circles with the same size and shape, have few colors, and are relatively symmetrical. Malignant lesions often have circles of different sizes and shapes, many colors, and are asymmetrical. Gray dots and granules indicate that the lesion may be malignant. The presence of gray dots and granules is called the annular–granular pattern (Fig. 9c.4) and is associated with a high suspicion of malignancy.

The reticular pattern is characterized by fine, thin hyperpigmented lines and is most commonly seen in solar lentigines (Fig. 9c.5). The lines may be interrupted and may appear to have a pattern similar to a fingerprint.

Solar lentigines have the following dermoscopic features (Figs. 9c.12 and 9c.13):

a. Annular pattern with areas of light brown and dark brown
b. Reticular pattern with fingerprinting and fine interrupted lines
c. Sharp borders
d. Moth-eaten borders

In addition to the characteristics of a solar lentigo, early SK may have the following features:

a. Fine interrupted lines that are often thicker than those seen in solar lentigines
b. Bulbous projections and ridge formation (fat finger-like structures or gyri)
c. A few milia-like cysts and/or comedo-like openings

The dermoscopic features of mature SK on the face are the same as on other areas of the body (Figs. 9c.14 and 9c.15):

a. Sharply demarcated borders
b. Milia-like cysts
c. Comedo-like openings (crypts)

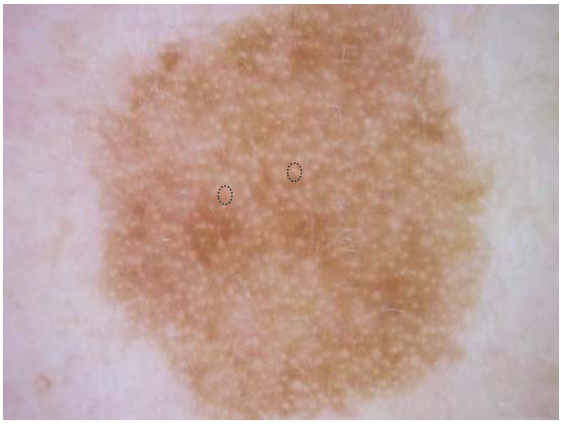


Figure 9c.1 Pseudonetwork (*dotted ovals*) are present throughout this lentigo. The light holes are due to the numerous non-pigmented follicular and sweat gland openings. Between the "holes" the pigment formation result in a "pseudo" network appearance.

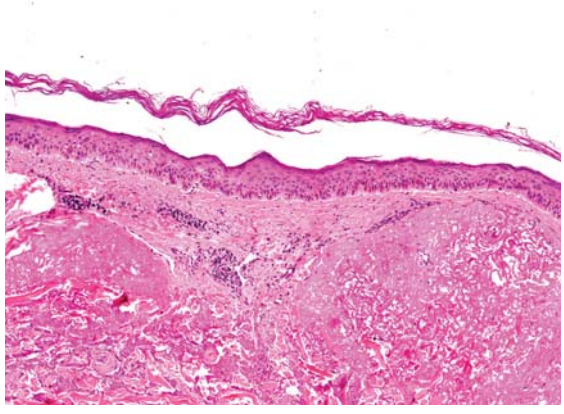
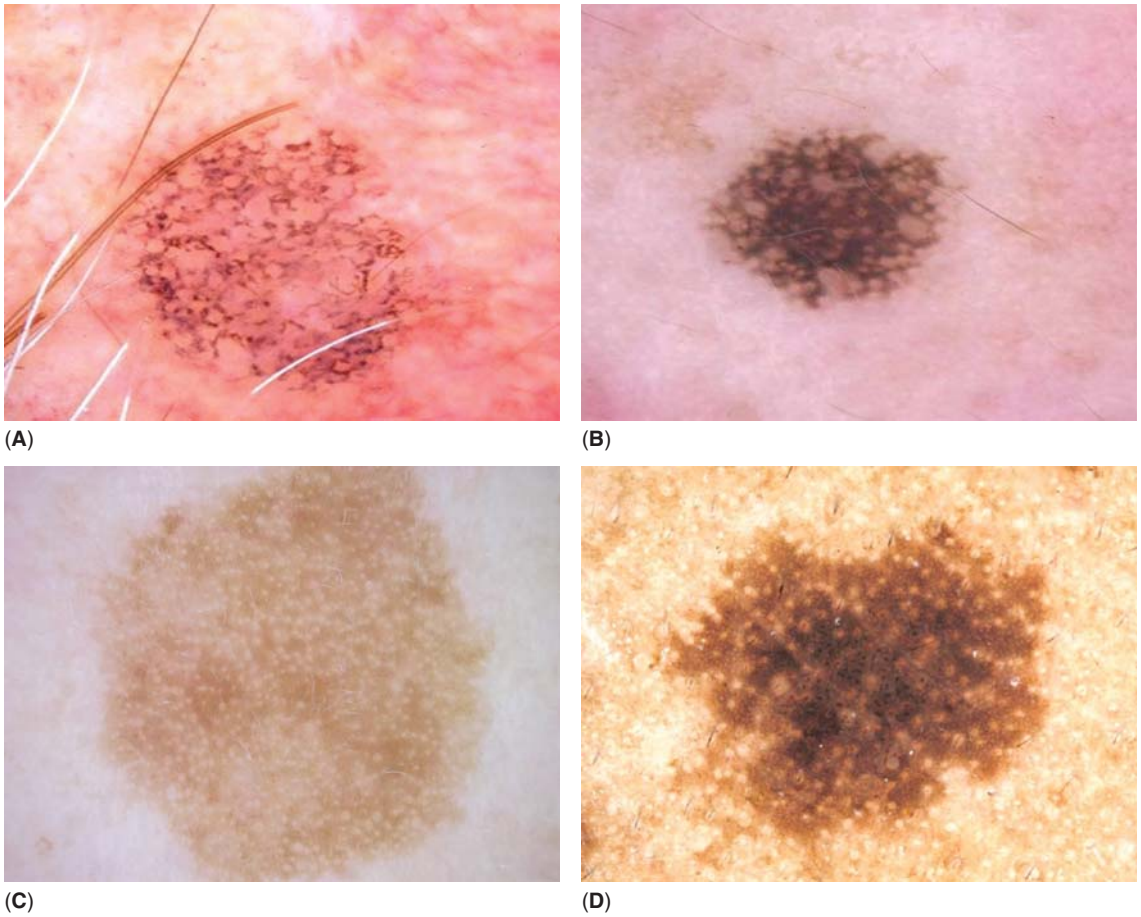


Figure 9c.2 Facial skin with characteristic flattening of rete ridges.



(**A**) (**B**) (**C**) (**D**)

Figure 9c.3 Examples of the pseudonetwork. (**A**) Lichen planus-like keratosis. (**B**)Clark nevus. (**C**) Solar lentigo. (**D**) Seborrheic keratosis. Lesions **A–D** are also examples of the annular pattern. Benign lesions typically have circles of the same size with even distribution of pigment.

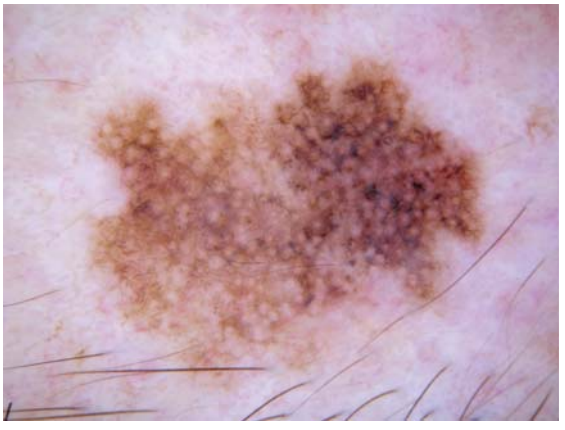
d. Fissures (sulci)
e. Ridges (gyri)
f. Hairpin vessels with a white halo

Flat pigmented lesions, such as Clark nevi junctional type, are characterized by an annular pattern (Fig. 9c.16). Nevi that are raised due to a prominent dermal component, such as in congenital nevi and compound Clark nevi, take on the same dermoscopic features of similar nevi seen on other areas of the body. For example, a dermal nevus with a globular pattern will appear the same on the torso as on the face (Fig. 9c.17).

FACIAL MELANOMA AND MELANOMA SIMULATORS

To say that the dermoscopy diagnosis of melanoma of the face is challenging is an understatement. Much of the difficulty of diagnosing facial melanomas lies in the fact that many other lesions, including pigmented actinic keratosis, LPLK, and occasionally pigmented BCC may simulate melanoma. Facial melanomas are typically found in the elderly, in the photo-damaged areas of the face. The elucidation of clinical and dermoscopic diagnostic criteria for facial melanoma and melanoma simulators are therefore critical.

(A)


(B)

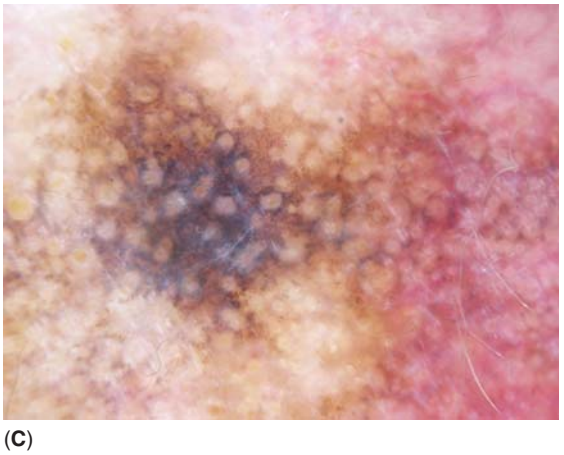
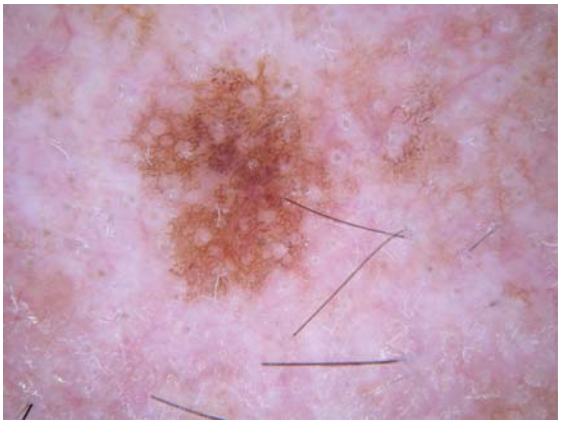

(C)

Figure 9c.4 (**A–C**) Malignant lesions often have circles of different sizes and shapes, many colors, and are asymmetrical. Gray dots/granules are a helpful sign (annular–granular pattern).

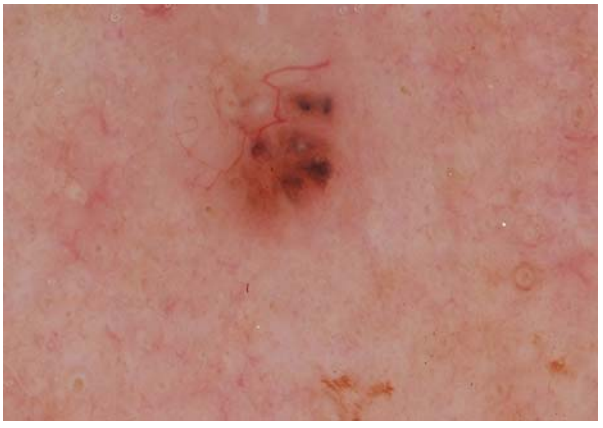
▲ **Figure 9c.5a** Clinical image.



◀ **Figure 9c.5b** The reticular pattern is often seen in solar lentigines.

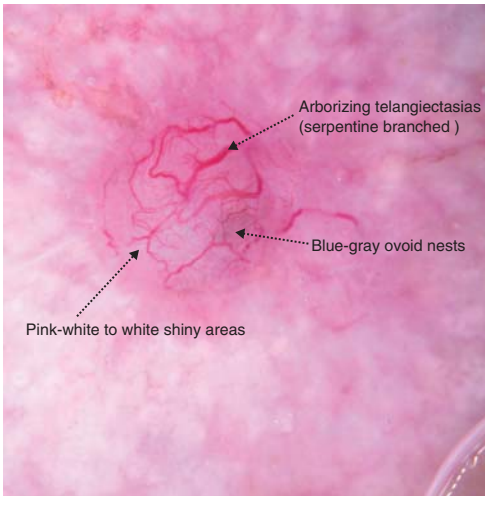
Understanding the patterns of early facial melanoma is critical for diagnosing this cancer. The pattern appears to change as the lesion evolves. A facial melanoma progression model has been described in which the earliest manifestation of melanoma in situ on sun-damaged skin are slate-gray dots and granules that may progress to form polygonal lines (zig-zag pattern) (Schiffner, 2000) (Figs. 9c.18–9c.24). The slate-gray dots represent either free melanin or melanin within macrophages. As the gray dots and granules accumulate around the follicles, the annular–granular pattern is formed. Later, short polygonal lines can be seen, which increase in size to become rhomboid structures. As melanoma cells within follicles multiply, asymmetric pigmented follicular openings can be visualized dermoscopically. Although asymmetric follicular openings can be seen in lentigines, in lentigines their color is tan to brown and in melanoma they often have a grayish hue. Asymmetric (grayish) pigmented follicular openings result when there is uneven invasion by melanoma cells located within hair follicles. In the final stage of the progression model, the rhomboid structures become thickened and the hair follicles are obliterated as the melanoma becomes more advanced. In advanced facial melanoma, white scar-like areas may also be present, representing regression. One last important point to highlight here is that amelanotic melanomas on the face have the same features as amelanotic melanomas on other body sites and the reader is encouraged to read the appropriate chapters in this book that describe the features of amelanotic tumors.

▲ **Figure 9c.6a** Clinical image of a pigmented BCC.



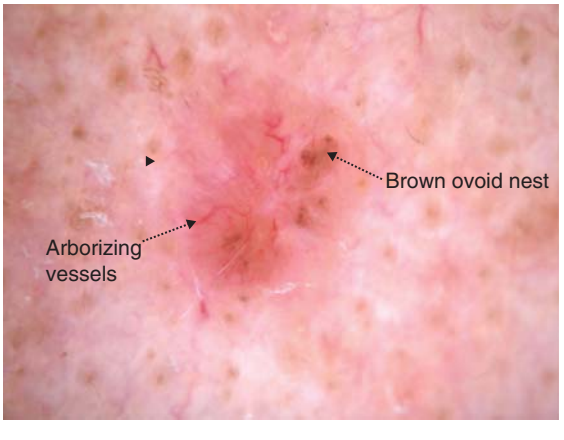
◀ **Figure 9c.6b** Dermoscopy of this BCC reveals blue-gray ovoid nests and arborizing vessels that are bright red and sharply in focus.

▲ **Figure 9c.7a** Clinical image of a BCC.



◀ **Figure 9c.7b** Dermoscopy image of a basal cell carcinoma demonstrating blue-gray ovoid nests, arborizing vessels, and a pink white shiny area.

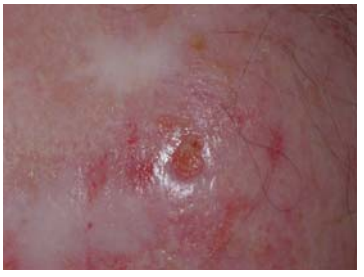
▲ **Figure 9c.8a** Clinical image.



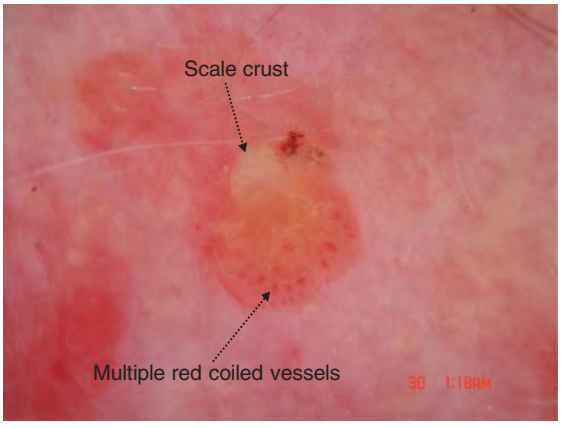
◀ **Figure 9c.8b** Basal cell carcinoma with telangiectasia and brown ovoid nests.

▲ **Figure 9c.9a** Clinical image.

◀ **Figure 9c.9b** Multiple dotted vessels (*arrow*) in a squamous cell carcinoma.

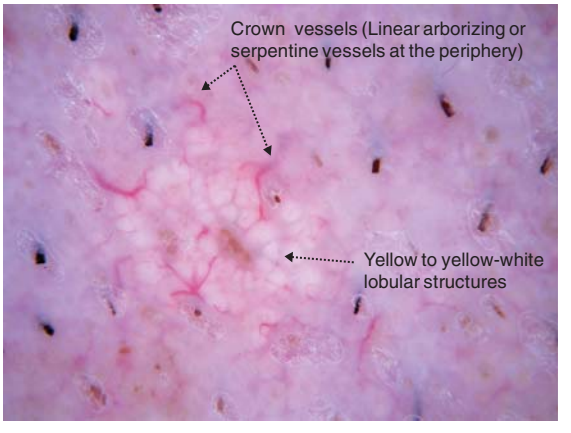


▲ **Figure 9c.10a** Clinical image.



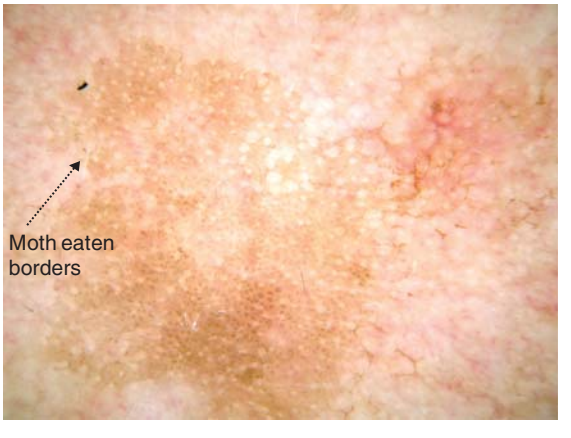
◀ **Figure 9c.10b** Glomerular vessels and scale crust in a squamous cell carcinoma.

▲ **Figure 9c.11a** Clinical image.



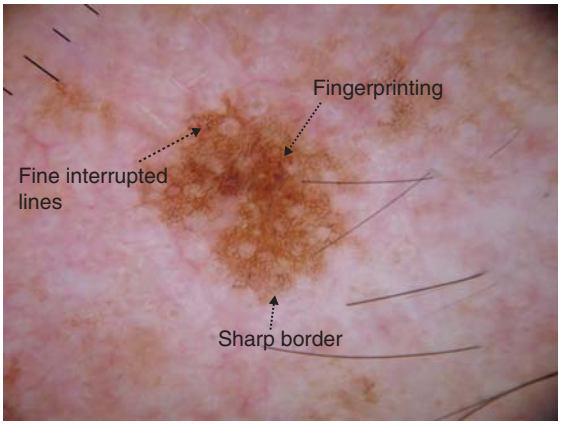
◀ **Figure 9c.11b** Sebaceous hyperplasia with yellow-white lobular structures and linear winding vessels at the periphery of the lesion, which are known as "crown vessels."

▲ **Figure 9c.12a** Clinical image.



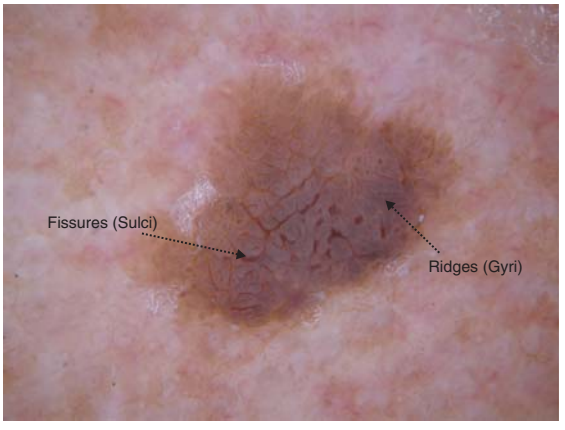
◀ **Figure 9c.12b** Solar lentigines may demonstrate the annular pattern with areas of light and dark brown and moth-eaten borders.

▲ **Figure 9c.13a** Clinical image.



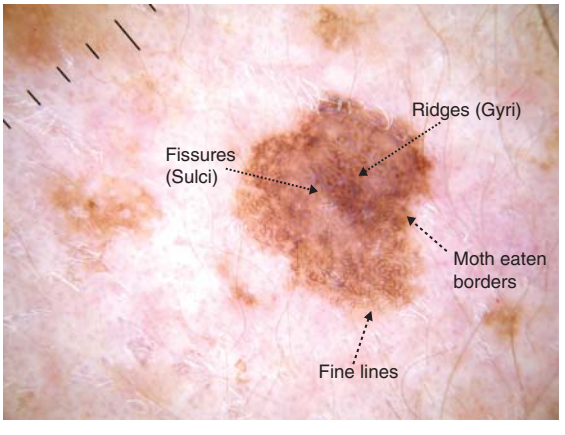
◀ **Figure 9c.13b** Reticular pattern with fingerprinting, fine interrupted lines and a sharp border may be seen in solar lentigines.

▲ **Figure 9c.14a** Clinical image.



◀ **Figure 9c.14b** Mature seborrheic keratosis on the face with ridges and fissures creating a cerebriform pattern.

▲ **Figure 9c.15a** Clinical image.



◀ **Figure 9c.15b** Seborrheic keratosis on the face with fine lines, ridges, fissures, and moth-eaten borders.

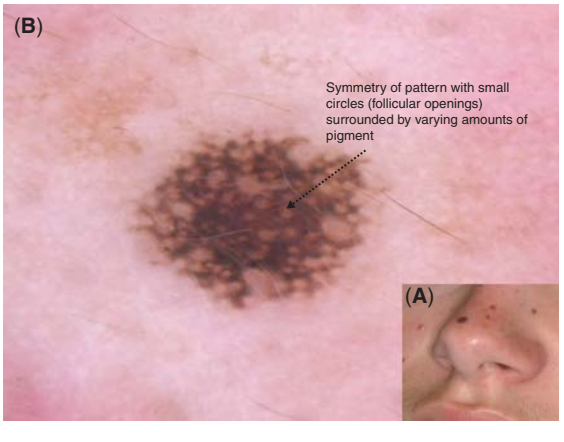
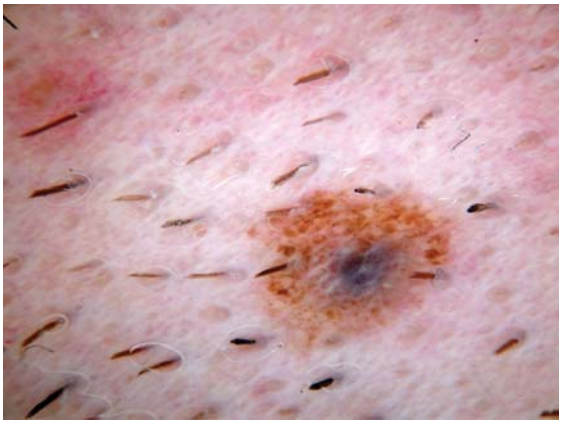


Figure 9c.16 (**A**) Clinical image. (**B**) Clark nevi junctional type with an annular pattern.

▲ **Figure 9c.17a** Clinical image.



◀ **Figure 9c.17b** Combined melanocytic nevi demonstrating a globular homogenous pattern.

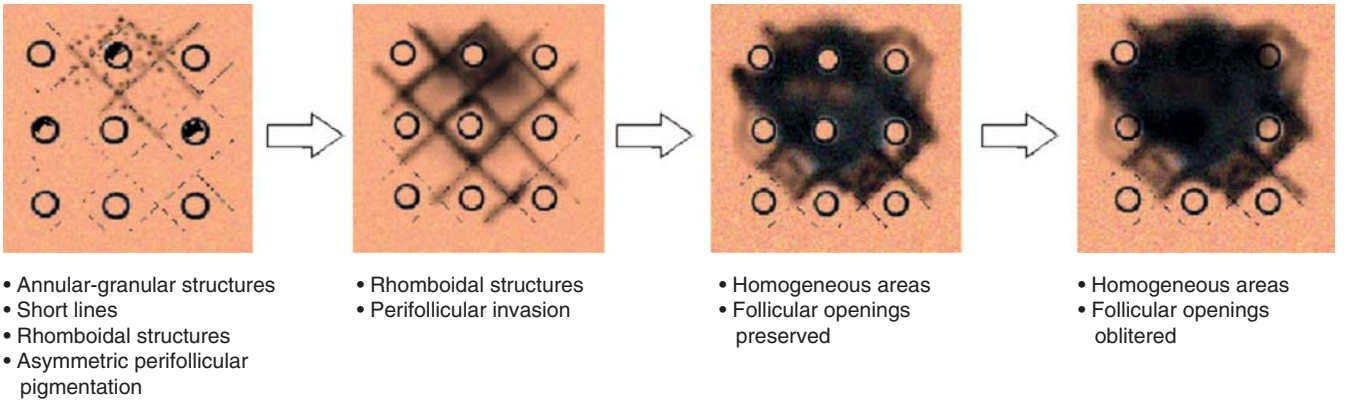


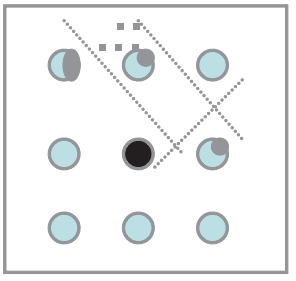
Figure 9c.18 Facial melanoma progression model with four stages whose characteristic features are outlined above. *Source*: From Schiffner, R., in: A.A. Marghoob, R.P. Braun, A.W. Kopf, eds. *Atlas of Dermoscopy*. Oxford: Taylor & Francis, 2005, Fig. 10.33.

Figure 9c.19 The facial melanoma progression model: stage 1 demonstrating annular–granular structures.

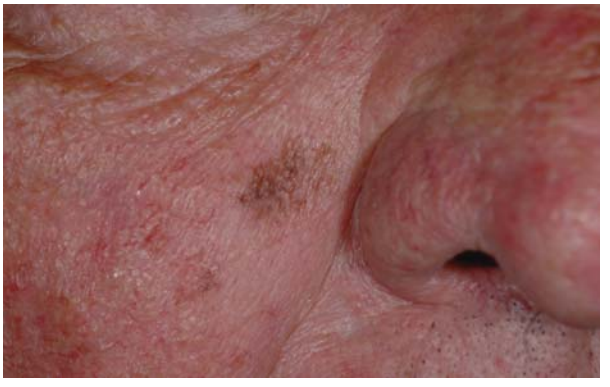
Dermoscopic features of facial melanoma include global features of asymmetry and multiple colors (Fig. 9c.25). Local features of facial melanoma include gray-brown pigmented follicular openings (Fig. 9c.26), irregular perifollicular hyperpigmentation (Fig. 9c.27), circles within circles (also known as isobars) (Fig. 9c.28), slate-gray to blue-gray dots and granules (Fig. 9c.29), rhomboid structures (Fig. 9c.30), and dark structureless areas obscuring the follicular openings (Fig. 9c.31) (Schiffner et al., 2000). Another criteria often seen in more advanced melanoma is the blue-white veil (Fig. 9c.32) (Zalaudek et al., 2003; Yadav et al., 1993) (also called by some authors a blue-white structure), which has been shown to correlate histologically with compact orthokeratosis overlying deeply located pigmented cells (Yadav et al., 1993).

Many of the criteria described for facial melanoma are not unique only to facial melanomas. For example, the annular–granular pattern can be seen in pigmented actinic keratoses and LPLK (Stolz et al., 2002; Schiffner et al., 2000). However, despite this overlap, when examining a facial lesion it is imperative that the entire lesion be evaluated dermoscopically and if any portion of the lesion manifests features suggestive of melanoma, even if only focally present, the lesion should be considered to be a possible melanoma (Argenziano et al., 2003). Facial melanoma patterns include annular patterns, reticular patterns, and nonspecific facial melanoma patterns (Fig. 9c.33).

The most common facial melanoma simulators include pigmented actinic keratoses, LPLK, and BCC. Pigmented actinic keratoses are



• Short polygonal lines



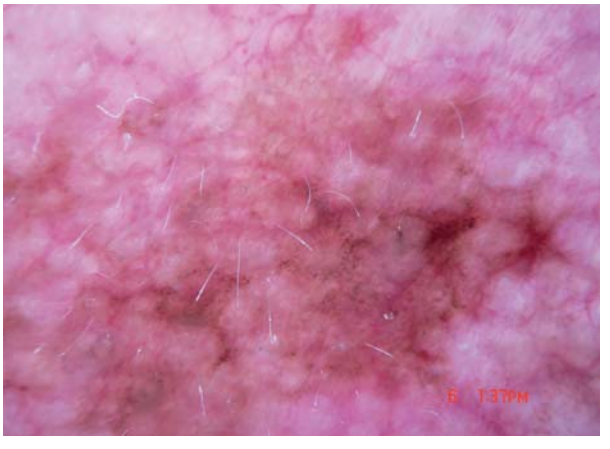
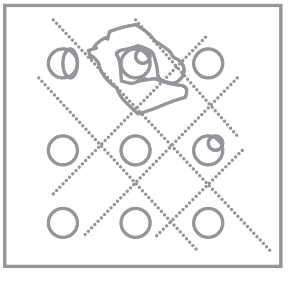
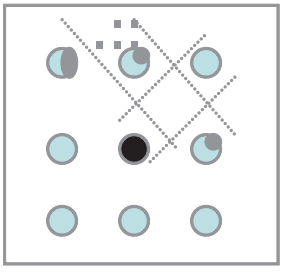


Figure 9c.20 The facial melanoma progression model: stage 1, demonstrating short polygonal lines.



• Romboidal structures

Figure 9c.21 The facial melanoma progression model: stage 1, demonstrating rhomboid structures.



• Romboidal structures
• Perifollicular invasion

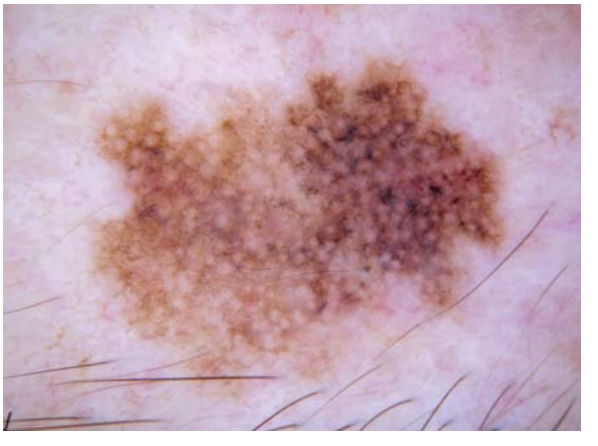
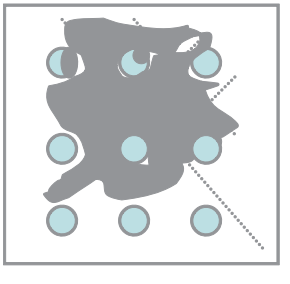
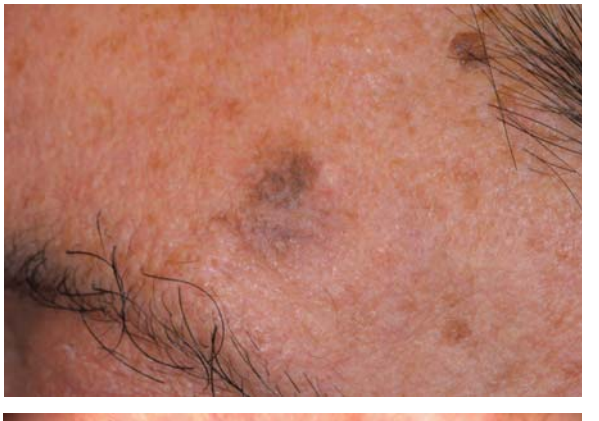


Figure 9c.22 The facial melanoma progression model: stage 2, demonstrating rhomboid structures and perifollicular invasion.



• Homogeneous areas
• Follicular openings preserved



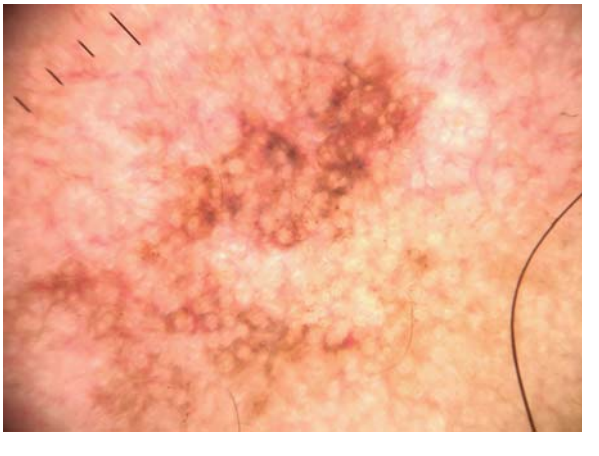


Figure 9c.23 The facial melanoma progression model: stage 3, demonstrating homogenous areas and follicular openings preserved.

• Homogeneous areas
• Follicular openings oblitered

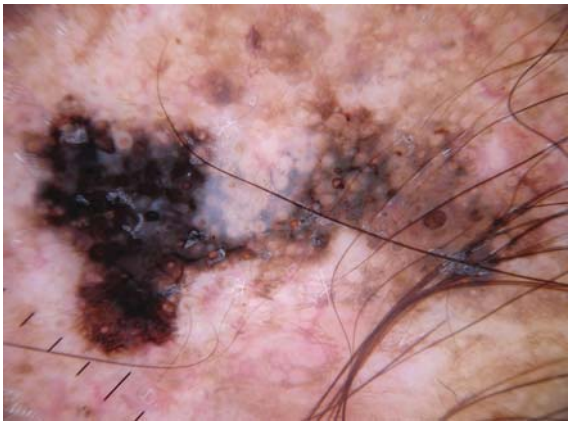
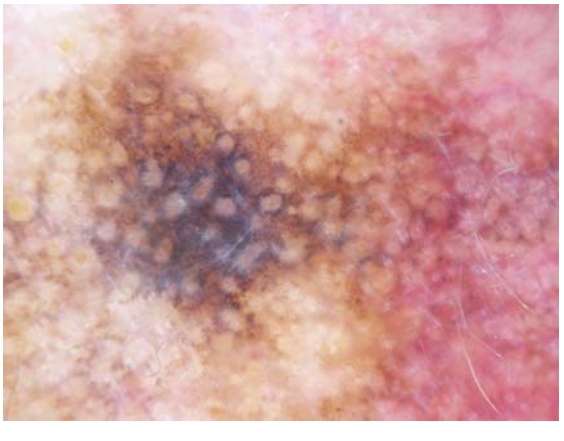


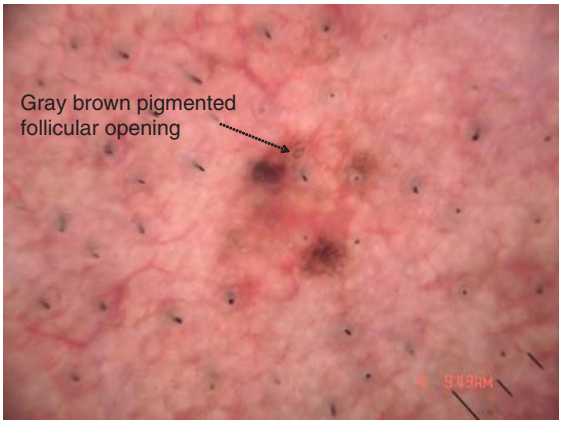
Figure 9c.24 The facial melanoma progression model: stage 4, demonstrating homogenous areas and follicular openings obliterated.

▲ **Figure 9c.25a** Clinical image.



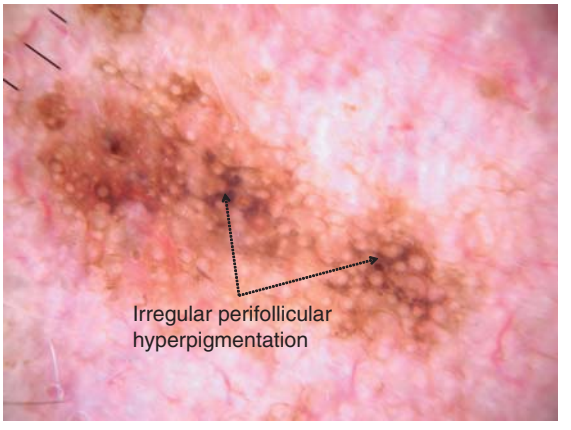
◀ **Figure 9c.25b** Facial melanomas have asymmetry and multiple colors. Diagnosis: lentigo maligna melanoma.

▲ **Figure 9c.26a** Clinical image.



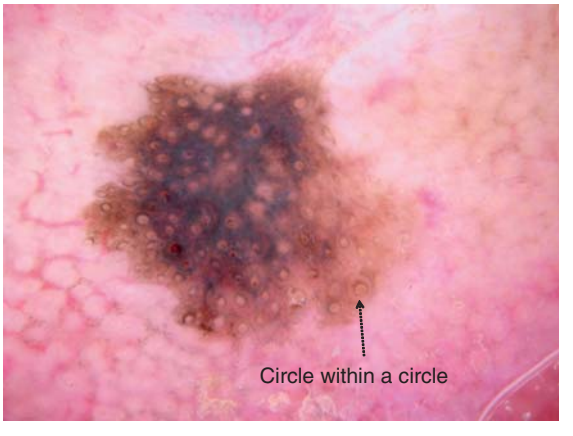
◀ **Figure 9c.26b** Gray-brown follicular openings. Diagnosis: lentigo maligna.

▲ **Figure 9c.27a** Clinical image.



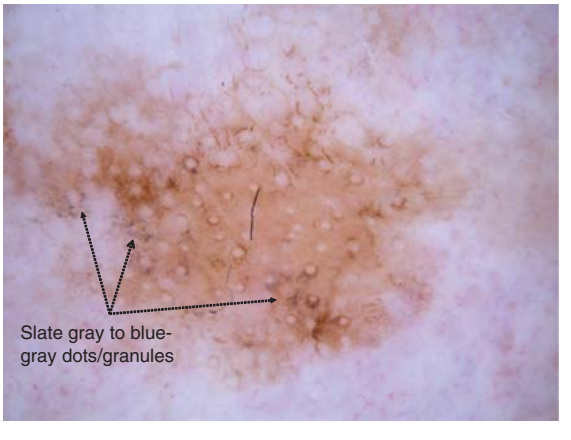
◀ **Figure 9c.27b** Irregular perifollicular hyperpigmentation. Diagnosis: lentigo maligna.

▲ **Figure 9c.28a** Clinical image.

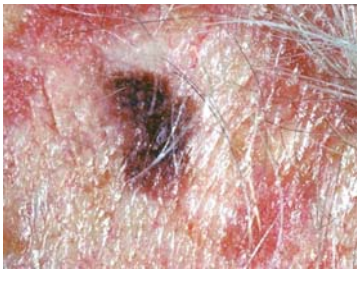


◀ **Figure 9c.28b** Circles within circles (isobars) are not commonly seen in lesions; however, when present they are suggestive of a diagnosis of lentigo maligna. Diagnosis: lentigo maligna.

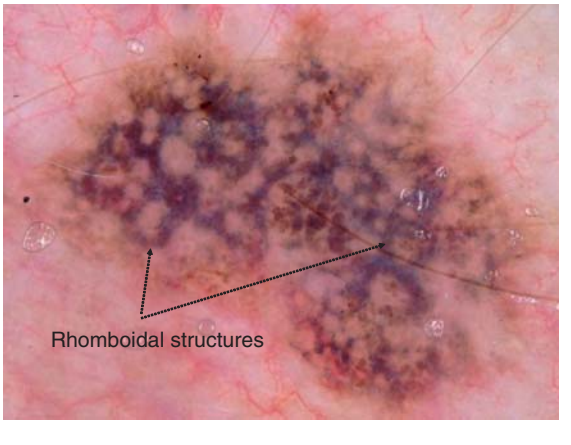
▲ **Figure 9c.29a** Clinical image.



◀ **Figure 9c.29b** Slate gray to blue-gray dots/granules. Diagnosis: lentigo maligna.

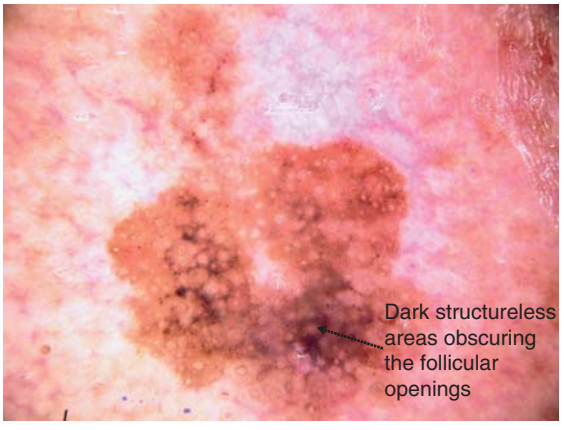


▲ **Figure 9c.30a** Clinical image.



◀ **Figure 9c.30b** Rhomboid structures. Diagnosis: lentigo maligna.

▲ **Figure 9c.31a** Clinical image.



◀ **Figure 9c.31b** Dark structureless areas obscuring the follicular openings. Diagnosis: lentigo maligna.

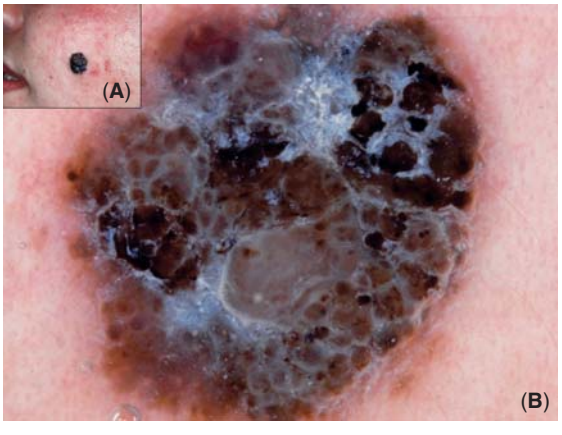


Figure 9c.32 (**A**) Clinical pattern. (**B**) The blue-white veil appearance on dermoscopy. Diagnosis: melanoma.

collision tumors of solar lentigines and actinic keratoses. They often have the dermoscopic features of melanoma, including asymmetrical pigmented follicular openings, polygonal lines, and gray dots/granules. The annular–granular pattern has been reported in pigmented actinic keratoses (Stolz et al., 2002; Schiffner et al., 2000). The helpful clues to the diagnosis of pigmented actinic keratoses include clinical feature of a fine scale, moth-eaten borders, fingerprinting, and fine interrupted lines, and a rough texture (Fig. 9c.34). However, there are many instances in which a clear diagnosis of pigmented actinic keratosis cannot be made dermoscopically and in these cases a histopathologic specimen should be obtained (Zalaudek, 2005).

Facial LPLK is another neoplasm difficult to differentiate from facial melanoma. LPLK is a fairly common lesion whose origin is not entirely certain; however, it is thought to be a process in which a pre-existing epidermal lesion undergoes regression (Prieto et al., 1993; Goette, 1980; Jang et al., 2000; Morgan et al., 2005). The pre-existing lesion is usually a solar lentigo, although it can also be an SK (Mehregan, 1975). In the literature, two general dermoscopic patterns have been described for LPLK: a diffuse granular pattern and a localized granular pattern (Mehregan, 1975; Elgart, 2001). The diffuse granular pattern is characterized by brownish-gray, reddish-brown, bluish-gray, or whitish-gray granules distributed throughout the lesion. The localized granular pattern is often seen in juxtaposition with dermoscopic features or criteria seen with solar lentigines and SK (Figs. 9c.35 and 9c.36). The granules in LPLK tend to be larger/coarser compared with the blue-gray fine dots that are seen in melanomas. However, it is important to remember that multiple blue-gray dots have been found in 45% of invasive melanomas and demonstrate a specificity of 91% for invasive melanoma (Zaballos et al., 2007). Thus, although the size of the granules in melanoma typically demonstrates fine granules as opposed to the coarse granules of LPLK, if the lesion does not manifest any other structures to confirm the diagnosis of LPLK, such as fingerprint-like lines, then the diagnosis should be considered uncertain and a biopsy should be contemplated (Mehregan, 1975).

Dark blue BCCs can at times be indistinguishable from thick melanomas. Sometimes focal areas within the basal cell may reveal structures, such as ovoid nests, arborizing vessels, or leaf-like areas, thus making the diagnosis relatively easy (Figs. 9c.37 and 9c.38). The diagnosis of a pigmented BCC precludes the presence of a pigment network or pseudonetwork, thus if a pigment network or pseudonetwork is present then the lesion is not a pigmented BCC (Zaballos et al., 2007). Furthermore, to diagnose a pigmented BCC, at least one of the following six criteria should be present: spoke-wheel-like areas, large gray-blue ovoid nests, arborizing telangiectasias, and leaf-like structures (Zaballos et al., 2007). However, it is important to remember that the decision to biopsy will not change even if a BCC is incorrectly diagnosed as a melanoma or vice-versa under dermoscopy—the fact that the lesion has features of a malignancy will remain undisputed.

The diagnosis of facial melanoma remains challenging. Many criteria have been described to aid in the differentiation between melanoma and melanoma simulators; however, if the diagnosis remains unclear, histopathologic confirmation is always the final arbitrator.

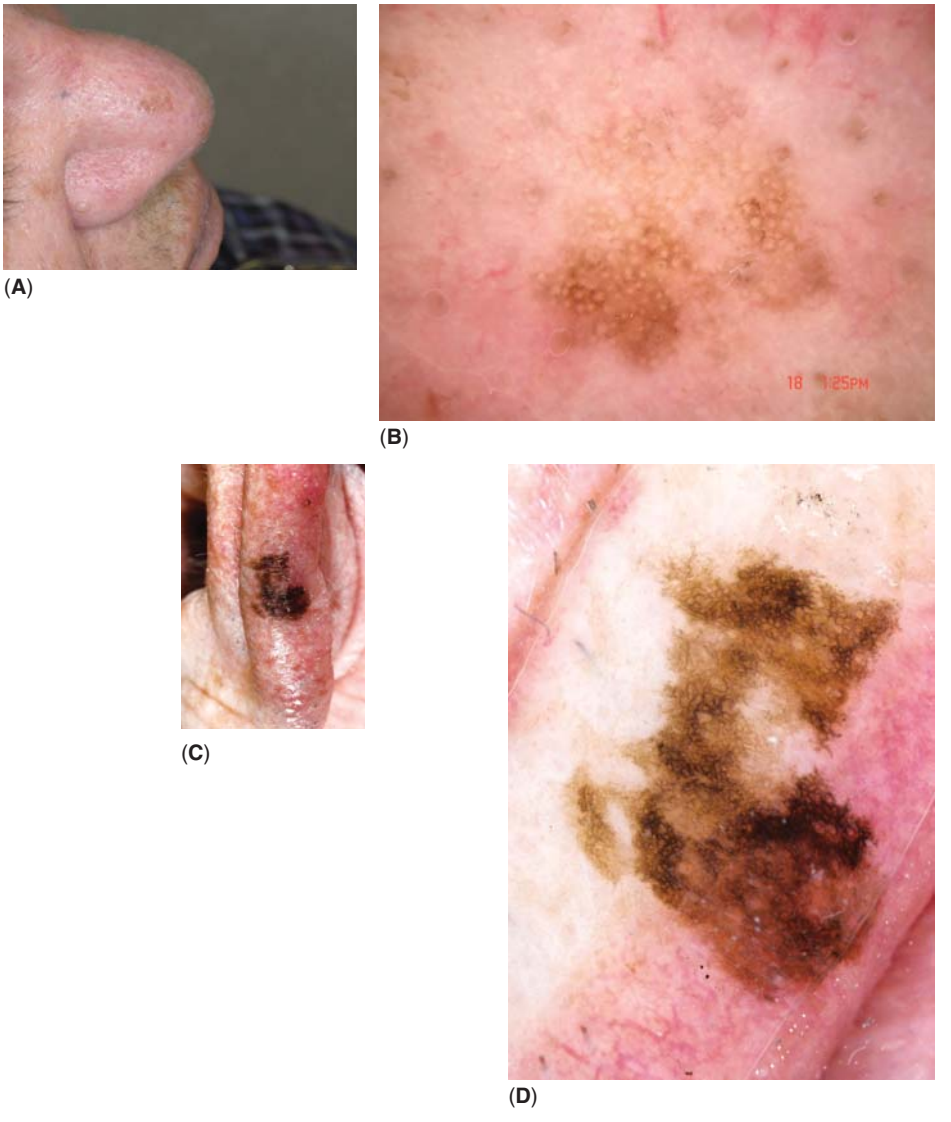
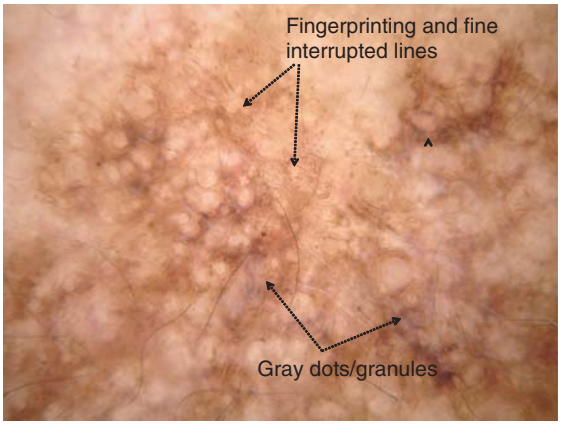


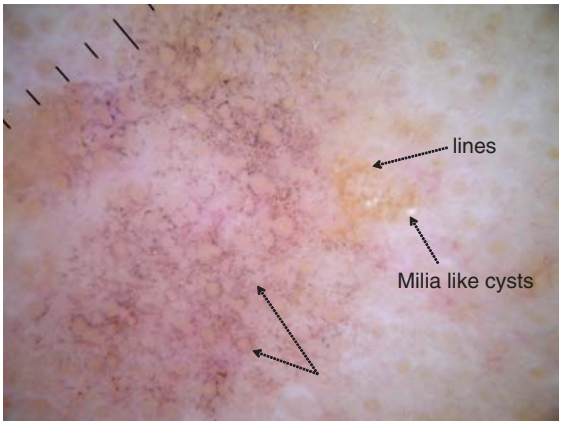
Figure 9c.33 Facial melanomas may have (A, B) annular or (C, D) reticular patterns.

▲ **Figure 9c.34a** Clinical image showing a fine scale (*arrowhead*).

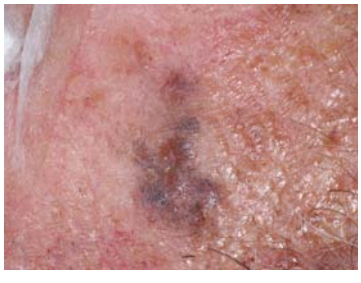


◀ **Figure 9c.34b** Pigmented actinic keratosis with fingerprinting and fine interrupted lines and gray dots/granules.

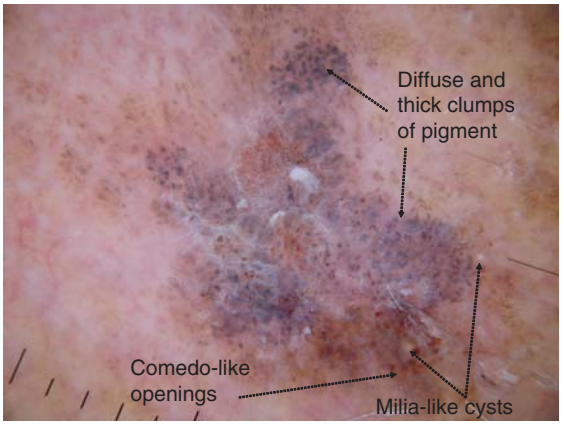
▲ **Figure 9c.35a** Clinical image.



◀ **Figure 9c.35b** Lichen planus-like keratosis with a diffuse granular pattern (*arrows*), milia-like cysts and a few fine lines.

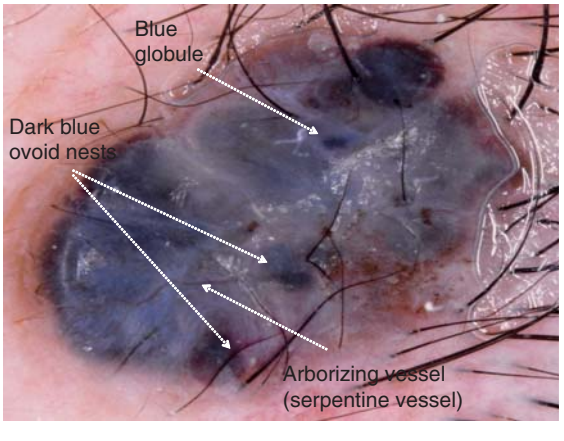


▲ **Figure 9c.36a** Clinical image.



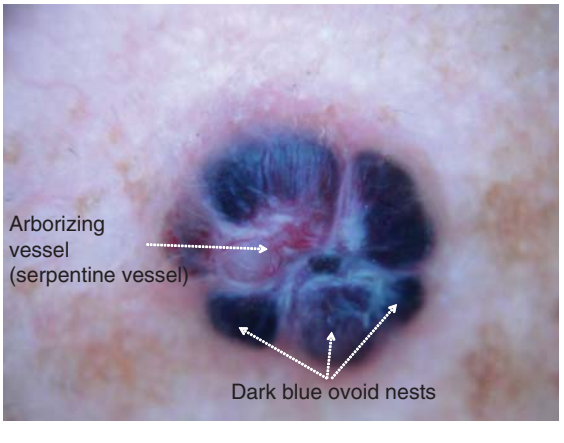
◀ **Figure 9c.36b** Lichen planus-like keratosis with milia-like cysts, comedo-like openings, and clumps of pigment.

▲ **Figure 9c.37a** Clinical image.



◀ **Figure 9c.37b** Pigmented basal cell carcinoma with a blue-white veil, blue globules, blue-brown ovoid nests, and arborizing vessels.

▲ **Figure 9c.38a** Clinical image.



◀ **Figure 9c.38b** Pigmented basal cell carcinoma with a blue-white veil, blue ovoid nests, and arborizing vessels.

Key Points

1. The dermoscopic features of BCC, SCC, and hemangioma on the face are the same as those found in the similar lesions on non-facial skin.
2. It is often a challenge to exclude the diagnosis of melanoma is some LPLK and solar lentigines on the face.
3. Pigmented lesions on the face manifest a pseudo-network pattern. The holes of the pseudo-network pattern correspond to adnexal openings.
4. The primary aim when evaluating a pigmented lesion on the face is to rule out melanoma. The management algorithm for facial lesions is located in chapter 8d, figure 8d.21.

REFERENCES

Argenziano, G., Soyer, H.P., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol*, 48, 679–93.

Carey, F.A. & Hogan, J.M., 1990, The relationship of sun exposure and solar elastosis to skin cancer in high risk population. *Ir J Med Sci*, 159, 44–7.

Elgart, G.W., 2001, Seborrheic keratoses, solar lentigines, and lichenoid keratoses. Dermatoscopic features and correlation to histology and clinical signs. *Dermatol Clin*, 19, 347–57.

Foley, P.A., Marks, R. & Dorevitch, A.P., 1993, Lentigo maligna is more common on the driver's side. *Arch Dermatol*, 129, 1211–12.

Goette, D.K., 1980, Benign lichenoid keratosis. *Arch Dermatol*, 116, 780–2.

Jang, K.A., Kim, S.H., Choi, J.H., et al., 2000, Lichenoid keratosis: a clinicopathologic study of 17 patients. *J Am Acad Dermatol*, 43, 511–16.

Magnus, K., 1981, Habits of sun exposure and risk of malignant melanoma: an analysis of incidence rates in Norway 1955–1977 by cohort, sex, age and primary tumor side. *Cancer*, 48, 2329–35.

Mehregan, A.H., 1975, Lentigo senilis and its evolution. *J Invest Dermatol*, 65, 429–33.

Morgan, M.B., Stevens, G.L. & Switlyk, S., 2005, Benign lichenoid keratosis: a clinical and pathologic reappraisal of 1040 cases. *Am J Dermatopathol*, 27, 387–92.

Prieto, V.G., Casal, M. & McNutt, N.S., 1993, Lichen planus-like keratosis. A clinical and histological reexamination. *Am J Surg Pathol*, 17, 259–63.

Schiffner, R., Schiffner-Rohe, J., Voft, T., et al., 2000, Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol*, 42, 25–32.

Stolz, W., Braun-Falco, O., Bilek, P. & Landthaler, M., 2002, *Color Atlas of Dermatoscopy*. Oxford: Blackwell Scientific Publications.

Walter, S.D., Marret, L.D., From, L., et al., 1990, The association of cutaneous malignant melanoma with the use of sunbeds and sunlamps. *Am J Epidemiol*, 131, 232–43.

Yadav, S., Vossaert, K.A., Kopf, A.W., et al., 1993, Histopathologic correlates of structures seen on dermoscopy (epiluminescence microscopy). *Am J Dermatopathol*, 15, 297–305.

Zaballos, P., Blazquez, S., Puig, S., et al., 2007, Dermoscopic pattern of intermediate stage in seborrheic keratosis regressing to lichenoid keratosis: report of 24 cases. *Br J Dermatol*, 157, 266–72.

Zalaudek, I., Argenziano, G., Soyer, H.P., et al., 2003, Clinically equivocal melanocytic skin lesions with features of regression – a dermoscopic-pathologic study. *Br J Dermatol*, 150, 64–71.

Zalaudek, I., Ferrara, G., Leinweber, B., et al., 2005, Pitfalls in the clinical and dermoscopic diagnosis of pigmented actinic keratosis. *J Am Acad Dermatol*, 53, 1071–4.

9d Hair and scalp (trichoscopy)

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TRICHOSCOPY: USING THE DERMOSCOPE FOR DIAGNOSING HAIR AND SCALP DISORDERS

The standard methods used to diagnose hair and scalp disorders are clinical inspection, pull test, trichogram, and histopathology. They vary in sensitivity, reproducibility, and invasiveness. Studies show that the use of dermoscopy of hair and scalp (trichoscopy) in the clinical evaluation of hair and scalp disorders improves diagnostic capability beyond simple clinical inspection (Inui et al., 2007; Inui et al., 2008b; Inui, 2011; Kossard & Zagarella, 1993; Lacarrubba et al., 2004; Olszewska et al., 2008; Ross et al., 2006; Rudnicka et al., 2008b; Toncić et al., 2007; Tosti, 2007; Trüeb, 2010). Thus, trichoscopy is gaining popularity as a valuable tool in differential diagnosis of hair and scalp disorders.

In clinical practice trichoscopy may be performed with the use of a hand-held dermoscope. Videodermoscopes have the additional benefit of allowing precise measurement of visualized structures (i.e., hair shaft thickness), making them more suitable for monitoring disease severity and for clinical trials (Olszewska & Rudnicka, 2005) than for rapid in-office diagnosis. Nonpolarized light trichoscopy may be performed with any interface solution, including 90% isopropanol, 70% ethanol, ultrasound gel, or water (Gewirtzman et al., 2003). In some cases it may be beneficial to perform dry dermoscopy in addition to trichoscopy with immersion fluid (Inui, 2007).

The images presented in this chapter were taken with a Dermlite Foto device attached to a canon G7 camera using an alcoholic solution as immersion liquid.

PATTERNS OF SCALP DISEASE REVEALED BY TRICHOSCOPY

Follicular Ostia

Follicular ostia encompass distinctive peripilar features that relate to the condition of the hair follicle.

Yellow dots (Fig. 9d.1) are characterized by an array of quite monomorphous, although variably sized, yellow to yellow-pink or yellow-brown, round or polycyclic dots that are devoid of hair or contain dystrophic or vellus hair. They may correspond to (dilated) follicular infundibula that contain sebaceous and keratinous material (Lacarrubba et al., 2004). Regularly distributed yellow dots are typical of alopecia areata (Ross et al., 2006; Inui et al., 2008a). They are found in a majority of patients with alopecia areata and are considered a marker of disease severity (Inui et al., 2008a; Rakowska et al., 2009a).

There are controversies regarding the presence and frequency of yellow dots in androgenetic alopecia. According to various literature sources yellow dots are present in 8–66% of these patients (Ross et al., 2006; Rakowska et al., 2009a; Inui et al., 2010). Yellow dots in androgenetic alopecia are usually homogenously colored from light-yellow to dark-brown. They are believed to correspond to sebaceous material secreted by intact sebaceous glands associated with miniaturized hair follicles (Olszewska et al., 2010). In androgenic alopecia the number of yellow dots is significantly higher in the frontal area as compared with the occipital area. Rakowska et al. (2010) evaluated the number of yellow dots in patients with female androgenetic alopecia and found $8.86 \pm 4.8/4$ yellow dots per field of vision (at 70-fold magnification) in the frontal area. The corresponding number in the occipital area was 1.59 ± 2.0 (Olszewska et al., 2010).

Large yellow dots are characteristic for discoid lupus erythematosus and folliculitis capitis abscedens and suphodiens (Rakowska et al., 2009a).

Thus, yellow dots can be observed in different types of hair loss. Their structure, number, distribution, and location on the scalp may provide a key to establish the correct diagnosis.

Black dots (Fig. 9d.2), formerly called "cadaverized hairs," represent pigmented hairs broken or destroyed at the level of the scalp. They are seen in acute alopecia areata, tinea capitis, trichotillomania, perifolliculitis abscedens et suffodiens of scalp, and anagen alopecia after chemotherapy (Rudnicka et al., 2008a, Rudnicka et al., 2011). In alopecia areata the presence of black dots is a marker of disease activity and is considered a negative prognostic marker (Inui et al., 2010). Black dots are not present in healthy individuals, androgenic alopecia, or telogen effluvium (Rudnicka et al., 2008a; Rakowska, 2009).

Follicular hyperkeratosis (Fig. 9d.3) is characterized by the accumulation of excessive keratin in hair follicles leading to follicular plugging, giving in trichoscopy the appearance of large yellow (or brown-yellow) dots.

Brown perifollicular discoloration ("*perifollicular hyperpigmentation*," *peripilar sign*) (Fig. 9d.4) is characterized by the presence of a brown halo, roughly 1 mm in diameter, at the follicular ostium around the emerging hair shaft or in the absence of a hair shaft. This finding was initially linked to superficial perifollicular lymphocytic infiltrates in early androgenic alopecia (Deloche et al., 2004; Ross et al., 2006). Later research showed that this is a nonspecific sign, present in various forms of hair loss and in healthy individuals (Rakowska, 2009; Rudnicka et al., 2011). In healthy females, the average number of follicular ostia with perifollicular discoloration is 4.6%, but numbers ranging up to 25% are occasionally observed in healthy females with no other features of hair or scalp disease (Rakowska, 2009b). A high percentage of follicular ostia surrounded by a brown discoloration is considered by some clinicians to be a feature of active telogen effluvium or "complicated androgenic alopecia" and a negative prognostic factor for hair loss within few months following this finding in trichoscopy.

Empty follicles or empty follicular ostia (Fig. 9d.5) may represent the physiologic interval of the hair cycle in which the hair follicle remains empty after the telogen hair has been extruded and before a new anagen hair emerges (called lag phase or kenogen: Rebora et al., 2002; Guarrera et al., 2005). During kenogen, the hair follicle rests physiologically. The number of empty hair follicles is visibly increased in telogen effluvium, androgenic alopecia, and alopecia areata. Some clinicians prefer to calculate the number of empty hair follicles and yellow dots together. The rationale behind this idea is that: (*i*) in a vast majority of cases the yellow dots represent empty hair follicles, which differ only by the presence of sebaceous or hyperkeratotic material in the infundibulum, (*ii*) it may be difficult to distinguish an empty hair follicle from a yellow dot.

White dots (Fig. 9d.6) and ***loss of follicular ostia*** (Fig. 9d.7) are a hallmark of scarring alopecia (cicatricial alopecia). The term scarring alopecia encompasses a diverse group of disorders characterized by permanent destruction of the hair follicle and irreversible hair loss. In primary folliculocentric scarring alopecia (i.e., lichen planopilaris,) white dots represent sites of selective follicular destruction. To be recognizable, a contrast between the focal loss of melanin and adjacent pigmented epidermis is essential. For this reason visibility of white dots in primary scarring alopecia is less conspicuous in light-skinned (skin phototype I) individuals. In advanced primary scarring alopecia white dots become confluent to form areas lacking follicular ostia. In some diseases leading to scarring alopecia (i.e., discoid lupus erythematosus) areas lacking follicular ostia develop without preceding the presence of white dots.

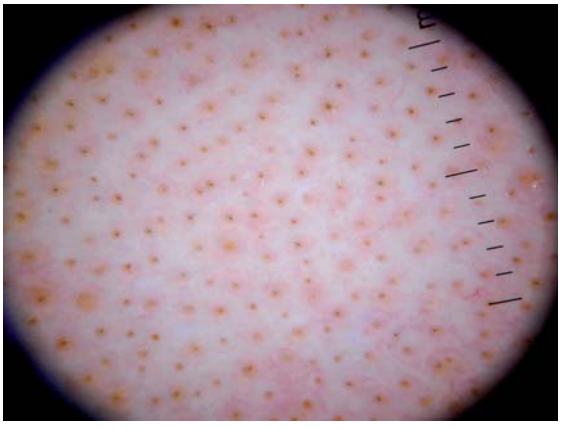


Figure 9d.1 Yellow dots. Multiple yellow round structures devoid of hair. Yellow dots in a regular distribution are characteristic of alopecia areata.

Figure 9d.2 Black dots are pigmented hairs broken or destroyed at the level of the scalp. Black dots are typically seen in active alopecia areata, but may be present in other diseases, such as trichotillomania, lichen planopilaris, monilethrix, and few others.

Figure 9d.3 Follicular keratosis (large yellow dots) in discoid lupus erythematodes.

Figure 9d.4 Peripilar signs (brown perifollicular discoloration; *black arrow*) may be observed in androgenetic alopecia and telogen effluvium. In this patient with androgenetic alopecia, yellow dots and hair shaft thickness diversity are also observed.

Figure 9d.5 Empty hair follicles. Other features seen in this image are coiled hairs and broken hairs. These features are indicative of trichotillomania.

Figure 9d.6 White dots in scarring alopecia representing selective follicular destruction.

Figure 9d.7 Loss of follicular ostia in scarring alopecia. Note also the actinic damage of the skin.

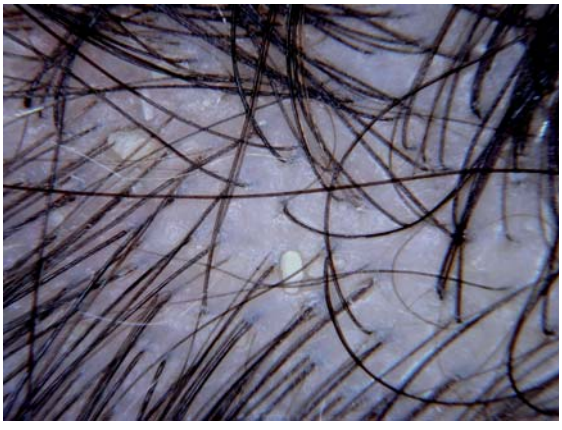


Figure 9d.9 Follicular filiform spicules of monoclonal paraprotein casts associated with multiple myeloma.

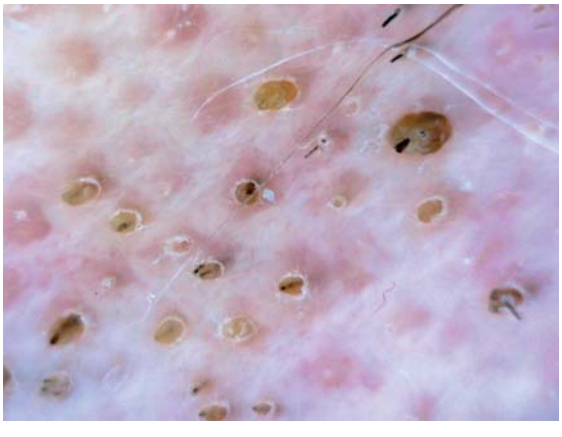


Figure 9d.8 Follicular mucinosis in a patient with folliculotropic mycosis fungoides (WHO-EORTC classification Stage IVa). Follicular plugs of mucin in dilated ostia.

Figure 9d.10 Vascular pattern of simple red loops in a normal epidermis.

White dots resulting from follicular/perifollicular fibrosis are usually over 200 μm in diameter, evenly colored with irregular borders.

In African-American patients (Fitzpatrick skin phototypes V and VI) with prominent perifollicular pigmentation, follicular ostia appear white giving a "pinpoint white dot" manifestation. These prominent small white dots are clearly visible on the contrasting background of pigment network. They are present in healthy individuals and in patients with frontal fibrosing alopecia, lichen planopilaris, alopecia areata, androgenetic alopecia, and central centrifugal cicatricial alopecia (Abraham et al., 2010).

Follicular mucinosis (Fig. 9d.8) is an uncommon condition, presenting clinically as follicular papules or plaques with associated hair loss, most commonly on the face, neck, and scalp. Follicular mucin presents by trichoscopy as follicular plugs of amorphous material in dilated follicular ostia. The disease may be primary (idiopathic) or secondary to mycosis fungoides, reticulosis, and a number of other diseases.

Follicular filiform spicules (Fig. 9d.9) represent another rare paraneoplastic phenomenon associated with multiple myeloma. The eruption is characterized by multiple hyperkeratotic spicules, usually of the face, nose, and scalp (Braun et al., 2002).

BLOOD VESSELS

Vascular features reflect abnormalities in the skin capillary loop network observed in various conditions of the scalp.

Simple red loops (Fig. 9d.10) are seen in a normal epidermis. The pattern is characterized by multiple, fine, red lasso- or hairpin-shaped structures that are regularly spaced.

Arborizing vessels (Figs. 9d.11, 9d.12) are characterized by a tree-like terminal branching of blood vessels. A few thin arborizing vessels may be present in healthy individuals. Multiple thin arborizing vessels are a hallmark of seborrheic dermatitis. Thick, focally arranged arborizing vessels are characteristic of discoid lupus erythematosus. This feature of discoid lupus erythematosus can lead to a misdiagnosis of basal cell carcinoma (Duque-Estrada et al., 2010; Rudnicka et al., 2011).

Very thin or absent blood vessels may be observed in healthy individuals, but are common in patients with diseases associated with systemic vasoconstriction, such as hyperthyroidism or scleroderma (Rudnicka et al., 2011).

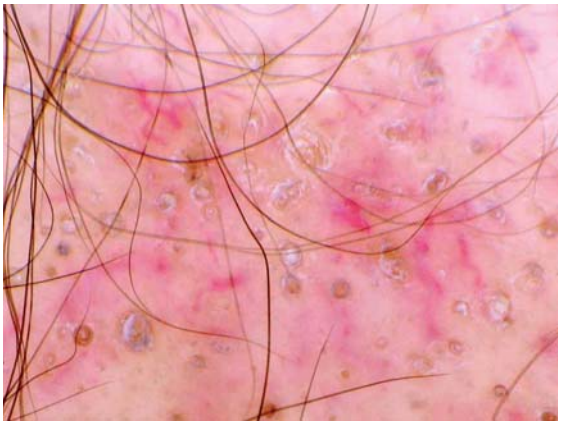


Figure 9d.11 Arborizing vessels in a patient with discoid lupus erythematodes. These vascular structures have a wider caliber than normal vascular loops.

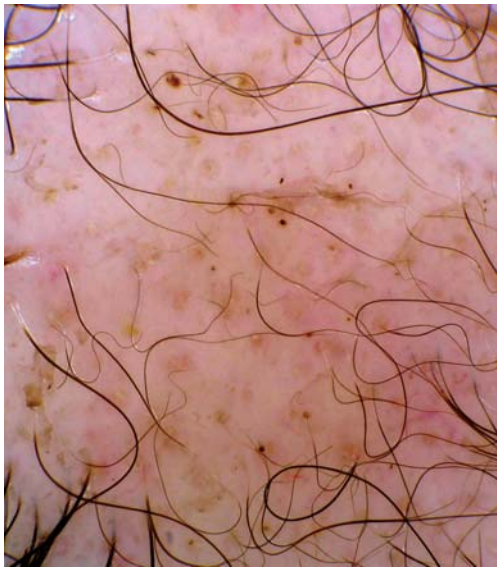


Figure 9d.12 A chronic scarred lesion of discoid lupus erythematosus. Absent vascular loops in the center of the lesion and arborizing vessels at the periphery, indicating peripheral disease activity.

Figure 9d.13 Twisted red loops in psoriasis with diffuse homogenous distribution.

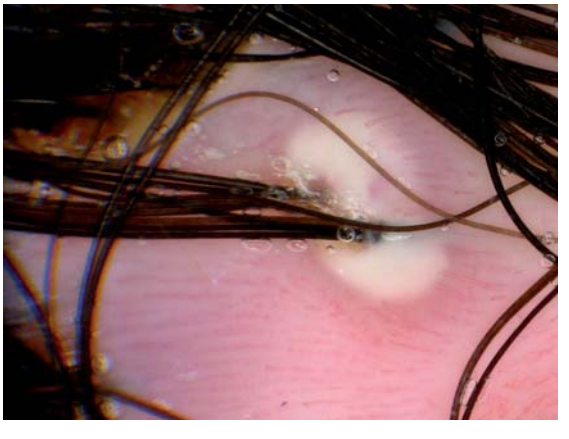


Figure 9d.14 Elongated vessels concentrated around affected follicles in a case of tufted folliculitis.

Twisted red loops are multiple, relatively evenly spaced, twisted loops in a homogenous distribution—a feature of psoriasis (Fig. 9d.13), Occasionally, twisted loops may be observed around affected follicles in folliculitis decalvans (Fig. 9d.14).

HONEYCOMB PIGMENT PATTERN

The honeycomb pigment pattern on the scalp is characterized by a relatively homogenous pigment network of adjoining brown rings and is observed in healthy individuals with darker skin phototypes. This finding is also common in persons with lighter phototypes, who, due to hair loss, receive increased sun exposure of the skin of the scalp. Its distribution is diffuse in bald scalp, and multifocal when some hairs remain in the area (Fig. 9d.15).

SCALING

Scaling is a nonspecific feature of reactive epidermal hyperproliferation with parakeratosis. The corneocytes are shed in large clumps, which appear as white or grayish patches on the scalp (Fig. 9d.16). Depending on the cause, the scales differ in localization, size, and greasiness (pityriasis simplex, pityrasis steatoides, pityriasis amiantacea). Scaling severity can be graded semi-quantitatively by trichoscopy from 0 to 4, where zero stands for no scaling and 4 for severe scaling in the whole field of vision (Ross et al., 2006, Rudnicka et al., 2011).

HAIR SHAFT PATTERNS

Hair shaft patterns reflect features that relate to the production and maintenance of the hair shaft.

Hair shaft diameter heterogeneity (Fig. 9d.17) relates to the presence of hairs with different caliber. This finding is typical of androgenetic alopecia and reflects progressive hair follicle miniaturization due to this condition (de Lacharrière et al., 2001; Rakowska et al., 2010).

Dystrophic hairs represent hairs that have fractured tips due to any process inhibiting cell division in the hair matrix. Severe inhibition leads to fracture, as a consequence of marked narrowing of the hair shaft. The hair

Figure 9d.15 Honeycomb pigment pattern due to actinic damage of the scalp in a patient with hair loss.

Figure 9d.17 Hair shaft thickness heterogeneity is a hallmark finding of androgenetic alopecia. Multiple hairs with different caliber are present. This finding is typical for progressive hair follicle miniaturization.

Figure 9d.16 Scaling in a patient with pityriasis simplex.

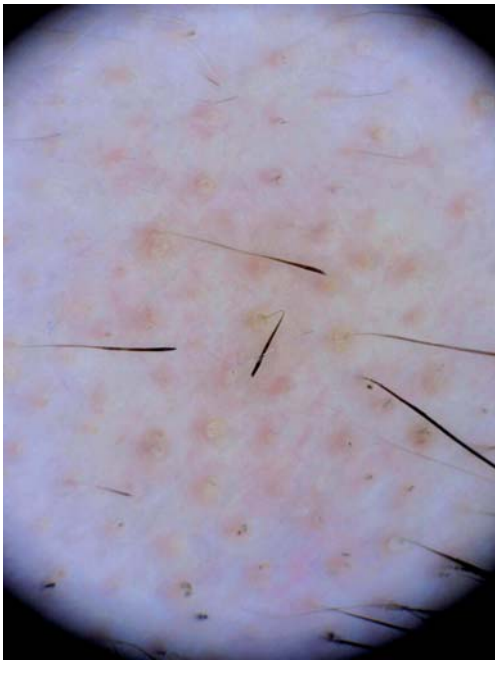


Figure 9d.18 Exclamation mark hairs in alopecia areata. Narrowing hair shafts toward the follicle ostia.

shafts may be fractured before emergence from the scalp and then appears as *black dots*. A hair shaft, which undergoes progressive thinning appears as a short **microexclamation mark hair** (Fig. 9d.18). This feature has to be distinguished from dystrophic hair roots seen in a trichogram, where the fiber is broken at the level of the keratogenous zone and a fractured proximal end is visible.

Hair tufting refers to the emergence of several hair shafts from dilated follicular ostia. In healthy individuals the number of hairs emerging from one follicular opening is 2–4 (Rakowska, 2009). In tufted folliculitis the number of hair shafts in follicular opening is significantly increased with the usual number ranging from 5 to 20 (Fig. 9d.19) (Smith et al.,1978).

Hair shaft abnormalities result form genetic conditions and/or exogenous factors affecting the integrity of the hair shaft. Hair shaft abnormalities may occur as localized or generalized disorders. Classic diagnosis is based on microscopic examination of the hair shaft. Trichoscopy is an effective tool for quick diagnosis of both congenital and acquired hair shaft disorders. Hair shaft abnormalities that can be visualized by dermoscopy include *monilethrix, pili torti, pili canaliculi et trianguli, pili annulati, trichorrhexis invaginata, trichorrhexis nodosa* and acquired features, such as microexclamation mark hairs, comma hairs, or vellus hairs.

TRICHOSCOPY IN HAIR DISORDERS

Monilethrix is characterized by a beaded appearance of the hair due to periodic thinning of the shaft. The uncommon hereditary condition is transmitted as an autosomal dominant trait. The phenotype results in hair fragility and patchy dystrophic alopecia. Alopecia is more severe in the occipital and parietal region that is more exposed to friction. Typically the occipital scalp also presents with follicular keratosis. Trichoscopy reveals hair shafts with uniform elliptical nodes and intermittent constrictions. Hairs are bent regularly at multiple locations and have a tendency to bend and fracture at constriction sites. The term "regularly bended ribbon sign" or "regularly twisted ribbon sign" was suggested for this specific trichoscopy feature of monilethrix (Rakowska et al., 2007).

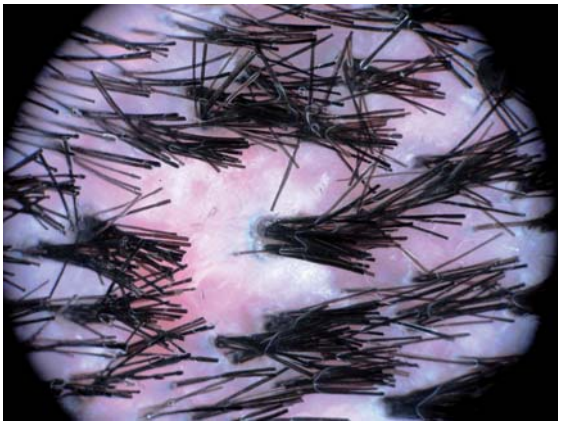


Figure 9d.19 Hair tufting. Emergence of several hair shafts together from one dilated ostia.

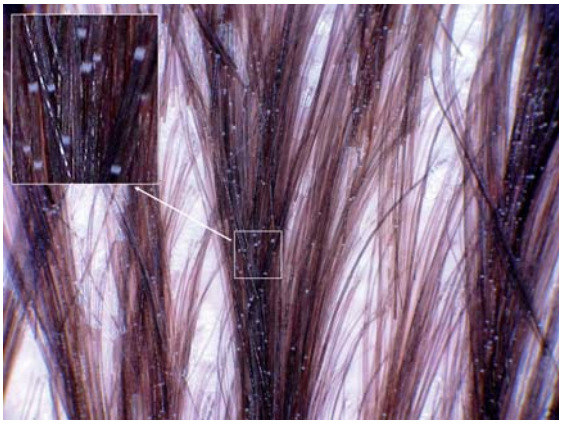


Figure 9d.21 Trichorrhexis nodosa. Broken hairs with nodes along the hair shaft.

Figure 9d.20 Pili torti in a patient with lichen planopilaris. Twisted hairs in an area of inflammatory and fibrotic changes.

Pili torti is characterized by hair that is flattened and twisted through 180° on its axis at varying intervals. The hair can additionally be grooved and has then also been termed ***pili torti et canaliculi*** (Trüeb et al., 1997). The hair shaft anomaly can be seen as an isolated hereditary trait, in a number of genetic syndromes, including Menkes kinky hair syndrome, Björnstad syndrome (with sensorineural deafness), and the ectodermal dysplasias. More commonly, it is found as *acquired pili torti* around the edges of patches of cicatricial alopecia, particularly lichen planopilaris (Fig. 9d.20), where local inflammatory and fibrosing processes distort the hair follicle. Trichoscopy of pili torti shows regular twists of the hair shaft along the long axis (at high magnification) and hair shafts bent at different angles at irregular intervals (with a handheld dermoscope). Usually only some of the hairs on the scalp, and only a part of the hair shaft length is affected (Rakowska et al., 2009b; Rudnicka et al., 2011).

Pili canaliculi et trianguli refers to the triangular hair shafts with longitudinal grooving underlying the uncombable hair syndrome. This feature may only be observed by videodermoscopy at high magnification (50-fold and higher).

Pili annulati are defined by characteristic alternating light and dark banding in the hair shaft, due to air-filled spaces between the macrofibrillar units of the hair cortex. Their significance lies in that affected hair is more susceptible to increased fragility, particularly in combination with androgenetic alopecia (Hofbauer et al., 2001).

Trichoscopy in patients with pili annulati demonstrates hair shafts with regular light bands, which correspond to dark cavities visible in microscopic examination (Rakowska et al., 2009b).

Trichorrhexis invaginata or bamboo hair is the marker for Netherton syndrome, a rare autosomal recessive condition with bamboo hair, ichthyosis, and atopic dermatitis. Trichoscopy shows characteristic bamboo hairs (nodes along the hair) and hairs with golf tee-type endings in the scalp hairs and eyebrows (Rakowska et al., 2009b).

Trichorrhexis nodosa refers to white knots with transverse fractures along the hair shaft. Trichoscopy reveals brush-like hair fracturing (Fig. 9d.21). In general, trichorrhexis nodosa is an unspecific finding related to excess stress of hair. It may be a genetic hair shaft dystrophy, but more frequently it is a consequence of hair weathering.

Exogenous Materials on the Scalp

A variety of exogenous materials of very different origin can be visualized by dermoscopy. These include hair dyes (Fig. 9d.22), camouflage products (Figs. 9d.23, 9d.24), residues from hair styling aids (Fig. 9d.25) (Itin et al., 1997), and ectoparasites (Fig. 9d.26) (Di Stefani et al., 2006; Tschandl et al., 2009). Camouflage products consist of dyes applied to the skin that makes the scalp appear to have more hair than it actually does.

Androgenetic Alopecia

Androgenetic alopecia is the most common reason for hair loss in women and men (Trüeb, 2003, Trueb, 2010). Trichoscopy features of androgenetic alopecia are hair shaft thickness diversity (anisotrichosis) (Fig. 9d.17), brown perifollicular discoloration (peripilar signs) (Fig. 9d.4), and empty follicles (Fig. 9d.5).

Hair shaft thickness diversity is a good marker of androgenetic alopecia, particularly in women. A diversity of over 20% is considered as diagnostic of androgenetic alopecia; however, there is no standardized method to calculate the "percentage of diversity."

Peripilar sign (brown perifollicular discoloration) is an early sign in female and male subjects with androgenetic alopecia (Deloche et al., 2004). A characteristic feature of the peripilar sign in androgenic alopecia is its predominance in the frontal scalp area (Olszewska et al., 2010).

Figure 9d.22 Hair dyes in a patient with androgenetic alopecia. Brown structureless blotches on the scalp.

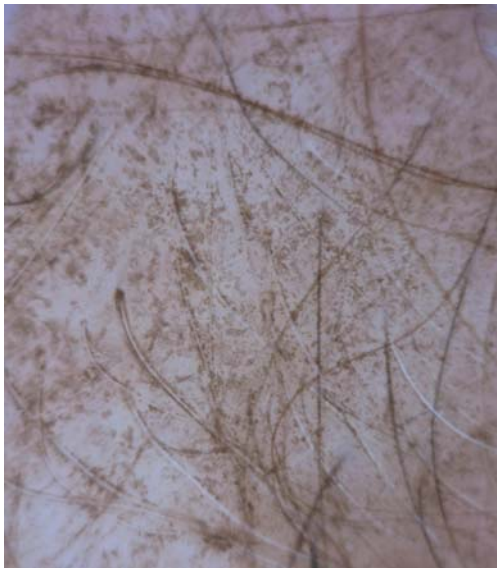


Figure 9d.23 Camouflage dye applied to the skin of the scalp.

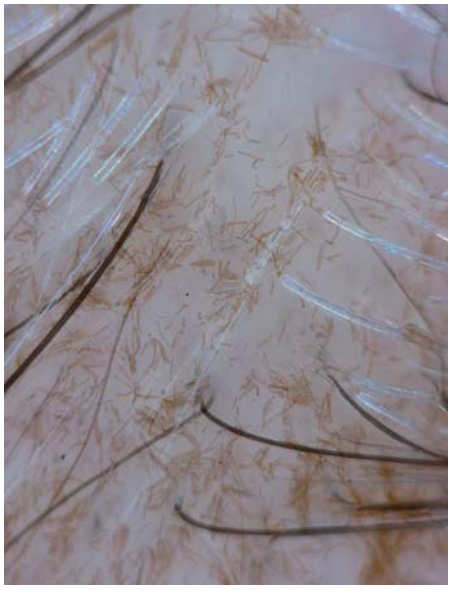


Figure 9d.24 Another type of camouflage product. This consists of exogenous pigment applied to the skin of the scalp to make it appear to have more hair than it actually does.

Figure 9d.25 Residues from hairspray. Multiple hairs glued together by this semi-translucent solution.

The presence of yellow dots in androgenetic alopecia is a matter of discussion (see: Yellow dots in the section "Follicular ostia"). According to Olszewska et al. (2010), the predominant presence of irregularly distributed yellow dots in the frontal scalp area is an important criterion of female androgenic alopecia. Ross et al. (2006) gives significantly less weight to this feature in androgenetic alopecia.

Kenogen frequency and duration are greater in androgenetic alopecia, which may be reflected by empty hair follicles.

Other characteristic trichoscopy features of androgenetic alopecia include the presence of multiple vellus hairs and multiple follicular ostia with only one hair shaft.

In general, a predominant presence of trichoscopy abnormalities in the frontal area compared with the occipital area is highly indicative of androgenetic alopecia (Olszewska et al., 2010).

Androgenetic alopecia is often associated with pain or burning of the scalp (trichodynia). In a series of 403 patients complaining of hair loss, presence of telangiectasia, usually arborizing red blood vessels (Fig. 9d.11) was found to strongly correlate with the presence of trichodynia (Willimann & Trüeb, 2002).

Figure 9d.26 Head louse (*Pediculus humanus capitis*) grasping hairs. The elongated body, structure of the head, and three pairs of clawed legs of this 1–2 mm large ectoparasite are visible (image taken with Fotofinder™ Trichoscan).

While performing trichoscopy it has to be borne in mind that androgenetic alopecia often coexists with other diseases causing hair loss, especially with telogen effluvium, and thus features of both diseases may be observed concomitantly (Rudnicka et al., 2011).

Scalp pigmentation with a reticular (honeycomb) pigment pattern (Fig. 9d.15) is eventually observed in patients with advanced androgenetic alopecia as a consequence of exposing the unprotected scalp to the sun (Ross et al., 2006).

Alopecia Areata

Alopecia areata is a common hair loss condition characterized by an acute onset of nonscarring hair loss, most commonly in sharply defined areas.

Trichoscopy features of alopecia areata consist of regularly distributed yellow dots (Fig. 9d.1), dystrophic hairs/black dots (Fig. 9d.18), and short, regrowing miniaturized hairs (Pawlowska et al., 2006; Ross et al., 2006; Inui et al., 2008a).

Exclamation mark hairs (exclamation point hairs) are a specific feature of alopecia areata. This trichoscopy finding is sometimes called "microexclamation mark hair" and consists of 1–2 mm long exclamation mark-shaped hairs seen by trichoscopy. The exclamation point hairs seen with the unaided eye are typically 5 to 15 mm in length (Pawlowska et al., 2006).

Yellow dots are a characteristic sign of alopecia areata that can be seen in all stages of the disease, and are considered a marker of disease severity.

Black dots are common in alopecia areata and are usually a marker of high disease activity. Short regrowing hairs (Fig. 9d.27) are a sign of hair regrowth in patients with alopecia areata.

Alopecia areata incognita is an uncommon variety of alopecia areata characterized by rapid diffuse shedding of telogen hairs in the absence of typical discrete patches. Clinically the disease has features of telogen effluvium, but hair loss is often more evident in the "androgen-dependent scalp area" (Rebora, 1987; Tosti et al., 2008). Concomitant presence of yellow dots and short regrowing hairs seen in the terminal hair-bearing scalp is an important trichoscopic clue to diagnosis (Fig. 9d.27)

The main pathology underlying alopecia areata incognita is a matter of controversy. According to Rakowska et al. (2009c) concomitant presence of yellow dots, hair shaft thickness diversity, and thin regrowing hairs with predominant presence in the "androgen-dependent" scalp area is indicative of acute telogen effluvium developing in a person with mild, previously unrecognized androgenetic alopecia.

Scarring Alopecia

Scarring alopecia is both a diagnostic and therapeutic challenge to the practitioner. On the basis of histopathology findings, the scarring alopecias has been classified into the categories of primary scarring alopecia, where the hair follicle is the primary target of destruction, and secondary scarring alopecia, where the follicular damage results incidentally from events surrounding the hair and impinging on the follicular unit (Ross et al., 2005; Stefanato, 2010).

In a retrospective study of scalp biopsy specimen from patients with scarring alopecia received for dermatopathology during a 5-year period Trachsler and Trüeb (2005) found the most prevalent diagnoses in order of frequency to be lichen planopilaris in 26%, lupus erythematosus in 21%, folliculitis decalvans in 20%, and pseudopelade in 10%. Scalp dermoscopy may be particularly helpful in differentiating these conditions.

Lichen planopilaris is the most common cause of scarring alopecia in the adult. It presents with pruritic central or multifocal alopecic patches with follicular hyperkeratosis and erythema at the hair-bearing margin. Histopathology reveals a lymphocytic primary scarring alopecia. The Lassueur–Graham Little syndrome is considered a disseminated variant, and frontal fibrosing alopecia (Kossard et al., 1997) as a pattern distribution variant of the disease (Zinkernagel & Trüeb, 2000).

Dermoscopic features of lichen planopilaris are follicular keratosis (Fig. 9d.3), loss of follicular ostia (Fig. 9d.7), white dots (Fig. 9d.6), and acquired pili torti (Fig. 9d.20).

Figure 9d. 27 Short regrowing miniaturized hairs in alopecia areata.

Discoid lupus erythematosus (*chronic cutaneous lupus erythematosus*) presents as erythematous scaly plaques with follicular plugs, telangiectases, and progressive central scarring. Histopathology reveals a lymphocytic primary scarring alopecia. Trichoscopy features of discoid lupus erythematosus are loss of follicular ostia, thick arborizing vessels, follicular keratotic plugs (big yellow dots), and scalp atrophy, occasionally with effaced or absent vascular loops (Fig. 9d.12).

Folliculitis decalvans represents a chronic and recurrent pustulofollicular scalp inflammation resulting in scarring alopecia. It usually presents in the central scalp area with exudative crusted areas and grouped follicular pustules at the hair-bearing margin with centrifugal progression. Histopathology reveals a neutrophilic primary scarring alopecia (Stefanato, 2010). Trichoscopy features of folliculitis decalvans are severe scaling and crusting, pronounced hair tufting (Fig. 9d.19), follicular pustules (Fig. 9d.14), numerous coiled capillary loops (Fig. 9d.14), loss of follicular ostia, and white dots.

Pseudopelade was first described by Brocq in 1888 as asymptomatic, noninflammed, ivory-white or flesh colored small oval-round, reticulate, or large, irregular patches of the central scalp area. It is considered a lymphocytic primary scarring alopecia with selective destruction of hair follicles. It is clinically and histologically indistinguishable from end-stage scarring alopecia of any origin. A distinction must be made from the *pseudopeladic state of Degos*, which represents the nonspecific, common end-stage of 60 different etiologies (Degos et al., 1954; Trüeb, 2010).

Trichoscopy features of classic pseudopelade of Brocq are nonspecific: loss of follicular ostia and occasionally white dots (Fig. 9d.6). Thus both clinically and by trichoscopy pseudopelade of Brocq remains a diagnosis of exclusion.

TRICHOTILLOMANIA

Trichotillomania is an impulse control disorder characterized by a compulsive urge to pull out one's own hair leading to noticeable hair loss. The most important differential diagnosis is alopecia areata. However, trichotillomania often coexists with alopecia areata (Trüeb & Cavegn, 1996), which may pose a special diagnostic challenge.

Trichoscopy features of trichotillomania are coiled fractured hairs, longitudinally split short hairs, black dots (Fig. 9d.2). Alopecia areata differs by the presence of regularly distributed yellow dots and microexclamation mark hairs, but absence of coiled hairs and longitudinally split short hairs (Ross et al., 2006; Inui et al., 2008a).

ALGORITHMS IN TRICHOSCOPY

As significant amount of data are accumulating on differential diagnosis of hair loss with trichoscopy, algorithms are being developed to simplify differential diagnosis in clinical practice. For example, according to Rakowska et al., (2010), female androgenic alopecia may be differentiated from

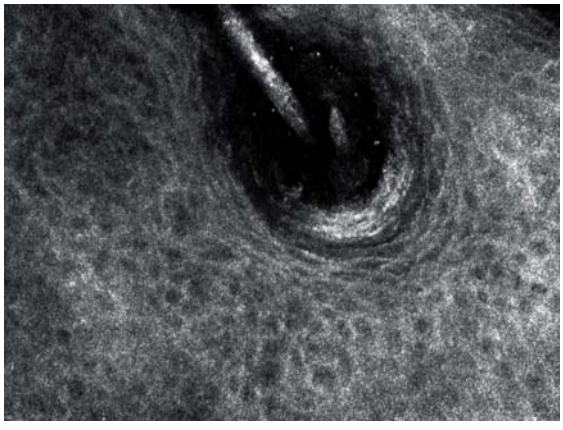


Figure 9d.28 A hair shaft emerging from a hair follicle visualized by reflectance confocal microscopy.

chronic telogen effluvium based on the following major and minor trichoscopy criteria. Major criteria are (*i*) more than four yellow dots in four images (70-fold magnification) in the frontal area, (*ii*) lower average hair thickness in the frontal area compared with the occiput, (*iii*) more the 10% of thin hairs (below 0.03 mm) in the frontal area. Minor criteria encompass increased frontal to occipital ratio of (*i*) single-hair pilosebaceous units, (*ii*) vellus hairs, and (*iii*) perifollicular discoloration. According to the authors' evaluation, fulfillment of two major criteria or one major and two minor criteria allows to diagnose female androgenic alopecia based on trichoscopy with a 98% specificity (Olszewska et al., 2010). Inui (2011) proposed a simplified algorithm to diagnose the most common diseases causing hair loss.

POSSIBLE APPLICATION OF IN VIVO REFLECTANCE CONFOCAL MICROSCOPY IN DIAGNOSING HAIR AND SCALP DISEASES

In vivo reflectance confocal microscopy (RCM) is a new imaging technique, which is gaining popularity in differential diagnosis of skin cancers and inflammatory skin diseases (Kolm et al., 2010). Attempts to employ this method in diagnosing hair loss are promising (Rudnicka et al., 2008). RCM allows visualization, with high precision, of most features known from trichoscopy in common hair diseases, such as alopecia areata or androgenetic alopecia (Rudnicka et al., 2008). Figure 9d.28 shows an RCM image of a hair shaft emerging from a hair follicle.

Key Points

- Hair and scalp dermoscopy or trichoscopy is helpful for the diagnosis of hair and scalp disorders. It can also give clues about the disease stage and progression
- Structures that may be visualized by trichoscopy include hair shafts of different types (terminal, vellus, and hair shaft dystrophies), follicular ostia (empty hair follicles, yellow, black, and white dots), vascular patterns, abnormalities of pigmentation, scaling, and exogenous materials. A single structure is rarely sufficient for diagnosis. Usually a disease may be suspected or diagnosed based on a combination of different structures, coexisting in one patient

REFERENCES

Abraham, L.S., Piñeiro-Maceira, J., Duque-Estrada, B., Barcaui, C.B. & Sodré, C.T., 2010, Pinpoint white dots in the scalp: dermoscopic and histopathologic correlation. *J Am Acad Dermatol*, 63, 721–2.

Braun, R.P., Skaria, A.M., Saurat, J.H. & Borradori, L., 2002, Multiple hyperkeratotic spicules and myeloma. *Dermatology*, 205, 210–12.

de Lacharrière, O., Deloche, C., Misciali, C., et al., 2001, Hair diameter diversity: a clinical sign reflecting the follicle miniaturization. *Arch Dermatol*, 137, 641–6.

Degos, R., Rabut, R., Duperrat, B. & Leclercq, R., 1954, L'état pseudopeladique. Réflexions a propos de cent cas d'alopöcies cicatricielles en airs, d'apparence primitive du type pseudo-pelade. *Ann Dermatol Syphiligr (Paris)*, 81, 5–26

Deloche, C., de Lacharrière, O., Misciali, C., et al., 2004, Histological features of peripilar signs associated with androgenetic alopecia. *Arch Dermatol Res*, 295, 422–8.

Di Stefani, A., Hofmann-Wellenhof, R. & Zalaudek, I., 2006, Dermoscopy for diagnosis and treatment monitoring of pediculosis capitis. *J Am Acad Dermatol*, 54, 909–11.

Duque-Estrada, B., Tamler, C., Sodré, C.T., Barcaui, C.B. & Pereira, F.B., 2010, Dermoscopy patterns of cicatricial alopecia resulting from discoid lupus erythematosus and lichen planopilaris. *An Bras Dermatol*, 85, 179–83

Gewirtzman, A.J., Saurat, J.H. & Braun, R.P., 2003, An evaluation of dermoscopy fluids and application techniques. *Br J Dermatol*, 149, 59–63.

Guarrera, M. & Rebora, A., 2005, Kenogen in female androgenetic alopecia. A longitudinal study. *Dermatology*, 210, 18–20.

Hofbauer, G.F., Tsambaos, D., Spycher, M.A. & Trüeb, R.M., 2001, Acquired hair fragility in pili anulati: causal relationship with androgenetic alopecia. *Dermatology*, 203, 60–2.

Inui, S., 2011, Trichoscopy for common hair loss diseases: algorithmic method for diagnosis. *J Dermatol*, 38, 71–5.

Inui, S., Nakajima, T. & Itami, S., 2007, Dry dermoscopy in clinical treatment of alopecia areata. *J Dermatol*, 34, 635–9.

Inui, S., Nakajima, T., Itami, S., 2010, Coudability hairs: a revisited sign of alopecia areata assessed by trichoscopy. *Clin Exp Derm,* 35, 361–50.

Inui, S., Nakajima, T., Nakagawa, K. & Itami, S., 2008a, Clinical significance of dermoscopy in alopecia areata: analysis of 300 cases. *Int J Dermatol*, 47, 688–93.

Inui, S., Nakajima, T., Shono, F. & Itami, S., 2008b, Dermoscopic findings in frontal fibrosing alopecia: report of four cases. *Int J Dermatol*, 47, 796–9.

Itin, P.H., Schiller, P., Mathys, D. & Guggenheim, R., 1997, Cosmetically induced hair beads. *J Am Acad Dermatol*, 36(2 Pt 1), 260–1.

Kolm, I., Kamarashev, J., Kerl, K., et al., 2010, Acral melanoma with network pattern: a dermoscopy-reflectance confocal microscopy and histopathology correlation. *Dermatol Surg*, 36, 701–3.

Kossard, S. & Zagarella, S., 1993, Spotted cicatricial alopecia in dark skin. A dermoscopic clue to fibrous tracts. *Australas J Dermatol*, 34, 49–51.

Kossard, S., Lee, M.S. & Wilkinson, B., 1997, Postmenopausal frontal fibrosing alopecia: a frontal variant of lichen planopilaris. *J Am Acad Dermatol*, 36, 59–66.

Lacarrubba, F., Dall'Oglio, F., Nasca, M.R. & Micali, G., 2004, Videodermoscopy enhances diagnostic capability in some forms of hair loss. *Am J Clin Dermatol*, 5, 205–8.

Olszewska, M. & Rudnicka, L., 2005, Effective treatment of female androgenic alopecia with dutasteride. *J Drugs Dermatol*, 4, 637–40.

Olszewska, M., Rudnicka, L., Rakowska, A., Kowalska-Oledzka, E. & Slowinska, M., 2008, Trichoscopy. *Arch Dermatol*, 144, 1007.

Olszewska, M., Warszawik, O., Rakowska, A., et al., 2010, Methods of hair loss evaluation in patients with endocrine disorders. *Endokrynol Pol,* 61, 406–11.

Pawlowska, M., Stasiak, T. & Olszewska, M., 2006, Trichoscopy in differentia diagnosis of alopecia areata. *J Invest Dermatol*, 126, S66.

Rakowska, A., 2009, Trichoscopy (hair and scalp videodermoscopy) in the healthy female. Method standardization and norms for measurable parameters. *J Dermatol Case Rep*, 3, 14–19.

Rakowska, A., Kowalska-Oledzka, E., Rudnicka, L. & Olszewska, M., 2009a, Numerous faces of yellow dots. *J Am Acad Dermatol*, 60(Suppl 1), AB98.

Rakowska, A., Kowalska-Oledzka, E., Slowinska, M., Rosinska, D. & Rudnicka, L., 2009b, Hair shaft videodermoscopy in Netherton syndrome. *Pediatr Dermatol*, 26, 320–2.

Rakowska, A., Slowinska, M., Czuwara, J., Olszewska, M. & Rudnicka, L., 2007, Dermoscopy as a tool for rapid diagnosis of monilethrix. *J Drugs Dermatol*, 6, 222–4.

Rakowska, A., Slowinska, M., Kowalska-Oledzka, E., et al., 2009c, Alopecia areata incognita: true or false? *J Am Acad Dermatol*, 60, 162–3.

Rebora, A. & Guarrera, M., 2002, Kenogen. A new phase of the hair cycle? *Dermatology*, 205, 108–10.

Rebora, A., 1987, Alopecia areata incognita: a hypothesis. *Dermatologica*, 174, 214–18.

Ross, E.K., Tan, E. & Shapiro, J., 2005, Update on primary cicatricial alopecias. *J Am Acad Dermatol*, 53, 1–37

Ross, E.K., Vincenzi, C. & Tosti, A., 2006, Videodermoscopy in the evaluation of hair and scalp disorders. *J Am Acad Dermatol*, 55, 799–806.

Rudnicka, L., Olsweska, M., Rakowska, A. & Slowinska, M., 2011, Trichoscopy update 2011. *J Dermatol Case Rep,* 12, 82–8.

Rudnicka, L., Olszewska, M. & Rakowska, M., 2008a, In vivo reflectance confocal microscopy: usefulness for diagnosing hair diseases. *J Dermatol Case Rep*, 4, 55–9.

Rudnicka, L., Olszewska, M., Rakowska, A., Kowalska-Oledzka, E. & Slowinska, M., 2008b, Trichoscopy: a new method for diagnosing hair loss. *J Drugs Dermatol*, 7, 651–4.

Smith, N.P. & Sanderson, K.V., 1978, Tufted hair folliculitis of the scalp. *J R Soc Med*, 71, 606–8.

Stefanato, C.M., 2010, Histopathology of alopecia: a clinicopathological approach to diagnosis. *Histopathology*, 56, 24–38.

Toncić, R.J., Lipozencić, J. & Pastar, Z., 2007, Videodermoscopy in the evaluation of hair and scalp disorders. *Acta Dermatovenerol Croat*, 1, 116–18.

Tosti, A., 2007, Dermoscopy of hair and scalp disorders with clinical and pathological correlations. Andover, Hampshire, UK: Informa Healthcare.

Tosti, A., Whiting, D., Iorizzo, M. & et al., 2008, The role of scalp dermoscopy in the diagnosis of alopecia areata incognita. *J Am Acad Dermatol*, 59, 64–7.

Trachsler, S. & Trueb, R.M., 2005, Value of direct immunofluorescence for differential diagnosis of cicatricial alopecia. *Dermatology*, 211, 98–102.

Trüeb, R.M. & Cavegn, B., 1996, Trichotillomania in connection with alopecia areata. *Cutis*, 58, 67–70.

Trüeb, R.M., 2003, Is androgenetic alopecia a photoaggravated dermatosis? *Dermatology*, 207, 343–8.

Trüeb, R.M., 2010, Systematic approach to hair loss in women. *J Dtsch Dermatol Ges*, 8, 284–97.

Trüeb, R.M., Tsambaos, D., Spycher, M.A., Müller, J. & Burg, G., 1997, Scarring folliculitis in the ectrodactyly-ectodermal dysplasia-clefting syndrome. Histologic, scanning electron-microscopic and biophysical studies of hair. *Dermatology*, 194, 191–4.

Tschandl, P., Argenziano, G., Bakos, R., et al., 2009, Dermoscopy and entomology (entomodermoscopy). *J Dtsch Dermatol Ges*, 7, 589–96.

Willimann, B. & Trüeb, R.M., 2002, Hair pain (trichodynia): frequency and relationship to hair loss and patient gender. *Dermatology*, 205, 374–7.

Zinkernagel, M.S. & Trüeb, R.M., 2000, Fibrosing alopecia in a pattern distribution: patterned lichen planopilaris or androgenetic alopecia with a lichenoid tissue reaction pattern? *Arch Dermatol*, 136, 205–11.

9e Mucosal lesions

Andreas Blum and Olga Simionescu

The mucosal surfaces encompass the lips, oral cavity, perianal skin and the genital skin of the penis and vulva. It is relatively uncommon to encounter pigmented or nonpigmented lesions on mucosal surfaces and this, in part, explains the paucity of literature available on this topic.

The clinical manifestation of mucosal lesions is at least in part dependent on the skin type, with darker skin types manifesting darker lesions (Table 9e.1) (Mannone et al., 2004; Wolf, 2007). The range of potential diagnoses for lesions on mucosal surfaces includes nevi, nonnevoid melanocytic macules (i.e., mucosal melanosis), melanomas, metastases of melanoma or other cancers, molluscum contagiosum, condylomata accuminata, hemangioma, lichen sclerosus et atrophicans, and Bowen's disease (i.e., squamous cell carcinoma), just to mention a few (Figs. 9e.1, 9e.2). In addition, peculiar benign melanocytic proliferations can develop within lichen sclerosus et atrophicans and these atypical pigmented lesions can prove challenging to diagnose and manage (Fig. 9e.3a, b) (Wolf, 2007; Bussen, 2009; El Shabrawi-Caelen et al., 2004; Carlson et al., 2002).

Dermoscopy of mucosal lesions reveals structures, colors, and patterns that may assist in differentiating benign from malignant lesions (Mannone et al., 2004; Wolf, 2007; Stolz et al., 2002; Ferrari et al., 2008; Lin et al., 2009; Blum et al., 2011; Ronger-Savle et al., 2011). To avoid contamination of dermoscopes requiring direct skin contact, the use of a polyvinyl chloride (PVC) film in the form of a "food wrap" was suggested by Dr. Alfred Kopf (Fig. 9e.4). However, when utilizing a plastic barrier (i.e., PVC film) between the scope and the skin it is imperative that oil or water be placed on both sides of the PVC film. If this is not done the dermoscopic structures will not be visualized adequately.

Numerous dermoscopic patterns have been observed on mucosal surfaces (Mannone et al., 2004; Wolf, 2007; Kato et al., 1987; Stolz et al., 2002; Tomicic & Wanebo, 2003; Matsushita et al., 2005; Wolf et al., 2005; Gencoglan et al., 2007; Lin et al., 2009; Blum et al., 2011; Ronger-Savle et al., 2011).

Parallel pattern: The parallel pattern consists of linear distribution of pigmentation. This linear pigment can appear as wispy linear streaks (Fig. 9e.5a, b). It is commonly seen in benign lesions on the lip (Fig. 9e.5a, b) and glans penis. The parallel linear lines can sometimes appear thickened and manifest a morphology reminiscent of hyphae (Fig. 9e.6A, B). Such thickened parallel lines can be seen in vulvar melanosis (Fig. 9e.6A, B). However, a similar parallel linear pattern can also be seen in mucosal melanoma (Fig. 9e.7A, B).

Structureless (i.e., homogeneous) pattern: Structureless pattern consists of diffuse light to dark brown, black, and/or gray-blue pigmented areas that are devoid of any visible dermoscopic structures. Structureless brown areas are commonly seen in melanosis of the vulva (Fig. 9e.8a, b). However, melanoma should be strongly considered in the differential diagnosis if the lesion manifests structureless areas with a blue, gray, or white color (Fig. 9e.9A, B) (Simionescu et al., 2008; Blum et al., 2011).

Reticular pattern: A honeycomb pattern or pigmented network pattern can also be seen in musosal lesions (Fig. 9e.10).

Dotted-globular pattern: This pattern consists of a lesion displaying dots and globules under dermoscopy (Fig. 9e.11A, B).

Ring-like patterns: Dermoscopy of mucosal melanotic macules will often reveal ring-like structures (Fig. 9e.12a, b). Ring-like structures that do not form a complete circle have been called "fish scale-like structures."

Any of the aforementioned patterns can be seen in both benign and malignant lesions. Benign lesions tend to display a single pattern that usually appears quite organized, whereas melanomas appear disorganized displaying more than one of the above-mentioned patterns (i.e., multicomponent pattern). In addition, melanomas frequently display blue, gray, and/or white colors (Fig. 9e.13a, b, Fig. 9e.14a, b).

Vascular lesions: Venous lakes and angiomas are common lesions on the lip. Dermoscopically these areas appear as light to dark red to bluish papules. These lesions can manifest lacunas (Fig. 9e.15).

Table 9e.1 Cell Types Involved in Mucosal Pigmented Lesions

	Normal melanocytes	Nevocytes	Malignant melanocytes	Keratinocytes
Origin	Neural crests	Neural crests	Uncertain	"Native" cells (from epidermis)
Distribution	Basal layer in skin types I, II, and III Basal and squamous layers in skin types IV, V, and VI	Dermis Dermoepidermal junction	Mucosal and submucosal invasion	Epidermis
Morphologic phenotype	Dendritic cells Small regular nuclei No contact with other melanocytes Melanosomes are poised and "ready" for transfer to surrounding keratinocytes	Ovoid to spindle shaped No dendritic projections Melanosomes retained but they have lost their ability to transfer melanin to adjacent keratinocytes No mitotic figures	Pleiomorphism Large irregular hyperchromatic nuclei No dendritic projections Mitotic figures	Columnar, polygonal Close contact with their corresponding melanocytes No mitotic figures, except in pigmented Bowen's disease
Mainly involved in	Mucosal melanosis Constitutive hyperpigmentation	Nevi	Mucosal melanoma	Mucosal melanosis Constitutive hyperpigmentation

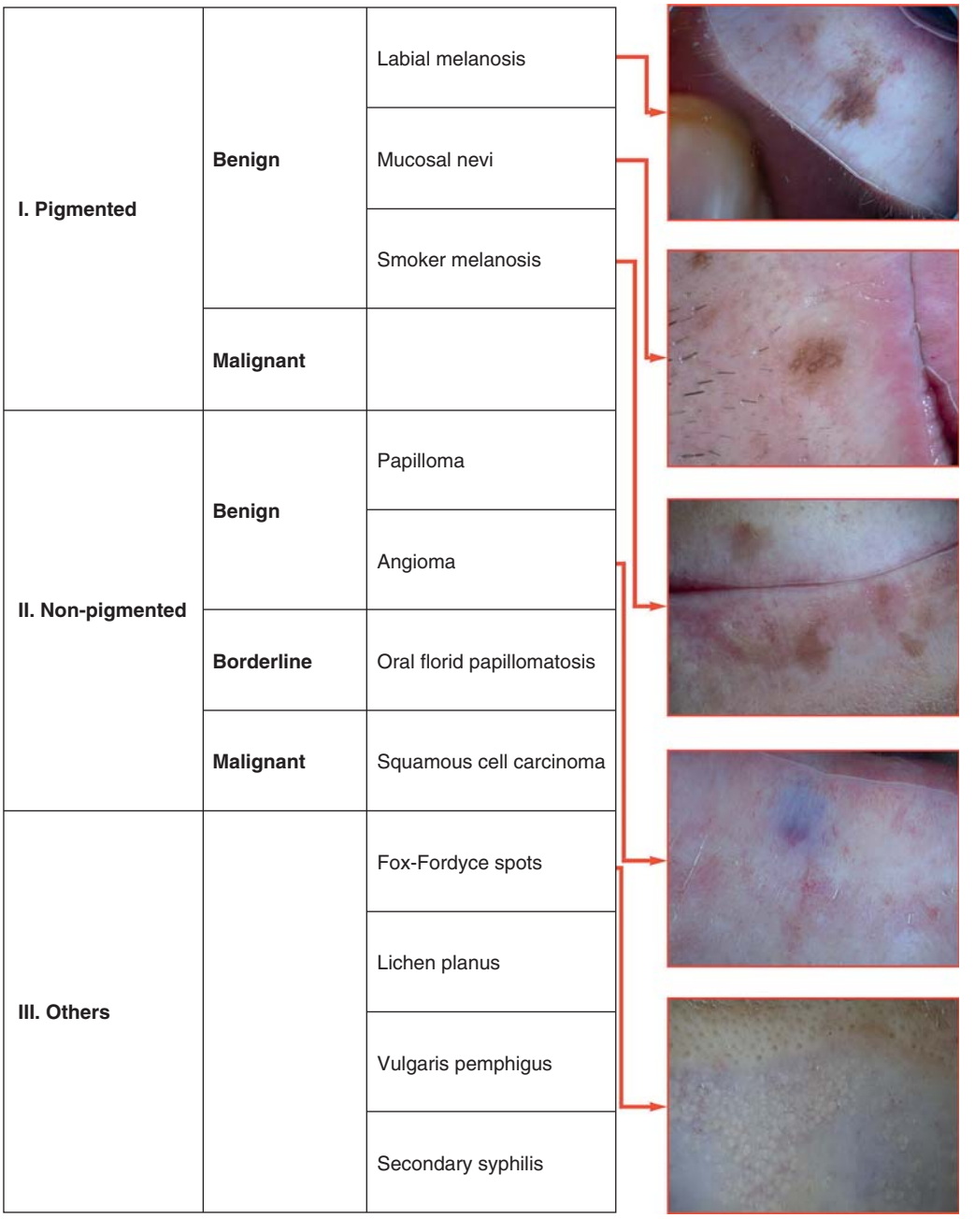


Figure 9e.1 Differential diagnosis for oral lesions.

The following pattern represent benign and malignant melanocytic and vascular lesions of the mucosa:

Benign melanosis of the mucosa

- Relatively symmetric lesions with an organized pattern and well-defined border
- Parallel pattern is often apparent in smaller lesions
- Structureless, diffuse pattern is usually seen in larger lesions
- Reticular or ring-like pattern can also be seen
- Brownish to black colors

Melanoma of the mucosa

- Asymmetric lesion with a disorganized pattern and ill-defined borders
- Structureless pattern with multiple colors including blue, gray, or white
- In addition to structureless areas melanomas will often also have focal areas with a parallel pattern, reticular pattern, ring-like pattern, or globular pattern.

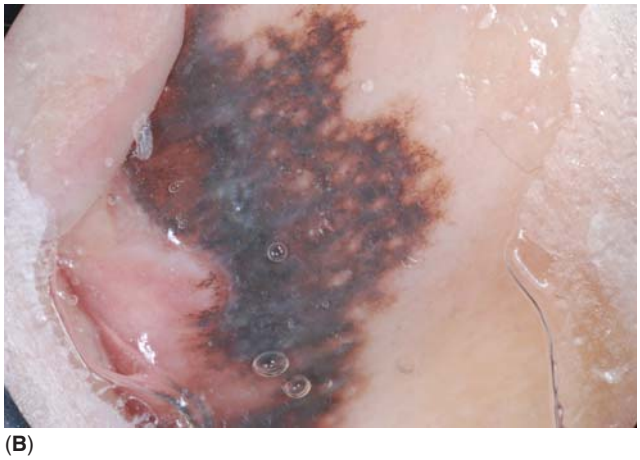
Vascular lesions:

- Light to dark red to bluish colors
- Lacunae

I. Pigmented	**Benign**	Vulvar/penile melanosis
		Vulvar/penile nevi
	Malignant	Pigmented Bowen
		Mucosal melanoma
II. Non-pigmented	**Benign**	Angioma
	Borderline	Vulvar/penile dysplasia
		Bowenoid papulosis
	Malignant	Squamous cell carcinoma
		Metastases
		Buschke-Löwenstein tumor
III. Sexually transmitted diseases	**Condylomata**	Lata (secondary syphilis)
		Acuminata (Human Papilloma Virus)
IV. Others		Lichen planus
		Lichen sclerosus et atrophicans
		Psoriasis
		Fox-Fordyce spots
		Vitiligo
V. Darker skin pigmentation (constitutive)		

Figure 9e.2 Differential diagnosis for genitoanal mucosal lesions.

(**A**)



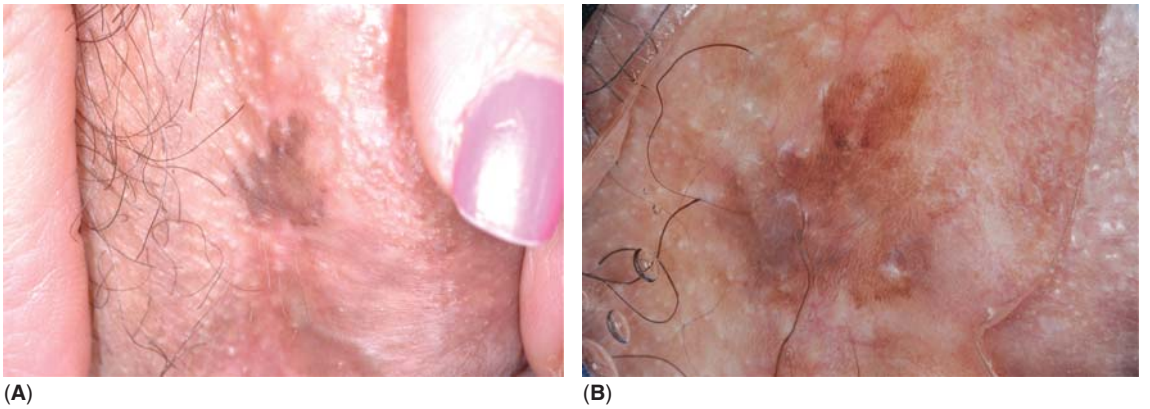
(**B**)

Figure 9e.3 (**A** and **B**) This young girl has lichen sclerosis et atrophicus. She developed this irregular-pigmented lesions within the sclerotic skin. A biopsy of this lesion revealed features that are commonly associated with recurrent nevi.

Figure 9e.4 Dermoscope covered with polyvinyl chloride film.

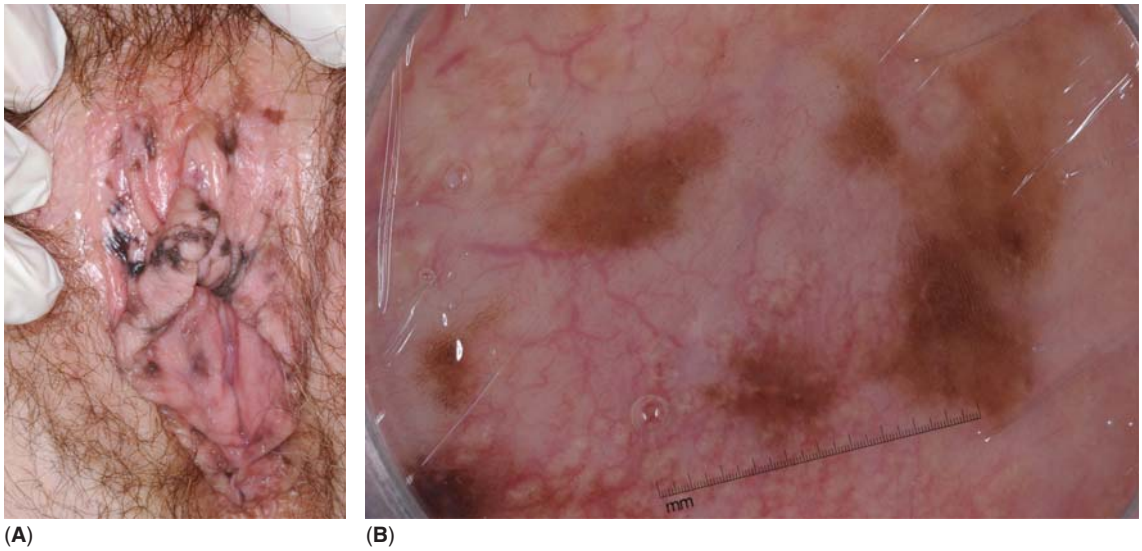
▲ **Figure 9e.5a** Clinical image of a benign melanocytic lesion on the lower lip.

◀ **Figure 9e.5b** Dermoscopic image of a benign melanocytic lesion of the lower lip. This lesion has a parallel pattern.



(**A**) (**B**)

Figure 9e.6 (**A** and **B**) Melanotic macule on the vulva displaying a thickened parallel pattern.

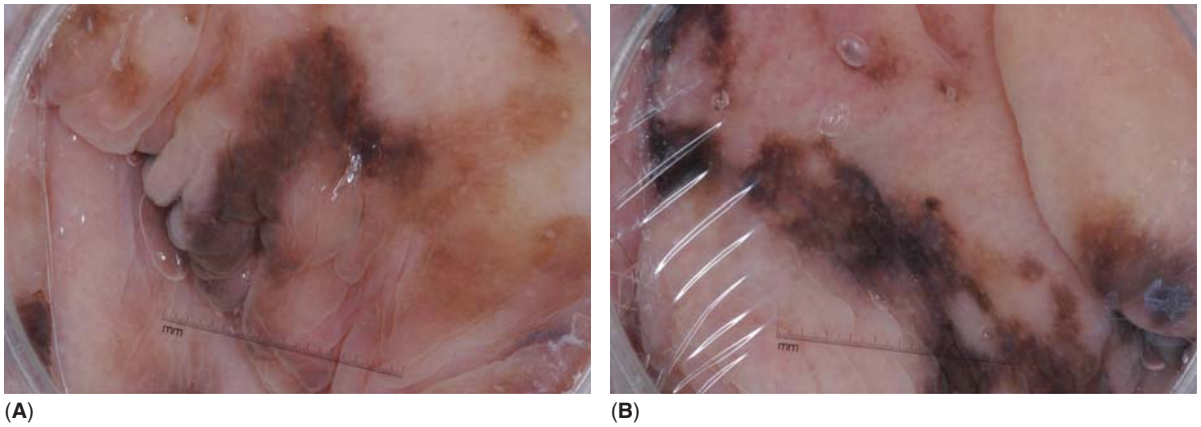


(A) (B)

Figure 9e.7 (**A** and **B**) One portion of this mucosal melanoma displays a parallel pattern.

▲ **Figure 9e.8a** Clinical image.

◀ **Figure 9e.8b** Dermoscopic image of a benign melanocytic lesion on the vulva. This lesion has a homogenous structureless pattern.



(A) (B)

Figure 9e.9 (**A** and **B**) Both dermoscopic images are taken from different areas within the melanoma shown in Figure 9e.7. The structureless areas in this melanoma have a blue-gray color, which is a common color seen in mucosal melanoma.

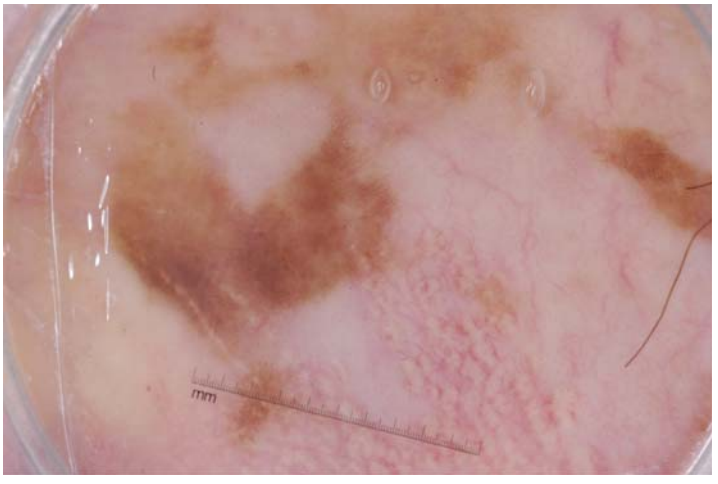
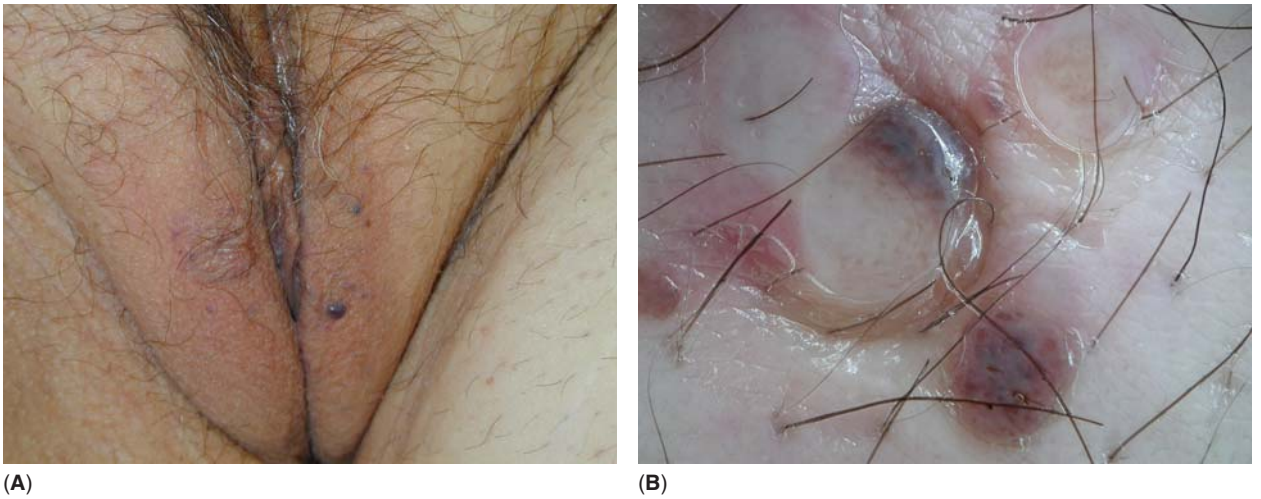


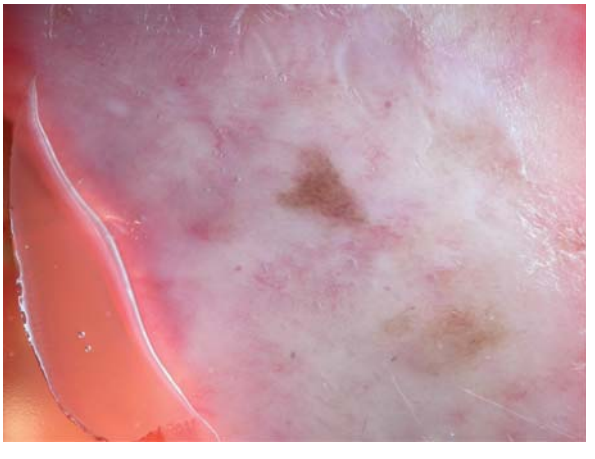
Figure 9e.10 This is an image taken from another portion of the melanoma shown in Figure 9e.7. The reticular pattern is quite evident here.



(**A**) (**B**)

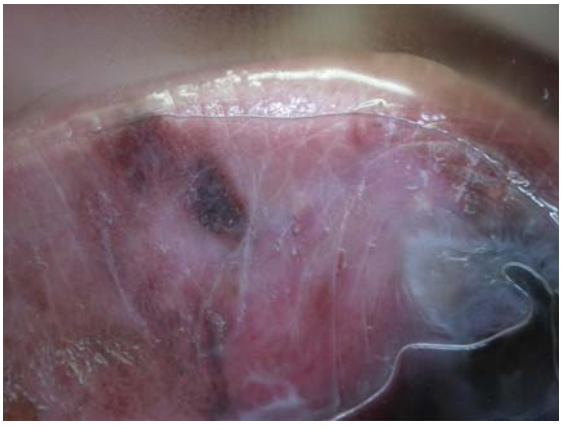
Figure 9e.11 (**A** and **B**) Dermoscopic image of a globular pattern in a benign melanocytic lesion on the vulva.

▲ **Figure 9e.12a** Clinical image.



◀ **Figure 9e.12b** Dermoscopic image of a benign melanocytic lesion on the lower lip. This lesion has a ring-like pattern.

▲ **Figure 9e.13a** Clinical image.



◀ **Figure 9e.13b** Dermoscopic image of an invasive melanoma on the upper lip. This melanoma has a multicomponent pattern and also has blue, gray and white colors.

▲ **Figure 9e.14a** Clinical image.

◀ **Figure 9e.14b** Dermoscopic image of pigmented Bowen's disease on anogenital skin. The blue-gray color and the presence of numerous blood vessels are clues to the diagnosis of a malignancy.

Figure 9e.15 Dermoscopic image of an angioma of the upper lip. This lesion has numerous lacunas.

Key Points

1. Dermoscopic structures seen in mucosal lesions include ring-like structures and fish scale like structures, lines, dots and globules, and homogeneous areas.
2. Benign lesions display one pattern consisting of one of the above mentioned structures.
3. 75% of melanomas manifest a multicomponent pattern and 25% manifest a homogeneous pattern.
4. Structureless areas with blue, gray or white color has a 100% sensitivity for melanoma, 93% sensitivity for any malignancy (including Bowen's disease) and specificity of between 82–83%.
5. Taking only colors into consideration, the presence of blue, gray or white within the lesion has a 100% sensitivity for malignancy with a specificity of approximately 60%.

REFERENCES

Blum, A., Simionescu, O., Argenziano, G., et al., 2011, Dermoscopy of Pigmented Lesions of the Mucosa and the Mucocutaneous Junction: Results of a Multicenter Study by the International Dermoscopy Society (IDS). *Arch Dermatol*, 147, 1181–7.

Bussen, S.S., 2009, Melanocytic proliferations associated with lichen sclerosus in adolescence. *Arch Gynecol Obstet*, 280, 1039–40.

Carlson, J.A., Mu, X.C., Slominski, A., et al., 2002, Melanocytic proliferations associated with lichen sclerosus. *Arch Dermatol*, 138, 77–87.

El Shabrawi-Caelen, L., Soyer, H.P., Schaeppi, H., et al., 2004, Genital lentigines and melanocytic nevi with superimposed lichen sclerosus: a diagnostic challenge. *J Am Acad Dermatol*, 50, 690–4.

Ferrari, A., Buccini, P., Covello, R., et al., 2008, The ringlike pattern in vulvar melanosis: a new dermoscopic clue for diagnosis. *Arch Dermatol*, 144, 1030–4.

Gencoglan, G., Gerceker-Turk, B., Kilinc-Karaarslan, I., Akalin, T. & Ozdemir, F., 2007, Dermoscopic findings in Laugier–Hunziker syndrome. *Arch Dermatol*, 143, 631–3.

Kato, T., Takematsu, H., Tomita, Y., Takahashi, M. & Abe, R., 1987, Malignant melanoma of mucous membranes. A clinicopathologic study of 13 cases in Japanese patients. *Arch Dermatol*, 123, 216–20.

Lin, J., Koga, H., Takata, M. & Saida, T., 2009, Dermoscopy of pigmented lesions on mucocutaneous junction and mucous membrane. *Br J Dermatol*, 161, 1255–61.

Mannone, F., De Giorgi, V., Cattaneo, A., et al., 2004, Dermoscopic features of mucosal melanosis. *Dermatol Surg*, 30, 1118–23.

Matsushita, S., Kageshita, T. & Ishihara, T., 2005, Comparison of dermoscopic and histopathological findings in a mucous melanoma of the lip. *Br J Dermatol*, 152, 1324–6.

Ronger-Savle S, Julien V, Duru G, Raudrant D, Dalle S, Thomas L., 2011 Features of pigmented vulval lesions on dermoscopy. *Br J Dermatol*, 164, 54–61.

Simionescu, O., Dumitrescu, D., Costache, M. & Blum, A., 2008, Dermatoscopy of an invasive melanoma on the upper lip shows possible association with Laugier-Hunziker syndrome. *J Am Acad Dermatol*, 59(Suppl 5), S105–8.

Stolz, W., Braun-Falco, O., Bilek, P., et al., 2002, Lesions on the mucosa. In: Stolz W, Braun-Falco O, Bilek P, Landthaler M, Burgdorf WHC, Cognetta AB, eds. *Color Atlas of Dermoscopy.* 2nd ed. Oxford, England: Blackwell; 110–2, 151–4.

Tomicic, J. & Wanebo, H.J., 2003, Mucosal melanomas. *Surg Clin North Am*, 83, 237–52.

Wolf, C., Haacke, T.C., Höft, S., Peters, K. & Hauschild, A., 2005, Malignant melanoma of the uvula and soft palate. *Hautarzt*, 56, 156–9.

Wolf, I.H., 2007, Melanocytic nevi on the genitalia and melanocytic nevi on other special locations. *Color Atlas of Melanocytic Lesions of the Skin.* Berlin, Heidelberg: Springer-Verlag, 119–23.

10 Exceptions to the two-step dermoscopy algorithm

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INTRODUCTION

The initial step of the two-step algorithm requires differentiating melanocytic from nonmelanocytic lesions based on the presence of pigment network, negative network, aggregated globules, streaks, and homogenous blue pigmentation. However, exceptions to this rule and potential diagnostic pitfalls can lead to incorrect classification (Scope et al., 2006). These exceptions and potential diagnostic pitfalls may occur when evaluating dermatofibromas (DFs), melanoma mimickers, such as seborrheic keratosis (SK) (see also chap. 8f, on equivocal lesions), lentigo, amelanotic and hypomelanotic melanomas, and melanomas manifesting nonmelanocytic features (see also equivocal lesion in chap. 8f). Therefore, knowledge of these exceptions is essential for maintaining a high diagnostic accuracy.

MISCLASSIFIED (OR MISCLASSIFICATION OF) NONMELANOCYTIC LESIONS

Nonmelanocytic lesions can on occasion display features resembling network, streaks, globules, or homogenous blue pigmentation. Following the criteria defined for the first step of the two-step dermoscopy algorithm, these lesions may incorrectly be classified as melanocytic tumors. Once misclassified as melanocytic tumors many of these lesions will be further misclassified in the second step of the two-step algorithm as lesions suspicious for melanoma. Here we describe the nonmelanocytic lesions that can resemble melanocytic tumors.

Pigment Network in Nonmelanocytic lesions

Pigment network and structures that resemble a pigment network (i.e., network-like structures) can be seen in DFs, solar lentigines, SKs, and accessory nipples.

Dermatofibromas

DF is a commonly encountered nonmelanocytic lesion that displays a fine pigment network at the periphery. Although the two-step dermoscopy algorithm classifies lesions based on the presence or absence of specific structures, for DF it is the pattern, not the presence of any one structure that helps to correctly identifying these lesions. The pattern of a delicate peripheral pigment network surrounding a central white scar-like patch (Ferrari et al., 2000; Arpaia, Cassano & Vena, 2005; Agero et al., 2006; Zaballos et al., 2008) trumps the presence of a pigment network leading to the diagnosis of a DF instead of a melanocytic lesion.

The dermoscopic structures seen in a DF can easily be correlated to the histology of these lesions. The network correlates with hyperpigmented rete ridges, which is due to the presence of increased melanin in keratinocytes overlying a DF. The ring-like globules correspond to broadened and hyperpigmented rete ridges, the scar-like area, and crystalline structures (NB: crystalline is seen primarely with polarized light) correlate with the collagenous stroma (Fig. 10.1). In addition, the presence of blood vessels and pink hue within the scar-like area correlates with increased vascularity, which is part of the collagenous stroma in DF (Figs. 10.1, 10.2).

Difficulty distinguishing DF from melanocytic lesions can lead to erroneously diagnosed melanoma and unnecessary biopsy. The reason for this is that the presence of the scar-like area, conspicuous crystalline structures, vessels, and a pink hue, may be interpreted as melanoma-specific structures. However, there are differences that can assist in differentiating the two. In melanoma the scar-like depigmented area will not reveal any blood vessels or pink hue (Argenziano et al., 1998). In addition, it is not common to see conspicuous crystalline structures in the scar-like regression areas seen in melanoma. Lastly, in melanoma the scar-like regression area is often associated with blue-gray granularity (also known as peppering), which is a feature not seen in DF.

Clues to help differentiate DF from a melanocytic lesion include the following:

1. Firm papule with a "dimple sign" is a feature of a DF. The dimple sign consists of the appearance of a central depression when the lesion is squeezed along its margin.
2. The network in a DF is fine/delicate and typical. It is located around the perimeter of the DF and is often associated with ring-like globules, which are located toward the center of the lesion adjacent to that scar-like area (Fig. 10.3).
3. The central scar-like area will often reveal vessels in a DF. Scar-like areas in a melanocytic neoplasm reflects regression and thus no blood vessels will be visible.
4. The central scar-like area in a DF will reveal conspicuous crystalline structures with polarized dermoscopy and there will be no evidence of regression structures, such as peppering. In melanoma the areas of regression tend not to reveal crystalline structures but they do tend to reveal peppering.

Seborrheic Keratoses

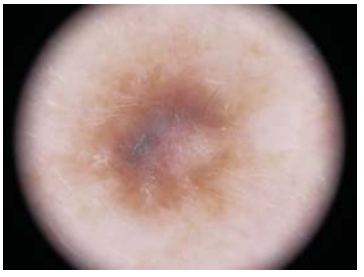
Between 7% and 46% of pigmented SK are reported to have network-like structures, appearing as hyperpigmented lines and often ending abruptly at the periphery (Fig. 10.4) (Braun et al., 2002). These lines form larger grids (meshwork) than the grids formed by a typical pigment network in a melanocytic lesion (Braun et al., 2002). The lines in a SK are due to the ridges of the skin and the holes of the network-like areas are due to the invaginations or sulci. The ridges may appear as thick dark lines, but more often they appear as sausage-shaped structures with a darker brown outline (Fig. 10.5) (De Giorgi et al., 2002). These structures have also been called "fat finger-like structures." The invaginations in the SK are often filled with keratin and are called comedo-like openings or crypts. If an SK is incorrectly classified as a melanocytic lesion then the presence of a blue-white veil, granularity as seen in regressing SK, and hairpin blood vessels, which are all features commonly seen in SK, may lead the observer to think that the lesion is a melanoma.

Misclassification rates of SK can be significantly reduced by knowing the specific dermoscopic features described in Table 10.1 (Braun et al., 2002). In some early lentigines that are transforming into SK, it may be very difficult to exclude the lesion as a melanocytic lesion (Fig. 10.6).

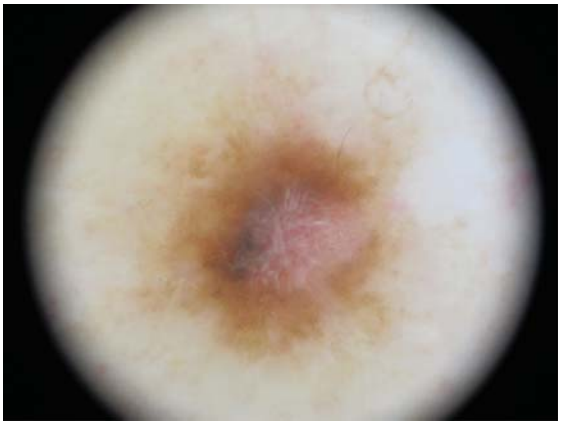
Other features that can assist in correctly classifying SK include the following:

1. Examining the network-like areas in an SK with the clinical eye (without dermoscopy) and with side lighting could help confirm that the grid is actually composed of ridges and keratin-filled invaginations.
2. Touching the lesion can confirm the keratotic and stuck-on consistency of the SK.
3. The border of an SK is sharply demarcated.

The wobble test can also provide clues to the diagnosis. The wobble sign is performed using a contact dermoscope and applying horizontal pressure to the lesion while moving the dermoscope back and forth horizontally across the skin surface (parallel to the surface). If the lesion slides across the skin surface, following the movement of the dermoscope, it favors a diagnosis of SK. If, on the other hand, the lesion rolls back and



▲ **Figure 10.1a** Clinical image of a DF.

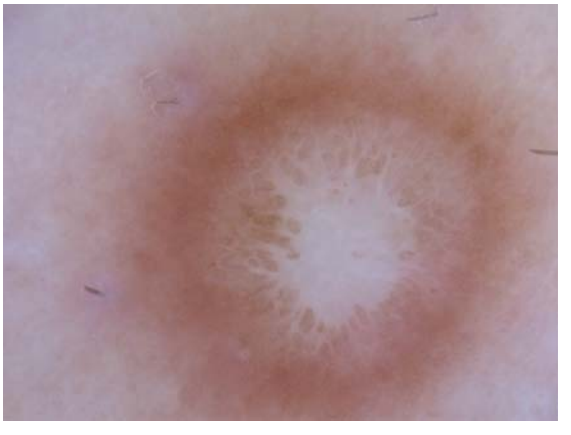


◀ **Figure 10.1b** Polarized dermoscopy image of this DF reveals a delicate pigment network, crystalline structures, and vessels. The presence of these structures may lead to a biopsy to rule out melanoma.

▲ **Figure 10.2a** Clinical image of a dermatofibroma.

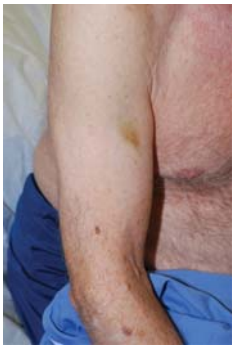
◀ **Figure 10.2b** Dermoscopy reveals a delicate pigment network and a few vessels within the central scar-like area. The presence of the blood vessels may raise concern for malignancy and result in an unnecessary biopsy.

▲ **Figure 10.3a** Clinical image of a DF.

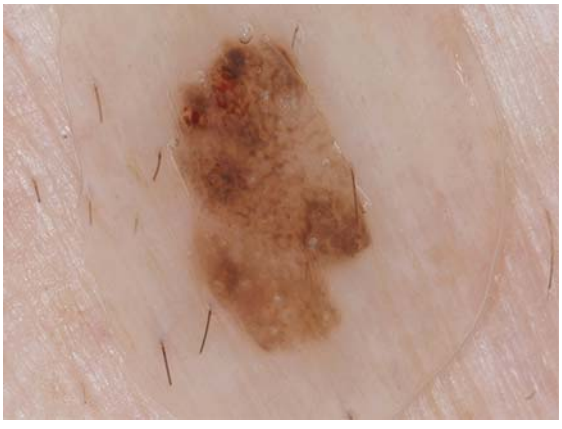


◀ **Figure 10.3b** Nonpolarized dermoscopy reveals a delicate peripheral network, central scar-like area and ring-like globules located between the network and scar-like area.

◀ **Figure 10.3c** Polarized dermoscopy highlights the crystalline structures in this DF. The ring-like globules and crystalline structures may lead to concern for melanoma.

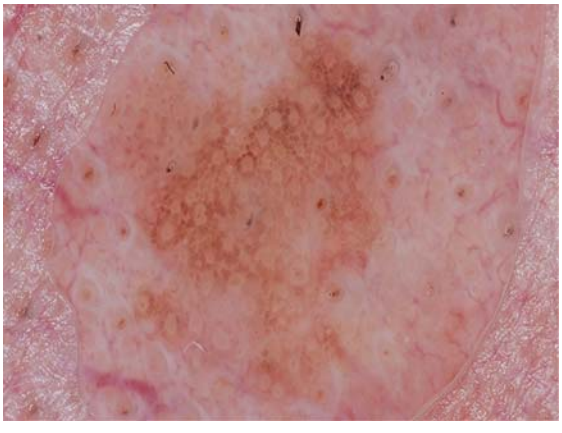


▲ **Figure 10.4a** Clinical image of an SK.



◀ **Figure 10.4b** Dermoscopy reveals ridges that are interconnecting and creating a network-like appearance.

▲ **Figure 10.5a** Clinical image of a SK.



◀ **Figure 10.5b** Dermoscopy shows ridges that manifest as globules and sausage-shaped structures with a darker outline. These structures have also been called "fat finger"-like structures. Notice their arrangement; appearing to form a meshwork pattern.

Table 10.1 Overlapping dermoscopic features and clues to differentiation

Dermoscopic structure	Melanocytic lesion	Dermatofibroma	Basal cell carcinoma	Seborrheic keratosis	Bowen's disease
PN	Typical	Delicate peripheral PN surrounding central, white scar-like area Homogenous pigmentation		Network-like: Thick, ends abruptly Various lengths, colors, and shapes; fissures and ridges, fat finger-like structures	Atypical PN Reticular, heterogenous pigment
Dots and Globules	Aggregated 3 or more brown, black, blue, or white	Within or at edges of central scar-like area Arranged in a grid-like pattern in scar-like area They have a ring-like appearance	Nonaggregated Multiple blue-gray globules Concentric structures	Rarely seen, associated with clonal seborrheic keratoses	Small, brown, globules in a patchy distribution Radially oriented linear brown and/or gray dots at the periphery
Streaks	Radiates away from tumor mass toward the surrounding normal skin Sharper in focus, tend to converge towards the geometric center of the lesion		May adiate toward tumor mass Tend to converge in a focal area creating a leaf-like structure Fuzzy	Peripheral, branched	Flossy, irregular At periphery
Homogenous blue pigmentation	Confluent blue-gray pigmentation	Hemosiderotic variant Diffuse or localized	Diffuse blue pattern Large blue-gray ovoid nests		
Other dermoscopic criteria	Facial pseudonetwork Acral parallel pattern	Dimple sign	Absence of typical PN Arborizing blood vessels Leaf-like areas Spoke-wheel-like structures	Multiple milia-like cysts Comedo-like openings Moth-eaten borders Fingerprint-like structures Waxy surface Lesion slides on the wobble test	Glomerular vessels Scaly surface

Abbreviation: PN, pigment network.

forward (wobbles) then the diagnosis of an intradermal or compound melanocytic neoplasm is favored (Braun, Krischer & Saurat, 2000).

Solar Lentigo
Densely pigmented keratinocytes found in solar lentigines result in the appearance of tan interrupted lines that can resemble an irregular pigment network with a sharply demarcated moth-eaten border (Fig. 10.7) (Marghoob, Braun & Kopf, 2005). Most lesions are easy to diagnose clinically and dermoscopically. However, in solar lentigines that are undergoing regression (i.e., lichen planus-like keratosis), the presence of gray peppering may raise concern for melanoma (Fig. 10.8). In the "ink-spot" variant of solar lentigo, the pigment network appears as a prominent black to dark brown network with thick or thin lines that have a relatively uniform color and texture (Figs. 10.9, 10.10) (Argenziano, 2004).

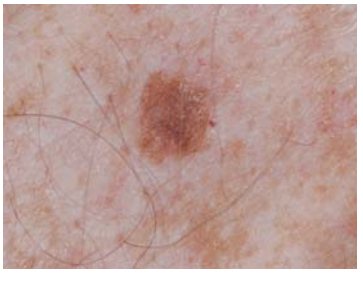
Accessory Nipple (Polythelia)
Accessory nipples have a dermoscopic morphology similar to DF. They present with a delicate peripheral pigment network, which corresponds to areolar epidermal hyperpigmentation of the basal layer with slight increase in melanocytes, and a central clear area (Fig. 10.11) (Blum & Roehm, 2003). However, unlike DF they are soft lesions. The presence of the network may result in the incorrect classification of these lesions as melanocytic. If this error occurs then an accessory nipple will usually be further classified as a benign nevus manifesting a peripheral network with central hypopigmentation pattern. The location, clinical examination, and history provide the necessary clues to help correctly identify accessory nipples and differentiate them form nevi and DF (Oztas & Gurer, 2007).

Dots and Globules in Nonmelanocytic Lesions
Dots and globular structures can be seen in nonmelanocytic lesions, such as DF, SK, basal cell carcinoma (BCC), pigmented Bowen's disease, and cutaneous metastasis.

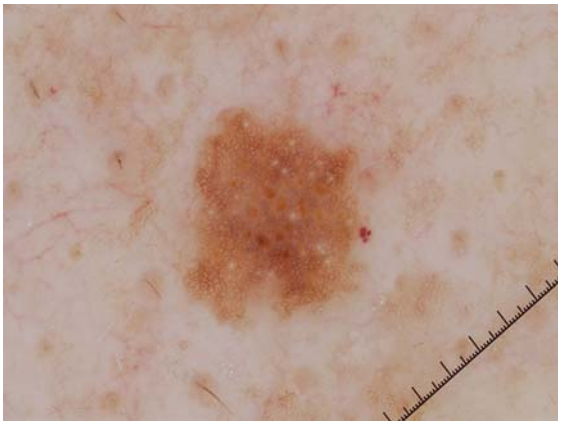
Dermatofibroma
The broadened and hyperpigmented rete ridges in a DF can appear as ring-shaped or donut-shaped globular structures when viewed with dermoscopy (Zaballos et al., 2008) (Fig. 10.3). The globules appear as light brown structures that have a darker brown peripheral rim giving them a ring-like appearance. These light brown globular structures are usually found in the zone between the delicate peripheral network and the central scar-like area of the DF (Ferrari et al., 2000; Arpaia, Cassano & Vena, 2005; Agero et al., 2006). These globular structures can also appear arranged in a grid-like pattern within the scar-like area (Kilinc Karaarslan et al., 2007). If these globular structures are misinterpreted as melanocytic nests (globules) then the lesion may end up being biopsied to rule out melanoma because of the presence of crystalline structures and vessels, which are commonly seen in DF. In addition, isolated, discrete red globules have also been reported in DF (Zaballos et al., 2006) and they can be confused for milky red globules sometimes seen in melanoma (Argenziano et al., 2004). The clues to correctly diagnose DF based on the clinical and dermoscopic examination have been discussed previously.

Seborrheic Keratosis or Epidermal Nevi
The presence of globules in SK is rare (Braun et al., 2002; De Giorgi et al., 2002). Out of 250 SK, only four clonal SK displayed light brown to bluish-black globules (Hirata et al., 2004). Histopathologically, these correlated to pigmented keratinocyte cell nests in the epidermis or pigmented intraepithelial horn cysts (Fig. 10.12) (Hirata et al., 2004; Provost et al., 1997). It should be noted that the features seen in a SK can also be seen in epidermal nevi and it is sometimes impossible to differentiate the two based on clinical, dermoscopic, and histopathology examination.

Another structure in SK that can sometimes be confused for globules (melanocytic nests) are short epidermal ridges (gyri). These ridges can take on the appearance of ring-like globular structures (Fig. 10.13). Despite the

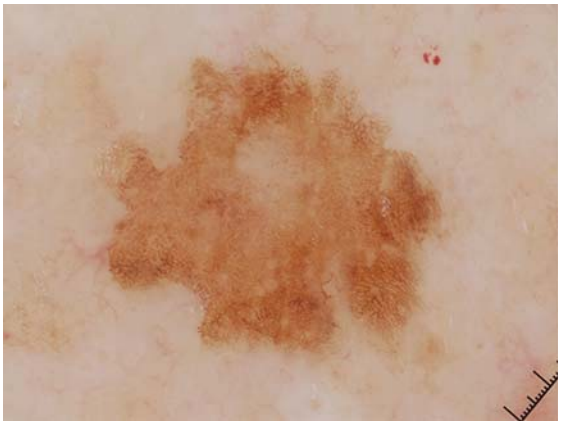


▲ **Figure 10.6a** Clinical image of an early SK. Notice the comedo-like openings on the clinical image.

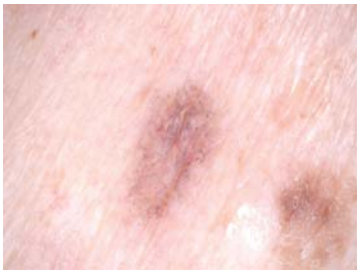


◀**Figure 10.6b** With dermoscopy the sharp demarcation of the network is easy to appreciate. The lesion also has numerous milia-like cysts and comedo-like openings. The network in this lentigo/SK is difficult to differentiate from the network seen in a melanocytic lesion.

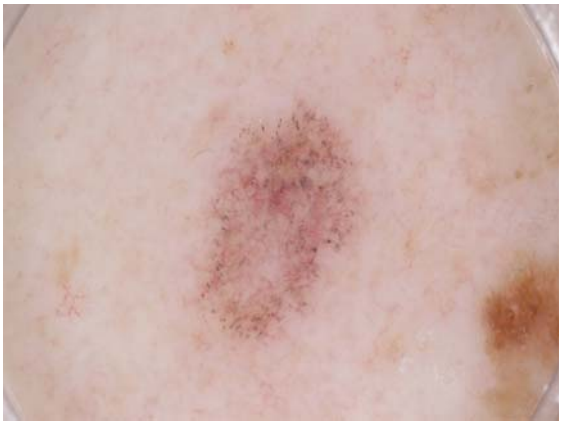
▲ **Figure 10.7a** Clinical image of a lentigo.



◀**Figure 10.7b** Dermoscopy reveals interrupted lines, sharp demarcation and moth eaten borders.



▲ **Figure 10.8a** Clinical image of lichen planus-like keratosis.



◀ **Figure 10.8b** Dermoscopy reveals peppering-type regression structures throughout the lesion. This is a lentigo undergoing regression. This lesion is suspicious for melanoma but turned out to be a lichen planus-like keratosis on biopsy.

▲ **Figure 10.9a** Clinical image of an ink spot lentigo.

◀ **Figure 10.9b** Dermoscopy reveals a relatively uniform darkly pigmented network. The network has an almost three dimensional quality to it. This is the classic morphology of an ink spot lentigo.

▲ **Figure 10.10a** Clinical image of an ink spot lentigo.

◀ **Figure 10.10b** Dermoscopy reveals the classic black network associated with an ink spot lentigo.

▲ **Figure 10.11a** Clinical image of polythelia.

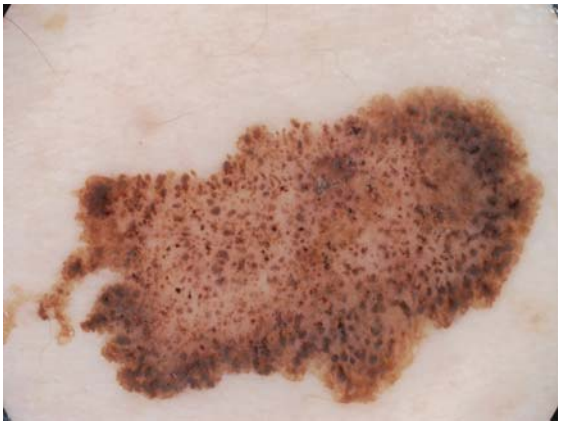
◀ **Figure 10.11b** Dermoscopy reveals a delicate peripheral network with central clearing.

clues to help differentiate SK from melanocytic nevi discussed previously, it is sometimes impossible to know the diagnosis without performing a biopsy. Some SK can have a blue-white veil, peppering [as seen in regressing SK (Figs. 8f.28 and 8f.29) in chap. 8f on equivocal lesions] vessels, dots, or homogenous structureless areas that may raise concern for melanoma (Figs. 10.14 and 10.15).

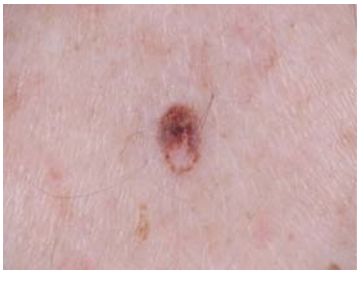
Pigmented Basal Cell Carcinoma

The presence of multiple non-aggregated gray-blue globules in a nonmelanocytic lesion is one of the specific dermoscopic criteria for pigmented BCC (97% specificity) (Menzies et al., 2000). The globules in BCC tend to have a blue-gray color and are not aggregated. For these blue-gray globules to be considered specific for BCC requires that the lesion does not manifest any features of a melanocytic lesion, such as network, aggregated brown globules, or streaks (Figs. 10.16 and 10.17). The features to help differentiate globules seen in melanocytic lesions from those seen in BCC are shown in Tables 10.1 and 10.2 (Figs. 10.18–10.20). Another clue to the diagnosis of BCC rests with the clinical view of the lesion; BCCs often have a shiny surface. In the event that a BCC is misclassified as a melanocytic neoplasm, the lesion will inevitably be biopsied to rule out melanoma. This is because the globules will be characterized as atypical. In addition, some BCCs will also reveal crystalline structures and fine brown to blue-gray dots, which can also be seen in melanoma (Altamura et al., 2010). With that said, incorrectly diagnosing a BCC as a melanoma or vice-versa has no bearing on the ultimate management because the lesion in question will be biopsied regardless.

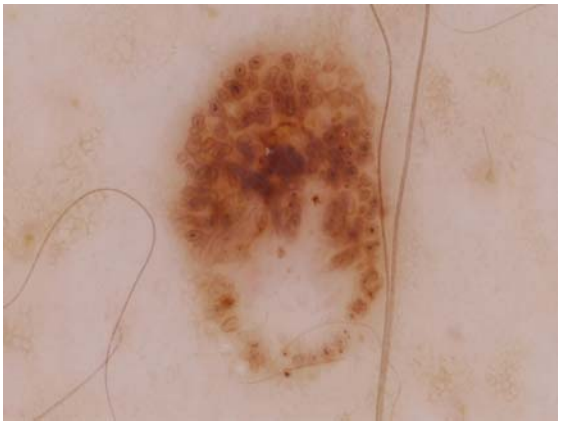
▲ **Figure 10.12a** Clinical image of a rough stuck-on appearing keratotic lesion that has been present for as long as the patient can remember.



◀ **Figure 10.12b** Dermoscopy reveals a sharply demarcated lesion with brown globular structures distributed throughout the lesion. Histopathology was consistent with a clonal seborrheic keratosis; however, the differential included a linear epidermal nevus. Based on the history and clinical findings this lesion is probably an epidermal nevus.



▲ **Figure 10.13a** Clinical image of a seborrheic keratosis.



◀ **Figure 10.13b** Dermoscopy reveals numerous ridges that are outlined by a darker brown color. Some of these ridges have a morphology resembling ring-like globules seen in dermatofibroma.

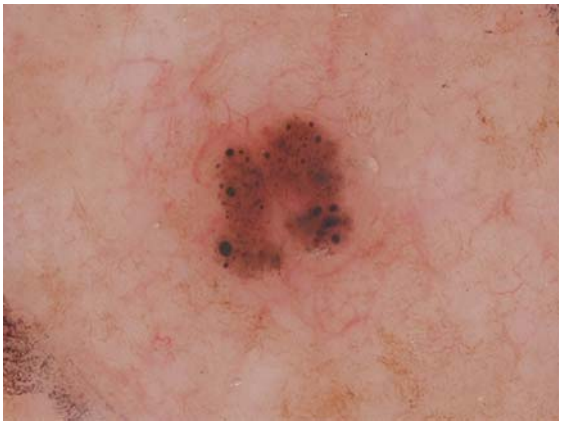
▲ **Figure 10.14a** Clinical image of a SK.

◀ **Figure 10.14b** Dermoscopy reveals a cluster of bluish globules with a blue-white veil. Despite the presence of sharp demarcation, a few ridges, comedo-like openings, and milia-like cysts, it is difficult to rule out melanoma in such lesions without a biopsy. This lesion was biopsied and was a clonal SK.

▲ **Figure 10.15a** Clinical image of a SK.

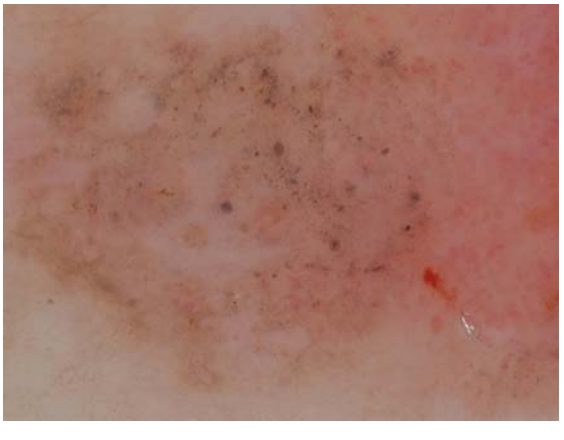
◀ **Figure 10.15b** Dermoscopy reveals no features to conclusively place this into either a melanocytic or nonmelanocytic category. Clues to the correct diagnosis include sharp demarcation and presence of milia-like cysts. However, the presence of dots and blue-white veil are concerning features for malignancy. This lesion was biopsied and was a SK.

▲ **Figure 10.16a** Clinical image of a pigmented BCC. Notice the shiny surface on this lesion.

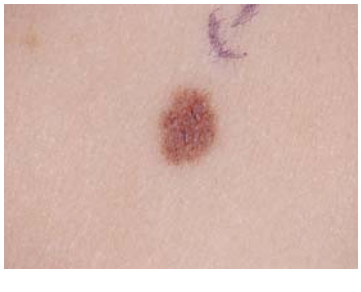


◀ **Figure 10.16b** This BCC has numerous globular structures but notice that these globules do not appear to be aggregated.

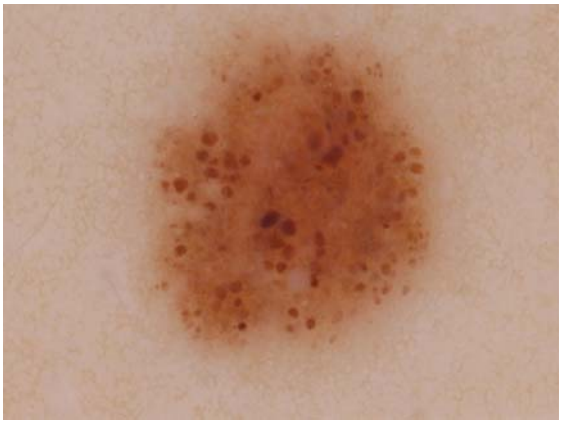
▲ **Figure 10.17a** Clinical image of a pigmented basal cell carcinoma.



◀ **Figure 10.17b** Dermoscopy reveals numerous fine grayish and brown dots and nonaggregated globules. Note that some of the globules have a central darker area or hub. Such globules are termed concentric globules and they are considered variants of spoke-wheel-like structures.



▲ **Figure 10.18a** Clinical image of a congenital nevus.

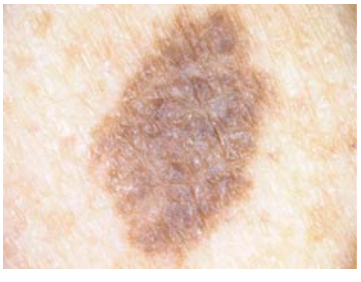


◀ **Figure 10.18b** Dermoscopy reveals globules. The globules in melanocytic lesions tend to be brown in color and are aggregated. Although concentric globules are not seen in nevi, the target globules seen in some congenital melanocytic nevi may look similar to the concentric globules seen in basal cell carcinoma.

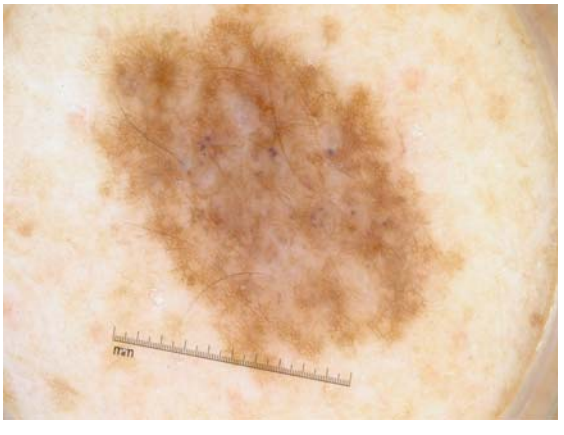
Table 10.2 Differential Features of BCC and Melanocytic Lesions

	BCC	Melanoma/CMN/Spitz
Globules	Color of the globules is usually blue-gray; however, on rare occasions they can be brown or pink in color. The globules tend not to be aggregated. Some globules may have a central darker hub. These are the so-called concentric globules. Usually there will be other features to help confirm the diagnosis of BCC, such as arborizing vessels	Color is usually brown. They can on occasion be black or blue or white in color The globules are usually aggregated. Usually there will be other structures to confirm that the lesion is melanocytic, such as network
Streaks	The streaks tend to be broader and appear less sharp (fuzzy or out of focus) compared with those seen in melanocytic neoplasms. Some of the streaks will radiate toward the tumor. The streaks will converge at multiple different focal points toward the periphery of the lesion. Each focal point will serve as the base for the convergence of a few streaks resulting in the formation of a leaf-like area. The center of gravity of each focal point will differ. The central part of the BCC will often appear shiny white, hypopigmented, and structureless	The streaks are thinner and sharper in focus. The streaks always radiate away from tumor mass toward normal uninvolved skin. In the portion of the lesion manifesting streaks, the streaks tend to converge toward the geometric central portion of the lesion. The central portion of the lesion is usually pigmented/hyperpigmented and often has a blue-white veil

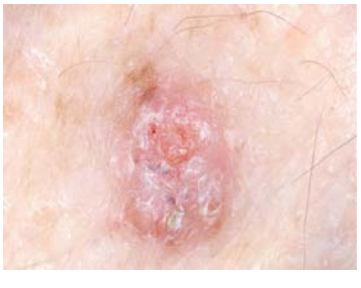
Abbreviations: BCC, basal cell carcinoma; CMN, congenital melanocytic nevus.



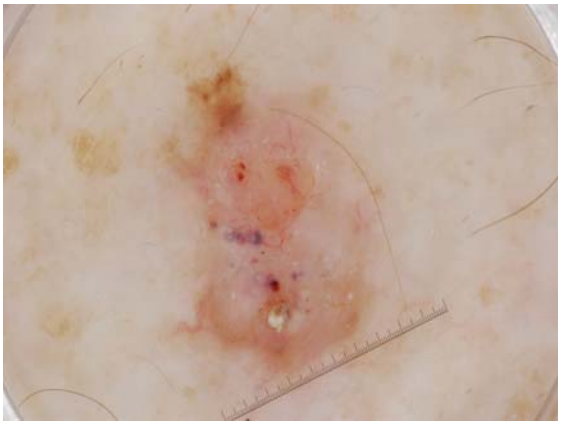
▲ **Figure 10.19a** Clinical image of a congenital nevus.



◀ **Figure 10.19b** Dermoscopy reveals a few bluish globules that appear not to be aggregated. This type of globular color and distribution is characteristic of basal cell carcinoma; however, in the presence of the reticular network the diagnosis of a melanocytic lesion was never in doubt. In addition, it is important to be aware that the presence of a network trumps the presence of globules for classification purposes. Thus, this is a melanocytic lesion based on the presence of network. The globules are a secondary clue in this lesion.



▲ **Figure 10.20a** Clinical image of a BCC.



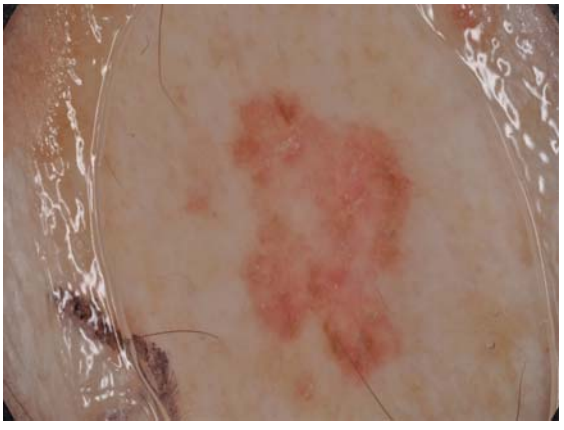
◀ **Figure 10.20b** Dermoscopy reveals nonaggregated bluish globules. In the context of the clinical view and in the presence of arborizing vessels the diagnosis of BCC is not in doubt.

Pigmented Bowen's disease

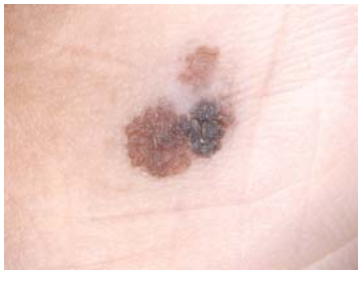
Pigmented Bowen's disease often appears structureless under dermoscopy. Based on the rules of the two-step dermoscopy algorithm, such structureless tan lesions are either subjected to short-term mole monitoring, confocal microscopy, or biopsy to rule out melanoma (Fig. 10.21). In some cases, such as the pigmented Bowen's disease, focal brown dots or globules are revealed at the periphery (Fig. 8f.21; see also chap. 8f, on equivocal lesions) (Fig. 10.22). These dots and globules are often aligned in centripetal linear tracks. The radially aligned linear arrangement of brown dots and globules at the periphery appears to be a fairly specific feature of Bowen's disease. These brown dots and globules correspond to clustered melanophages in the superficial dermis or to a proliferation of malignant pigmented keratinocytes in the epidermis (Zalaudek et al., 2004). The benign dermoscopic and histopathologic counterpart to these globules are the globules seen in clonal SK. Clues to the correct diagnosis of Bowen's include a rough texture and scale, radially aligned dots/globules at the periphery, and the presence of glomerular vessels.

In the event that a squamous cell carcinoma (SCC) is misclassified as a melanocytic neoplasm, the lesion will inevitably be biopsied to rule out melanoma. Thus, errors in clinical diagnosis of a Bowen's patch as a melanoma will have no bearing on management because the lesion will be biopsied regardless.

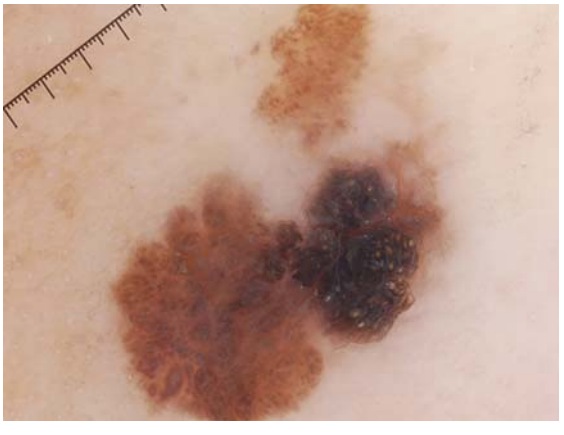
▲ **Figure 10.21a** Clinical image of a biopsy-proven squamous cell carcinoma in situ of the Bowen's type.



◀ **Figure 10.21b** Dermoscopy reveals a tan structureless lesion. The two-step dermoscopy algorithm considers all structureless lesions to be melanocytic with melanoma as the rule out. The reason for this is that this algorithm's main goal is to avoid missing a structureless melanoma. This is why it is recommended that structureless lesions be followed or monitored. NB: monitoring is recommended only for flat nonpalpable lesions. For raised lesions a biopsy is recommended.



▲ **Figure 10.22a** Clinical image of a keratotic tumor on the foot.



◀ **Figure 10.22b** The lesion has milia-like cysts and multiple brown globules at the periphery that are aligned centripetally. This is a biopsy-proven Bowen's disease.

Cutaneous Metastasis

Noncutaneous malignancies can metastasize to the skin. On occasion the foci of metastatic cells can come in close proximity to the epidermodermal junction or hair follicles and become colonized with melanocytes or the cutaneous melanocytes can transfer melanin to the tumor clusters (Micallef et al., 2004). Once melanized these metastatic foci mimic melanocytic nests and appear as globules under dermoscopy. These globular structures can appear as light brown, dark brown, or gray globules that are irregularly and asymmetrically distributed. Based on the aforementioned dermoscopic morphology it should come as no surprise that melanoma often enters the differential diagnosis for such metastatic lesions (Fig. 10.23) (Micallef et al., 2004; Wyatt et al., 2006).

Streaks in Nonmelanocytic Lesions

A streak or structures that resemble streaks can be seen in SK, BCC, and pigmented Bowen's disease.

Seborrheic Keratosis

Peripheral streaks were observed in 13 of 402 pigmented SK (Fig. 8f.27; see also chap. 8f). These streaks correlated to a proliferation of pigmented basaloid cells and they can on occasion be seen in growing SK (De Giorgi et al., 2002). On occasion these streak-like structures in an SK correspond to the epidermal ridges (i.e., fat finger-like structures) commonly seen in SK (Fig. 10.24).The waxy stuck-on feel of SK can help in correctly diagnosing these SKs. Other clues to the correct diagnosis include sharp demarcation, a negative wobble test (instead of wobbling, the lesion slides), and the presence of milia-like cysts and comedo-like openings.

Basal Cell Carcinoma

Streaks were reported in 2.8% of pigmented BCCs by Menzies et al. (2000), whereas Altamura et al. (2010) found streaks in 0.6% of studied BCCs (Fig. 8f.20; see also chap. 8f). Differences between streaks seen in BCCs and in melanocytic lesions are described in Tables 10.1 and 10.2, and Figures 10.25 and 10.26.

Bowen's Disease

Streaks seen in Bowen's disease have been described as flossy (Hayashi et al., 2009; Inoue et al., 2010), irregular, and are located at the periphery of the lesion (Gutierrez-Mendoza et al., 2010). These streaks correlate to pigmented dendritic melanocytes (Gutierrez-Mendoza et al., 2010). Peripheral, regularly distributed radial streaks have also been seen in pigmented SCC (De Giorgi et al., 2009). Such lesions will invariably be biopsied with a rule out diagnosis of melanoma. Thus, although the clinical diagnosis may be incorrect, the management decision to perform a biopsy will usually be correct. Clues to the correct clinical diagnosis include a scaly surface that is commonly present in SCC.

Cutaneous Metastasis

As was mentioned above noncutaneous malignancies can metastasize to the skin. On occasion streak-like structures can be seen in metastatic foci (Fig. 10.27). The reasons for seeing melanocytic structures in metastatic foci have been discussed previously.

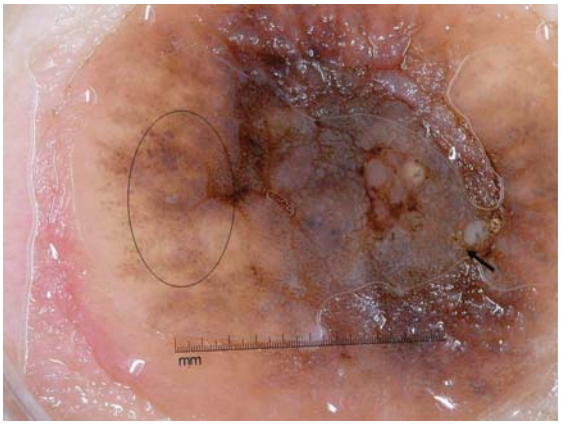
Homogenous Blue Pigmentation in Nonmelanocytic Lesions

Structureless, homogenous blue pigmentation is typical of blue nevi as well as 39% of cutaneous metastatic melanomas (Bono et al., 2004). However, hemosiderotic DF, Kaposi's sarcoma, BCC, vascular lesions, and tattoos also could display a homogenous blue pattern.

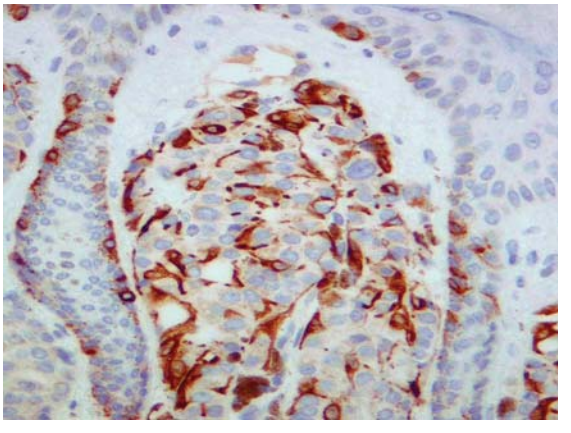
Dermatofibroma

Although DF are usually diagnosed with ease, the hemosiderotic variant can display a diffuse or localized homogenous blue (Ozdemir, Kilinc & Akalin,

▲ **Figure 10.23a** Clinical image of a focus of breast cancer that has metastasized to the skin of the breast. The metastatic focus has brown pigmentation.

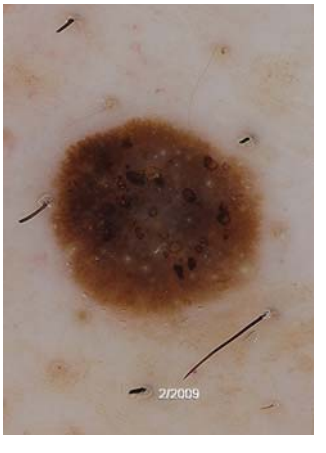


◀ **Figure 10.23b** With dermoscopy one can appreciate numerous globules as can be seen within the highlighted oval.

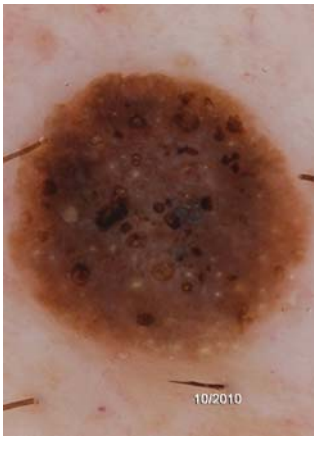


◀ **Figure 10.23c** Histopathology reveals clusters of breast cancer metastatic cells in the papillary dermis. This metastatic focus appears to have been colonized with melanocytes. The breast cancer metastatic cells seen here have melanin in their cytoplasm, which presumably was transferred from melanocytes to the breast cancer cells.

▲ **Figure 10.24a** Clinical image of a SK.



◀ **Figure 10.24b** This dermoscopic image reveals small streak-like structures at the periphery.



◀ **Figure 10.24c** This image was taken 1.5 years later and shows that this SK has grown larger, with the streak-like structures no longer visible.

2006), blue-gray (Kilinc Karaarslan et al., 2007), blue-yellow, blue-violaceous, or red-bluish (Zaballos et al., 2006) pigmentation. The homogenous pigmentation has been attributed to siderophages containing hemosiderin granules in the superficial and reticular dermis (Ozdemir, Kilinc & Akalin, 2006), as well as prominent blood-filled spaces and hemosiderin deposition (Zaballos et al., 2006). Although a peripheral pigment network, vascular structures, and white linear and homogenous structures also might be the features of this variant DF, it can be difficult to differentiate from melanoma and typically warrants biopsy (Zaballos et al., 2006).

Vascular Lesions and Kaposi's Sarcoma

Vascular lesions, such as cherry hemangiomas and angiokeratomas, can mimic melanoma when the vasculature is deeper in the dermis and displays a fuzzy blue pigmentation (Fig. 10.28). Similarly, Kaposi's sarcoma can sometimes display a structureless blue (Scope et al., 2006) to blue-red pattern due to the same phenomenon (Coates & Bowling, 2010).

Basal Cell Carcinoma

On rare occasions a BCC can present as a homogenous blue lesion (Figs. 10.29–10.31). Clues to the correct diagnosis of BCC include a shiny appearance on clinical view and shiny white areas seen with polarized dermoscopy. However, some BCC will not manifest any clues that can help the clinician make a clinical diagnosis with confidence (Fig. 10.32).

Tattoos Including Radiation Tattoos

Carbon dye or India ink are commonly used as tattoo inks, including for tattoos used to position radiation fields (Haselow & Krause, 1980). These tattoos can simulate melanin by appearing blue under dermoscopy (Scope et al., 2006). Clinical history, prior radiation, patterned tattoo placement, and radiation-induced skin changes can aid in the diagnosis (Fig. 10.33).

MISCLASSIFIED MELANOCYTIC LESIONS

Misclassification of melanocytic lesions can occur when lacking structures that define the lesion as melanocytic, such as network, aggregated globules, or streaks. In addition, misclassification of melanocytic lesions as nonmelanocytic lesions can also occur if the tumor manifests both melanocytic and nonmelanocytic features, but in which the nonmelanocytic features are more conspicuous, leading the observer to focus their attention only on the nonmelanocytic features (known as anchoring bias or first impression) (Croskerry, 2002). Indeed, 15% of biopsy-proven melanomas simulated nonmelanocytic lesions under dermoscopy (Puig et al., 2007).

Dermatofibroma-Like Lesions

Melanoma masquerading as DF-like lesions are exceedingly rare. They are reported as atypical lesions presenting with multiple central white scar-like patches with a peripheral pigmented network (Blum & Bauer, 2003) or central, homogenous reddish pigmentation with linear irregular vessels, surrounded by a blue-white to brown pigmentation with focal brown globules (Zalaudek et al., 2005). In fact, cases of DF demonstrating an atypical pattern, which includes an atypical pigment network, atypical scar-like area, negative network, atypical homogenous pigmentation or irregular distribution of these structures, may be difficult to differentiate from melanoma (Zaballos et al., 2008). However, there are other clues that can assist in the correct classification of DF, including the dimple sign and the clinical history. Nevertheless, it is important to not rely only on palpation or dermoscopy to render a final diagnosis, instead apply the different components of the cognitive process and consider melanoma in the differential diagnoses when there is lack of clinicodermoscopic correlation or a DF-like lesion that presents with an atypical pattern (Zalaudek et al., 2005; Marghoob & Scope, 2009)

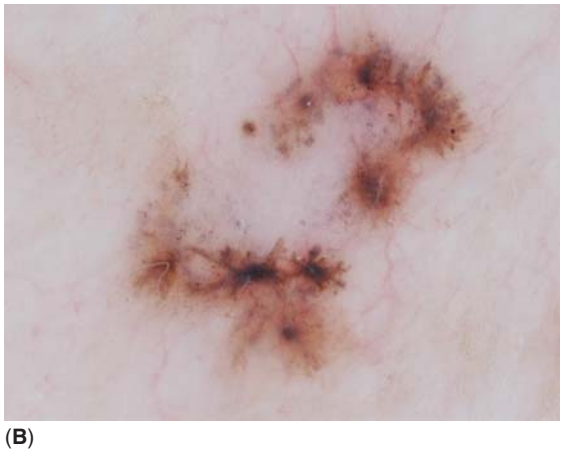
Basal Cell Carcinoma-Like Lesions

Although arborizing vessels have a positive predictive value of 94% for BCCs (Argenziano et al., 2004), they can also appear in some melanocytic lesions, such as melanomas and cutaneous melanoma metastases. It has been suggested that thick melanomas can present arborizing vessels, which are usually more irregular and with less branches than BCCs (Zalaudek et al., 2010). In a series of 97 cases of difficult-to-diagnose melanomas, four lesions presented with arborizing vessels, resembling a BCC. However, all melanoma mimicking a BCC were biopsied because a skin cancer diagnosis was in the differential (Puig et al., 2007) (Fig. 8f.11; chap 8f). Therefore, despite this diagnostic pitfall, melanomas displaying arborizing vessels and classified as BCCs will ultimately undergo a skin biopsy with the correct diagnosis being rendered by the pathologist.

Hemangioma-Like Lesions

On occasions melanomas can simulate hemangiomas. However, lacunas seen in hemangiomas are red, blue-red, or blue-black, separated by well-defined septae (Marghoob, Braun & Kopf, 2005). In contrast, lacunas seen in melanomas tend to be ill-defined, not well-demarcated, and may

▲ **Figure 10.25a** Clinical image of a pigmented lesion on the chest of a 70-year-old man.



(**B**)

Figure 10.25 (**B**) Dermoscopy reveals numerous streak-like structures. However, notice that some of these streak-like structures, especially those located at the bottom left corner of the lesion, have the appearance of large spoke-wheel-like structures with some of the streaks radiating toward the tumor. These structures correspond with BCC tumor islands. In melanocytic lesions the streaks will never radiate toward the tumor, they always radiate away from the tumor toward normal skin and they represent the radial growth phase of the tumor. Also notice that the streak-like areas on the top right side converge at a focal area toward the periphery of the lesion creating a leaf-like area. Streaks in a melanocytic lesion tend to converge toward the center and not toward the periphery. Lastly, notice that the center of this BCC is hypopigmented. In melanocytic lesions having streaks, the center is usually hyperpigmented and will often have a blue-white veil.

▲ **Figure 10.26a** Clinical image of a melanoma.

◀ **Figure 10.26b** Dermoscopy reveals streaks. Notice that all the streaks radiate away from the tumor. The streaks converge at a point toward the center of the lesion, and the center of the lesion is hyperpigmented.

▲ **Figure 10.27a** Clinical image of a cutaneous metastatic focus of breast cancer.

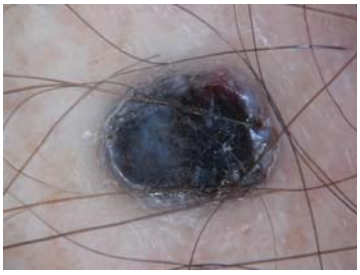
◀ **Figure 10.27b** Dermoscopy reveals streak-like structures.

▲ **Figure 10.28a** Clinical image of a hemangioma.

◀ **Figure 10.28b** Dermoscopy reveals a bluish color throughout the entire lesion.

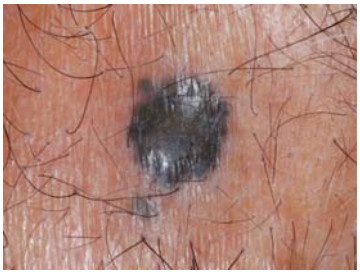
▲ **Figure 10.29a** Clinical image of a biopsy-proven BCC on the right temple of an 83-year-old woman.

◀ **Figure 10.29b** Dermoscopy reveals a homogenous blue nodule. The blue areas have differing hues. The differential diagnosis is between a melanoma, BCC, and blue nevus. There are no dermoscopic clues in this lesion to help with the diagnosis. On histopathology this was a BCC.



▲ **Figure 10.30a** Clinical image of a nodular melanoma.

◀ **Figure 10.30b** Dermoscopy reveals a homogenous blue lesion with differing shades of blue and a blue-white veil. The differential diagnosis for this lesion is between melanoma, basal cell carcinoma, and cellular blue nevus.



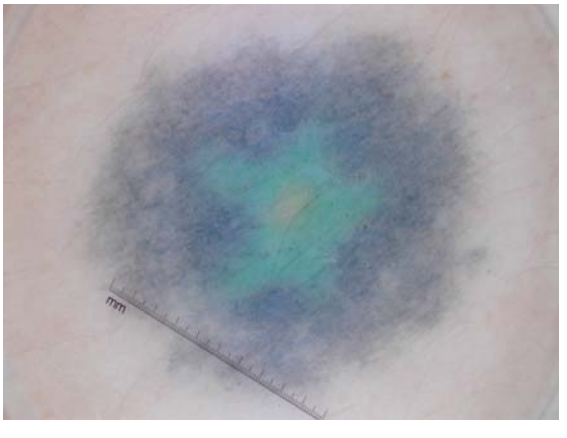
▲ **Figure 10.31a** Clinical image of a blue nevus.

◀ **Figure 10.31b** Dermoscopy has a homogenous blue color. The difference between this lesion and the malignancies shown in Figures 10.29 and 10.30 is that this blue nevus does not display as many differing hues of blue. However, ultimate diagnosis rests with histopathology.

▲ **Figure 10.32a** Clinical image of a sessile lesion on the back of this patient.

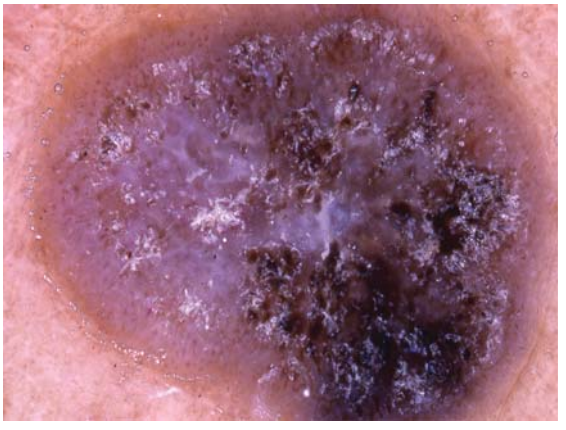
◀ **Figure 10.32b** Dermoscopy reveals no features to help with the diagnosis. Knowing that the patient has the basal cell nevus syndrome leads one to make an educated guess that the lesion in question is probably a BCC. Biopsy of this lesion confirmed the diagnosis of BCC.

▲ **Figure 10.33a** Clinical image of a tattoo of a star.



◀ **Figure 10.33b** Dermoscopy reveals a homogenous blue color, which is reminiscent of the blue color seen in blue nevi.

▲ **Figure 10.34a** Clinical image of a rough stuck-on appearing lesion on the thigh.



◀ **Figure 10.34b** Dermoscopy reveals a lesion with a blue-white veil and polymorphous vessels. This lesion was biopsied and was a verrucous melanoma.

▲ **Figure 10.35a** Clinical image of a firm papule on the thigh of this patient. The lesion dimples when squeezed.

◀ **Figure 10.35b** Dermoscopy reveals a tan patch superimposed by a papule. The papule has vessels arranged in a string of pearls distribution. This lesion was a dermatofibroma with a superimposed clear cell acanthoma.

present with small linear vessels within the lacuna-like structures (Puig et al., 2007) (Figs. 8f.8, 8f.9; see also chap. 8f).

Seborrheic Keratosis-Like Lesions

Melanoma can mimic and share dermoscopic features with SK, such as milia-like cysts and comedo-like openings (Braga et al., 2008). However, to avoid misclassification of melanocytic lesions as SK, it is important to realize that once a lesion has been defined as melanocytic in the first-step of the two-step algorithm, the presence of milia-like cysts or comedo-like openings should be ignored—if not ignored the presence of milia and comedos may lead to the incorrect diagnosis of SK (Fig. 8f.14; see also chap. 8f). Why does this occur? Structures such as milia-like cysts and comedo-like openings are very conspicuous and are detected almost immediately without requiring a thorough inspection of the entire lesion. This may result in errors, such as anchoring bias or first impression bias where the diagnosis is based on the most conspicuous structures, and the subtler diagnostic structures go unnoticed. Following the two-step algorithm as outlined in this textbook and in the concluding chapter (chap. 17) will help minimize such errors from occurring (Croskerry, 2002). Lastly, verrucous melanoma can clinically, dermoscopically, and histologically mimic SK (Fig. 10.34) (Blessing, Evans & al Nafussi, 1993). Dermoscopic clues to the diagnosis of verrucous melanoma include the presence of atypical vessels and irregular pigment distribution (De Giorgi et al., 2011; Gencoglan et al., 2011).

Pyogenic Granuloma-Like Lesions

Amelanotic melanomas can clinically and dermoscopically mimic pyogenic granulomas (Elmets & Ceilley, 1980; Junck, Huerter & Sarma, 2011). Not only can they have similar clinical histories, summarized by the EFG rule (elevated, firm lesions with continuous growth) (Zalaudek et al., 2010), they share common dermoscopic features, including a reddish homogenous area and linear, irregular vessels or polymorphous/atypical vessels (Zaballos et al., 2010). Because there are no accurate criteria differentiating pyogenic granulomas from melanoma, the histopathology inspection of any suspected pyogenic granuloma is recommended to exclude the diagnosis of amelanotic melanoma (Zalaudek et al., 2010).

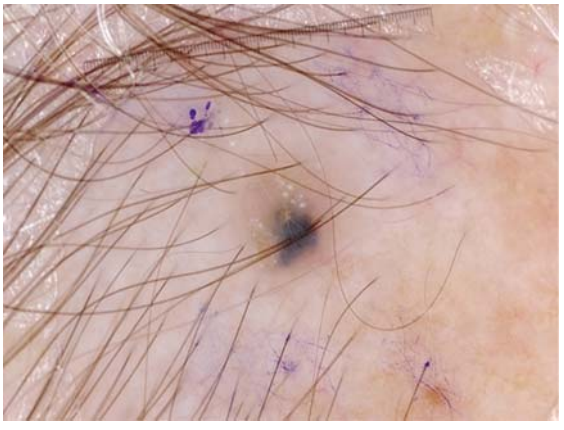
COLLISION TUMORS

The coexistence of two different neoplasms in a single lesion, so-called collision or compound tumors, may display two separate dermoscopic patterns (Fig. 10.35) (Salerni et al., 2011; Martorell et al., 2010; Zaballos et al., 2005). Numerous combinations have been described, including the co-existence of melanoma with SK (Birnie & Varma, 2008), SCC (Mopuri, Laitung & Cardozo, 2009), and BCC (Pierard et al., 1997) (Fig. 8f.15; see also chap. 8f). Management of these lesions should be based on the worst and most concerning diagnosis (Fig. 10.36).

SUMMARY

Awareness of these common exceptions and potential diagnostic pitfalls can help in avoiding diagnostic errors when using the two-step algorithm. Integration of dermoscopic and clinical features, context, and history is often required to determine the correct diagnosis. If conflicting dermoscopic and/or morphologic features are present, pathologic confirmation to rule out the worst possible diagnosis may be necessary. Ultimately, it is important to remember that the main purpose of dermoscopy is to determine whether a lesion needs to be biopsied so as not to miss a malignancy. Following the rules and sequence outlined in the two-step algorithm will almost always lead to the correct management decision with cutaneous malignancies being subjected to a biopsy.

▲ **Figure 10.36a** Clinical image of a pigmented lesion on the temple.



◀ **Figure 10.36b** Dermoscopy reveals multiple milia-like cysts and a blue ovoid nest. This lesion was biopsied and pathology revealed a basal cell carcinoma arising within an seborrheic keratosis.

REFERENCES

Agero, AL., Taliercio, S., Dusza, SW., et al., 2006, Conventional and polarized dermoscopy features of dermatofibroma. *Arch Dermatol*, 142, 1431–7.

Altamura, D., Menzies, SW., Argenziano, G., et al., 2010, Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *J Am Acad Dermatol*, 62, 67–75.

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., 2004, Dermoscopy of melanocytic hyperplasias: subpatterns of lentigines (ink spot). *Arch Dermatol*, 140, 776.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Arpaia, N., Cassano, N. & Vena, G.A., 2005, Dermoscopic patterns of dermatofibroma. *Dermatol Surg*, 31, 1336–9.

Birnie, A.J. & Varma, S., 2008, A dermatoscopically diagnosed collision tumour: malignant melanoma arising within a seborrhoeic keratosis. *Clin Exp Dermatol*, 33, 512–13.

Blessing, K., Evans, A.T. & al-Nafussi, A., 1993, Verrucous naevoid and keratotic malignant melanoma: a clinico-pathological study of 20 cases. *Histopathology*, 23, 453–8.

Blum, A. & Bauer, J., 2003, Atypical dermatofibroma-like pattern of a melanoma on dermoscopy. *Melanoma Res*, 13, 633–4.

Blum, A. & Roehm, S., 2003, Accessory nipple looks like dermatofibroma in dermoscopy. *Arch Dermatol*, 139, 948–9.

Bono, R., Giampetruzzi, AR., Concolino, F., et al., 2004, Dermoscopic patterns of cutaneous melanoma metastases. *Melanoma Res*, 14, 367–73.

Braga, JC., Scope, A., Klaz, I., et al., 2008, Melanoma mimicking seborrheic keratosis: an error of perception precluding correct dermoscopic diagnosis. *J Am Acad Dermatol*, 58, 875–80.

Braun, RP., Rabinovitz, HS., Krischer, J., et al., 2002, Dermoscopy of pigmented seborrheic keratosis: a morphological study. *Arch Dermatol*, 138, 1556–60.

Braun, R.P., Krischer, J. & Saurat, J.H., 2000, The "wobble sign" in epiluminescence microscopy as a novel clue to the differential diagnosis of pigmented skin lesions. *Arch Dermatol*, 136, 940–2.

Coates, D. & Bowling, J., 2010, Dermoscopy is not always helpful in the diagnosis of vascular lesions. *Australas J Dermatol*, 51, 292–4.

Croskerry, P., 2002, Achieving quality in clinical decision making: cognitive strategies and detection of bias. *Acad Emerg Med*, 9, 1184–204.

De Giorgi, V., Massi, D., Stante, M., & Carli P., 2002, False "melanocytic" parameters shown by pigmented seborrheic keratoses: a finding which is not uncommon in dermoscopy. *Dermatol Surg*, 28, 776–9.

De Giorgi, V., Alfaioli, B., Papi, F., et al., 2009, Dermoscopy in pigmented squamous cell carcinoma. *J Cutan Med Surg*, 13, 326–9.

De Giorgi, V., Grazzini, M., Savarese, I., et al., 2011, What can hide under exophytic verrucous appearance? *Acta Derm Venereol*, 91, 100–1.

Elmets, C.A. & Ceilley, R.I., 1980, Amelanotic melanoma presenting as a pyogenic granuloma. *Cutis*, 25, 164–6, 168.

Ferrari, A., Soyer, HP., Peris, K., et al., 2000, Central white scarlike patch: a dermatoscopic clue for the diagnosis of dermatofibroma. *J Am Acad Dermatol*, 43, 1123–5.

Gencoglan, G., Inanir, I., Miskioglu, M. & Temiz, P., 2011, Acral amelanotic verrucous melanoma: dermoscopic findings. *Dermatol Surg*, 37, 107–10.

Gutiérrez-Mendoza, D., Narro-Llorente, R., Karam-Orantes, M., et al., 2010, Dermoscopy clues in pigmented Bowen's disease. *Dermatol Res Pract*, 1–9.

Haselow, R.E. & Krause, D.A., 1980, Problems with India ink skin markings. *Radiology*, 134, 542–3.

Hayashi, Y., Tanaka, M., Suzaki, R., Mori, N. & Konohana, I., 2009, Dermoscopy of pigmented Bowen's disease mimicking early superficial spreading melanoma. *Case Rep Dermatol*, 1, 11–15.

Hirata, SH., Almeida, FA., Tomimori-Yamashita, J., et al., 2004, "Globulelike" dermoscopic structures in pigmented seborrheic keratosis. *Arch Dermatol*, 140, 128–9.

Inoue, T., Kobayashi, K., Sawada, M., et al., 2010, Dermoscopic features of pigmented Bowen's disease in a Japanese female mimicking malignant melanoma. *Dermatol Res Pract*.

Junck, M., Huerter, C.J. & Sarma, D.P., 2011, Rapidly growing hemorrhagic papule on the cheek of a 54-year-old man. *Dermatol Online J*, 17, 11.

Kilinc Karaarslan, I., Gencoglan, G., Akalin, T. & Ozdemir F., 2007, Different dermoscopic faces of dermatofibromas. *J Am Acad Dermatol*, 57, 401–6.

Marghoob, A.A. & Scope, A., 2009, The complexity of diagnosing melanoma. *J Invest Dermatol*, 129, 11–13.

Marghoob, A., Braun, R. & Kopf, A., 2005, *Atlas of Dermoscopy*, New York: Taylor & Francis.

Martorell, A., Botella-Estrada, R., Nagore, E. & Guillen-Barona, C., 2010, Dermoscopic features of a collision tumour composed of a pigmented basal cell carcinoma and a melanoma. *J Eur Acad Dermatol Venereol*, 24, 982–4.

Menzies, SW., Westerhoff, K., Rabinovitz, H., et al., 2000, Surface microscopy of pigmented basal cell carcinoma. *Arch Dermatol*, 136, 1012–16.

Micallef, RA., Boffa, MJ., DeGaetano, J. & Muscat, V., 2004, Melanoma-like pigmented cutaneous metastases from breast carcinoma. *Clin Exp Dermatol*, 29, 144–6.

Mopuri, N., Laitung, J.K. & Cardozo, C., 2009, Collision tumour of squamous cell carcinoma and invasive malignant melanoma of scalp - a case report. *J Plast Reconstr Aesthet Surg*, 62, e104–5.

Ozdemir, F., Kilinc, I. & Akalin, T., 2006, Homogeneous blue pigmentation in dermatofibroma simulating a blue naevus. *J Eur Acad Dermatol Venereol*, 20, 733–4.

Oztas, M.O. & Gurer, M.A., 2007, Dermoscopic features of accessory nipples. *Int J Dermatol*, 46, 1067–8.

Piérard, GE., Fazaa, B., Henry, F., Kamoun, MR. & Piérard-Franchimont, C., 1997, Collision of primary malignant neoplasms on the skin: the connection between malignant melanoma and basal cell carcinoma. *Dermatology*, 194, 378–9.

Provost, N., et al., 1997, Globulelike dermoscopic structures in pigmented seborrheic keratosis. *Arch Dermatol*, 133, 540–1.

Puig, S., Argenziano, G., Zalaudek, I., et al., 2007, Melanomas that failed dermoscopic detection: a combined clinicodermoscopic approach for not missing melanoma. *Dermatol Surg*, 33, 1262–73.

Salerni, G., Lovatto, L., Carrera, C., et al., 2011, Correlation among dermoscopy, confocal reflectance microscopy, and histologic features of melanoma and basal cell carcinoma collision tumor. *Dermatol Surg*, 37, 275–9.

Scope, A., Benvenuto-Andrade, C., Agero, AL. & Marghoob, AA., 2006, Nonmelanocytic lesions defying the two-step dermoscopy algorithm. *Dermatol Surg*, 32, 1398–406.

Wyatt, AJ., Agero, AL., Delgado, R., Busam, KJ. & Marghoob, AA., 2006, Cutaneous metastatic breast carcinoma with melanocyte colonization: a clinical and dermoscopic mimic of malignant melanoma. *Dermatol Surg*, 32, 949–54.

Zaballos, P., Llambrich, A., Puig, S. & Malvehy, J., 2005, Dermoscopy is useful for the recognition of benign-malignant compound tumours. *Br J Dermatol*, 153, 653–6.

Zaballos, P., Llambrich, A., Ara, M., et al., 2006, Dermoscopic findings of haemosiderotic and aneurysmal dermatofibroma: report of six patients. *Br J Dermatol*, 154, 244–50.

Zaballos, P., Puig, S., Llambrich, A. & Malvehy, J., 2008, Dermoscopy of dermatofibromas: a prospective morphological study of 412 cases. *Arch Dermatol*, 144, 75–83.

Zaballos, P., Carulla, M., Ozdemir, F., et al., 2010, Dermoscopy of pyogenic granuloma: a morphological study. *Br J Dermatol*, 163, 1229–37.

Zalaudek, I., Argenziano, G., Leinweber, B., et al., 2004, Dermoscopy of Bowen's disease. *Br J Dermatol*, 150, 1112–16.

Zalaudek, I., Ferrara, G., Di Stefani, A. & Argenziano, G., 2005, Dermoscopy for challenging melanoma; how to raise the 'red flag' when melanoma clinically looks benign. *Br J Dermatol*, 153, 200–2.

Zalaudek, I., Kreusch, J., Giacomel, J., 2010a, How to diagnose nonpigmented skin tumors: a review of vascular structures seen with dermoscopy: part I. Melanocytic skin tumors. *J Am Acad Dermatol*, 63, 361–74.

Zalaudek, I., Kreusch, J., Giacomel, J., et al., 2010b. How to diagnose nonpigmented skin tumors: a review of vascular structures seen with dermoscopy: part II. Nonmelanocytic skin tumors. *J Am Acad Dermatol*, 63, 377–86.

11 Dermoscopy in general dermatology

Iris Zalaudek

INTRODUCTION

Despite the classic application of dermoscopy for diagnosing skin tumors, dermoscopy has been increasingly used for the evaluation of skin diseases, conditions, and manifestations in general dermatology (Zalaudek et al., 2006a). This has been greatly facilitated by the easy availability and accessibility of handheld noncontact dermoscopes. These instruments have enabled clinicians to effortlessly and rapidly view any and all skin conditions under dermoscopy, leading to observations linking particular dermoscopic morphologies with specific skin diseases. Although the use of dermoscopy in general dermatology is relatively new, many reports and studies have already been published and it is beyond the scope of this chapter to cover them all. This chapter will focus only on those entities that have well-established and recognized dermoscopic findings. It is imperative that dermoscopic morphology not be viewed in a vacuum and this is especially true when it comes to interpreting findings in nontumoral skin diseases. Clinical information, including patient history, clinical features, laboratory tests, radiographic imaging, and histopathologic findings, are all important and need to be integrated with the dermoscopic findings.

Among the list of new applications of dermoscopy, five main fields of dermoscopy in general dermatology can be distinguished, namely, dermoscopy of skin infections and infestations (entomodermoscopy), dermoscopy of inflammatory skin diseases (inflammoscopy), dermoscopy of hair disorders (trichoscopy), dermoscopy of the nailfold capillaries (capillaroscopy), and dermoscopy for treatment decisions or treatment monitoring.

ENTOMODERMOSCOPY: A NEW TOOL FOR THE DIAGNOSIS OF SKIN INFECTIONS AND INFESTATIONS

The term "entomodermoscopy" originates from the words dermoscopy and entomology and has been introduced to describe the use of dermoscopy in the diagnosis of infectious skin disorders (Zalaudek et al., 2008). Dermoscopy patterns have been described for a number of viral, bacterial, fungal, and parasitic skin infections (Table 11.1). Of those, the dermoscopic patterns of molluscum contagiosum, scabies, or lice infestations are highly specific and have been shown to aid in their rapid and accurate diagnosis in the daily routine.

Molluscum Contagiosum

This skin infection is caused by a contagious human-specific poxvirus. Dermoscopically, molluscum contagiosum displays a central pore or umbilication in association with polylobular white to yellowish amorphous structures, which are typically surrounded by linear, fine and blurred telangiectasias ("corona"-like vessels, also known as crown vessels) (Fig. 11.1) (Morales et al., 2005; Zaballos et al., 2006).

Scabies

Scabies is caused by a skin infestation with the mite *Sarcoptes scabiei* var. *hominis*, which is a ubiquitous human ectoparasite. Dermoscopic findings can often rapidly provide the diagnosis of scabies without the need to resort to the procedure of obtaining multiple skin scrapings followed by the time-consuming endeavor of searching the scraped material under a microscope for the presence of the scabies mite, their eggs, or feces (Argenziano et al., 1997; Bauer et al., 2001; Brunetti et al., 1998; Dupuy et al., 2007; Prins et al., 2004; Weinstock et al., 2000). The dermoscopic patterns of scabies are particularly well observable on the lateral sites of the fingers, toes, palms, and soles, as well as around the mamilla or umbilicus or on genital areas. Placing the dermoscope over the end of a suspected burrow often reveals a small, dark brown, delta-shaped structure, representing the anterior body of the adult female mite (her mouth and two front legs); this shape reminds some of a jet airplane (Fig. 11.2) (Argenziano et al., 1997; Bauer et al., 2001; Brunetti et al., 1998; Dupuy et al., 2007; Prins et al., 2004; Weinstock et al., 2000). Trailing the delta-shaped structure is a thin tract of whitish scale, representing the burrow, and which is reminiscent of a whitish condensation trail (contrail) following the delta-shaped "jet" (Fig. 11.2). Dupuy et al. (2007) found that the sensitivity of dermoscopy for the diagnosis of scabies was comparable to that of conventional microscopic examination of skin scrapings (91% *vs* 90%). Additionally they found that when dermoscopy was used to influence decisions regarding treatment, there were fewer patients left with untreated scabies, compared with when dermoscopy was not utilized.

As mentioned above, the brown triangle observed with dermoscopy corresponds to the anterior part of the mite, whereas the posterior part of the mite is usually translucent and often not visible. The "contrail" is caused by the mites' burrow in the skin, which may sometimes contain feces. The latter appear as small brown dots. Some training and experience is required to accurately differentiate the brown triangle of the mite from small brown dots or ovoid blotches (superficial blood crusts due to erosions) seen in other itchy skin conditions, such as eczematous dermatitis or prurigo.

Lice Infestations

Pediculus humanis capitis and *Phthirus pubis* are worldwide ectoparasites causing thousands of infestations per year. Dermoscopy allows a rapid and reliable diagnosis by permitting the identification of the louse or the nits fixed to the hair shaft (Bakos & Bakos, 2007b; Di Stefani et al., 2006a; Scanni & Bonifazi, 2006). The identification of cemented nits (eggs) located within 1–2 mm from the scalp's surface suggests active pediculosis infestation. Although the adult louse can be elusive and difficult to find, the diagnosis can be confirmed simply by identifying nits on the hair shaft. Dermoscopy confirms the presence of nits and also helps in determining whether these nits contain viable nymphs, dead nymphs, or are empty (Fig. 11.3A, B). Under dermoscopy, nits containing nymphs have a brown color and ovoid shape, while empty nits appear translucent with an oval shape that is disfigured by a flattened free end (Fig. 11.3C). Empty nits typically have a flattened free end, whereas dead birth nits contain a collapsed nymph, which dermoscopically appears as a focal brown area within the nit; and in addition, there is an air pocket, which appears dermoscopically as a translucent area within the egg (Fig. 11.3C). Noncontact polarized dermoscopy is preferred over contact dermoscopy since the former minimizes the risk for disease transmission to other patients. Alternatively, one can snip hairs on which presumed adherent nits are present, place them on the sticky side of transparent tape, followed by placement of the standard contact dermoscope on the nonsticky side of the tape. Such a method enables direct visualization of the hair and can help differentiate nits from pseudonits (i.e., hair casts, debris of hair spray or gel, or scales from seborrheic dermatitis) while obviating the risk of cross-contamination. Since it can distinguish viable nits from empty or dead ones, dermoscopy has been used to monitor treatment progress in scabies.

Phthiriasis

Pubic lice or "crabs" are usually found attached to the terminal hair shaft within hair-bearing areas, such as the genitalia, eyelashes, and scalp; however, they may on occasion be found on other body sites

Table 11.1 Dermoscopic Patterns Associated with Skin Infections and Infestations

	Diagnosis	Dermoscopy pattern	References
Viral	Facial-plane warts	Regularly distributed dotted vessels on a brown to flesh colored background, often intermingled by whitish lines	Zalaudek et al., 2008
	Common warts	Frogspawn patterns. Looped or dotted vessels within papillae that are typically whitish	Teoli et al., 2006; Vázquez-López et al., 2004a
	Plamoplantar warts	Yellowish structureless pattern typically with brownish to reddish lines or dots (corresponding to hemorrhages)	Dalmau et al., 2006; Kim et al., 2006
	Genital warts	Whitish reticulation	Zalaudek et al., 2008
	Molluscum contagiosum	Polylobular whitish structureless areas in the center surrounded by elongated blurred telangiectasias	Morales et al., 2005; Zaballos et al., 2006
Fungal	Tinea corporis	Coarse scale and chaotic direction/orientation of scaling: mixed vascular pattern	Vázquez-López et al., 2004a
	Tinea nigra	Fine superficial wispy-like gray to brownish lines that do not follow the anatomic structures of the furrows or ridges on glabrous skin. Clue: The superficial pigmentation can be easily removed by scraping the stratum corneum with a scalpel	Smith et al., 2001; Xavier et al., 2008
Bacterial	Follicultis	White to yellow dot filling the hair follicle surrounded sometimes by dotted vessels	Zalaudek et al., 2008
	Lupus vulgaris	Fine focused telangiectasias on a typically yellow to golden background. Sometimes a few milia-like cysts or whitish lines can be present	Brasiello et al., 2008
	Trichomycosis palmellina	Yellowish casts around the hair shafts	Personal observation
Parasites	Cutaneous larva migrans	Translucent brownish structureless areas in a segmental arrangement, which corresponded to the body of the larva, whereas the empty burrow revealed red-dotted vessels on dermoscopy	Elsner et al., 1997; Zalaudek et al., 2008
	Ixodex ricinus	Double pair of anterior legs protruding from the surface of the skin, whereas the chitinous body is seen as a brown to gray translucent "shield" with pigmented streaks	Pagliarello et al., 2006; Zalaudek et al., 2008
	Lice/nits	Vital nits: ovoid, brown structures fixed to the hair shaft Empty nits: Cases are translucent and typically show a plane and fissured free ending	Bakos & Bakos, 2007b; Di Stefani et al., 2006a; Di Stefani et al., 2006b; Scanni & Bonifazi, 2006
	Myiasis	Central opening surrounded by dilated blood vessels from which a yellowish structure with black barb-like spines can be seen. Movements of the larva can be seen	Bakos & Bakos, 2007a
	Scabies	Brown triangle at the end of a curved whitish line (jet with contrail)	Argenziano et al., 1997; Bauer et al., 2001; Brunetti et al., 1998; Dupuy et al., 2007; Prins et al., 2004 Weinstock et al., 2000
	Tungiasis	Central pigmented ring with a pore in the middle, eccentric gray-bluish blotch, in a whitish background	Bakos & Bakos, 2008; Bauer et al., 2004; Bauer et al., 2005; Cabrera et al., 2008; Di Stefani et al., 2005

containing vellous hair. Dermoscopy can easily help to diagnose this condition by identifying the crab via its characteristic louse morphology (Fig. 11.4).

Tinea Nigra

Tinea nigra (TN) is a superficial fungal infection caused by *Hortaea (Phaeoannellomyces) werneckii*, formerly called *Cladosporium werneckii* or *Exophilia werneckii*. TN characteristically presents as an asymptomatic, irregular, brown-black macules often mottled in coloration and darkest at the advancing border. It most commonly infects the stratum corneum of the palms and/or soles of children living in or visiting South and Central America, Asia, and Africa and, rarely, in the U.S.A. and Europe. Potassium hydroxide (KOH) examination of TN reveals brown to olive-colored, thick, branching hypha as well as budding yeast cells. TN may mimic junctional nevi or acrolentiginous melanoma. Although the diagnosis of TN is easy to confirm by KOH examination, more often than not, the diagnosis of TN is overlooked and many of these patients are subjected to unnecessary biopsies to rule out melanoma. Fortunately, dermoscopy may circumvent the physician's inclination to biopsy these lesions. Under dermoscopy, TN does not reveal the parallel pattern, fibrillar pattern, or lattice-like pattern characteristic of melanocytic lesions of the palms and soles. Instead, there are fine, wispy brown strands or "pigmented spicules," which represent pigmented hyphae in the stratum corneum. The pigment in TN does not follow or respect the dermatoglyphic furrows and ridges (Fig. 11.5).

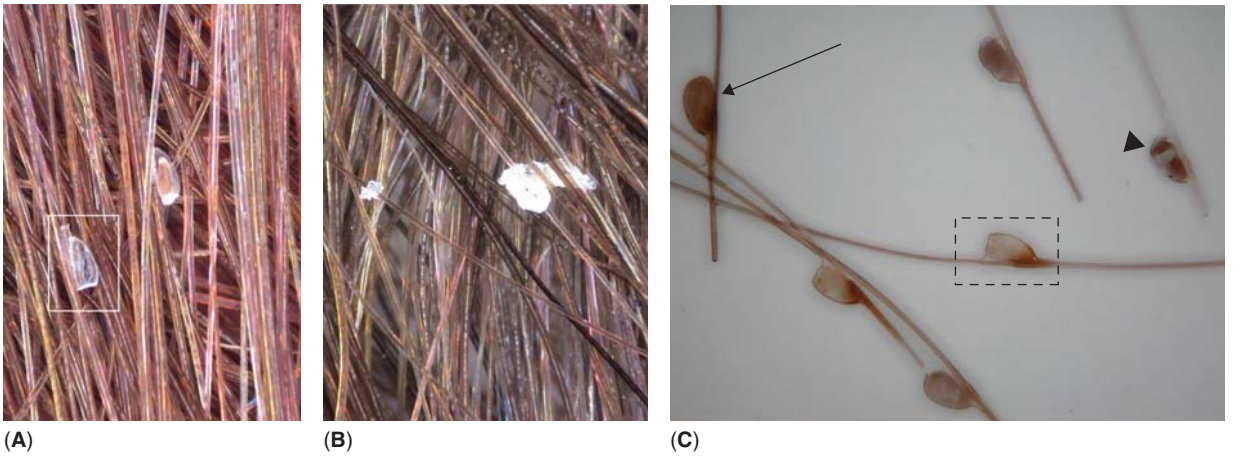
Verrucae

Cutaneous warts are due to localized benign epithelial hyperplasia with overlying surface hyperkeratosis that manifest as papules to large plaques; lesions may become confluent, forming a mosaic. Human papillomovirus infects epidermal keratinocytes and is the causative agent of the disease. On close examination, one can appreciate a disruption of dermatoglyphics as well as thrombosed capillaries. Warts can sometimes be difficult to distinguish from other cutaneous lesions, such as callus, corn, or even melanoma. Dermoscopic examination of these lesions can aid in distinguishing between these various entities. Under dermoscopy, verruca vulgaris displays, "multiple densely packed papilla, each containing a central red or black dot or loop, which is surrounded by a whitish halo" (Fig. 11.6). The red dots and loops and the black dots and loops represent normal and

▲ **Figure 11.1a** Clinical manifestation of two mollusca contagiosa on the forearm of an 8-year-old boy.

◀ **Figure 11.1b** Although the clinical features raise the suspicion of molluscum contagiosum, dermoscopy leaves little doubt about the diagnosis, exhibiting structureless central polymorphous structures surrounded by elongated telangiectasias (i.e., crown vessels).

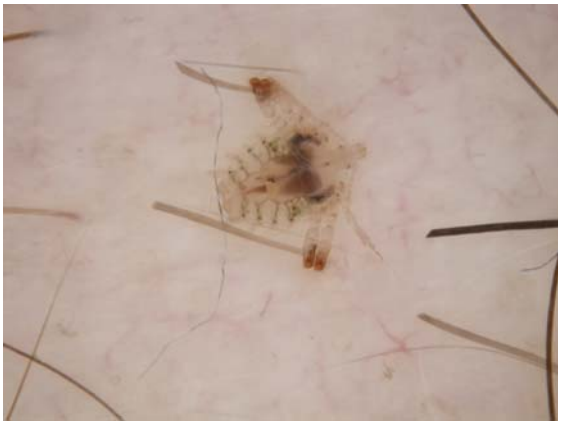
Figure 11.2 Dermoscopy of scabies showing brown triangles and whitish appearing burrow. One serpiginous burrow can clearly be seen. At each end of the burrow is a small dark triangular structure called a delta. Each delta-shaped structure represents one scabies mite.



(**A**) (**B**) (**C**)

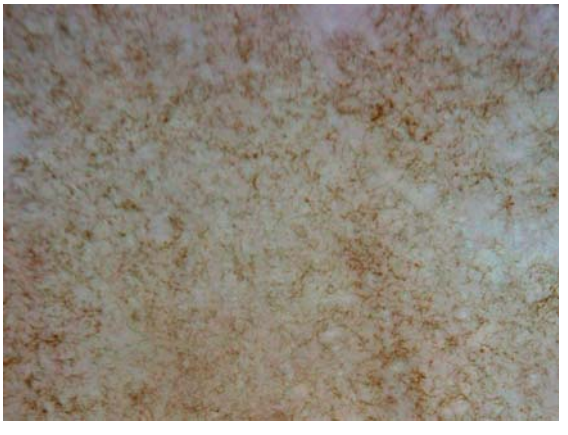
Figure 11.3 Side-by-side comparison of the clinical appearance of head lice nits (**A**) and pseudonits (**B**) attached to the hair shaft. With dermoscopy (C) the vital nits appear as roundish structures with a brownish center (arrow), while empty nits appear translucent with one side of the nit having a flat end (*square*). Dead birth nits appear with a focal brown color together with an air pocket (arrowhead).

▲ **Figure 11.4a** Clinical image of phthiriasis. Crab louse may be difficult to identify by naked-eye examination, especially if found in nongenital hair-bearing areas.



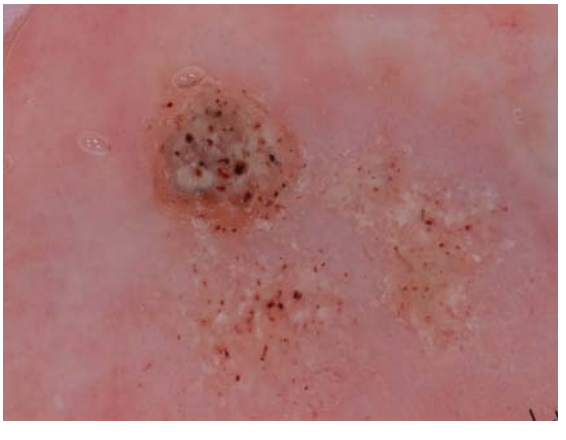
◀ **Figure 11.4b** Dermoscopic image showing the louse clinging onto hair shafts.

▲ **Figure 11.5a** Clinical image of tinea nigra on the sole of the foot.



◀ **Figure 11.5b** Dermoscopy exhibiting "pigmented spicules" or wispy lines that do not respect the dermatoglyphic ridges or furrows. Source: Images courtesy of Wilhelm Stolz.

▲ **Figure 11.6a** Clinical image of a wart.



◀ **Figure 11.6b** Dermoscopy reveals a verrucous lesion with numerous thrombosed capillaries. Nonthrombosed vessels are often surrounded by a white halo.

thrombosed capillaries, respectively. Plantar warts show slightly different features under dermoscopy. The effects of pressure due to weight bearing and trauma on the sole, results in an irregular distribution of black dots or streaks corresponding to thrombosed vessels and microhemorrhages. In contrast, calluses demonstrate homogenous opacities, whereas corns exhibit a translucent central core.

Bae et al. (2008) performed a study using dermoscopy to better assess complete resolution of the warts after treatment. They examined 111 lesions that were suspected of being plantar warts and after dermoscopy it was determined that 88% of the lesions were in fact warts, 8% were corns, and 4% were calluses. The group reported that their ability to visualize the lesions after treatments helped in determining whether clearance was achieved or further treatments were indicated.

DERMOSCOPY OF INFLAMMATORY DISEASES (INFLAMMOSCOPY)

The spectrum of inflammatory skin diseases is broad and their diagnosis is often clinically challenging. A large spectrum of different dermoscopic patterns associated with a variety of inflammatory skin disorders has been described (Table 11.2).

Table 11.2 Dermoscopy Patterns of Inflammatory Skin Disorders

Diagnosis	Dermoscopy patterns	References
Acute spongiotic dermatitis/eczema	Homogenous structureless erythema and scales	Vázquez-López et al., 2004a
Darier's disease	Central giant pseudocomedones, occasionally red dots, red lines, and erythema	Vázquez-López et al., 2004b
Drug rashes	Homogenously distributed linear vessels or mixed vascular patterns	Vázquez-López et al., 2004a
Erythema multiforme	Rim at the border (corresponding to the clinical red area) and centrally located bluish patch (corresponding to the clinical bluish area)	Vázquez-López et al., 2004a
Lichen planus	Radially arranged, horizontally oriented red lines or red dots surrounding reticular whitish striae (Wickham striae)	Vázquez-López et al., 2004a; Vázquez-López et al., 2003a; Vázquez-López et al., 2007; Zalaudek et al., 2006a
Morphea	Linear vessels within a lilac ring	Vázquez-López et al., 2004a
Panniculitis	Irregularly distributed mixed vascular patterns	Vázquez-López et al., 2004a
Psoriasis	Regularly distributed dotted vessels and scales	Blum et al., 2001; Bugatti et al., 2003; Vázquez-López et al., 2004a; Zalaudek et al., 2003
Scaling spongiotic dermatitis/eczema	Regularly distributed dotted and linear vessels, scales	Vázquez-López et al., 2004a
Urticaria	Linear vessels or reddish structureless areas	Vázquez-López et al., 2004a; Vázquez-López et al., 2003b
Venous stasis dermatitis	Regularly distributed glomerular vessels	Vázquez-López et al., 2004a
Annular erythema	Homogenously distributed red lines	Vázquez-López et al., 2004a
Henoch–Schönlein purpura	Red patches with blurred borders	Vázquez-López et al., 2004a
Pigmented purpuric dermatosis	Purple round-to-oval red dots, globules, and patches on a red-brownish or red-coppery diffuse background coloration	Vázquez-López et al., 2004a; Zaballos et al., 2004a; Zalaudek et al., 2006
Lichen simplex chronicus	Irregularly distributed small brownish-red dots	Vázquez-López et al., 2004a
Livedo reticularis	Linear vessels	Vázquez-López et al., 2004a
Necrobiosis lipoidica	Red lines on a yellow-to-red background	Vázquez-López et al., 2004a
Perniones	Diffuse structureless bluish patches	Vázquez-López et al., 2004a
Pityriasis rosea	Central mixed vascular pattern and peripheral colarette of scales	Chuh, 2001; Chuh, 2002; Vázquez-López et al., 2004a
Porokeratosis	Whitish yellow, erythematous or skin-colored annular structures, such as "outlines of a volcanic crater observed from a high point," which is due to the double rim of scale. The central component of the lesion has numerous dotted vessels (Fig. 11.21)	Delfino et al., 2004
Sarcoidosis	Red lines on a homogenous red-to-yellow background	Vázquez-López et al., 2004a
Sweet syndrome	Diffuse structureless bluish patches	Vázquez-López et al., 2004a
Urticaria pigmentosa	Tanned patches and pale pigment network	Vázquez-López et al., 2004a
Urticarial vasculitis	Irregularly distributed red to purple globules	Vázquez-López et al., 2004a

Although histopathology remains the standard for diagnosis, dermoscopy patterns of some inflammatory conditions, including lichen planus, psoriasis, pityriasis rosea, urticarial vasculitis, and pigmented purpuric dermatosis are quite specific, allowing for their in vivo diagnosis using dermoscopy with confidence (Lallas et al., 2012).

Lichen Planus

The dermoscopic features of lichen planus are specific enough that dermoscopy can replace the need for a histopathologic diagnosis in most cases. This is because dermoscopy allows for the rapid identification of the Wickham striae, which appear as whitish lines on a purple to reddish background, often surrounded by dotted or linear vessels (Figs. 11.7, 11.8) (Vázquez-López et al., 2003a; Vázquez-López et al., 2004a; Vázquez-López et al., 2007b; Zalaudek et al., 2006a). The presence of linear or dotted vessels located around the whitish striae are typically seen during the active phase of inflammation (Figs. 11.8, 11.9). In contrast to active lesions, regressing lesions exhibit either a structureless homogenous brown to gray coloration or gray dots (granularity) (Fig. 11.10). The granularity correlates with the presence of pigment-laden melanophages in the dermis. The difference between the two patterns of regressing lichen planus may prove helpful in predicting the clinical course. Lesions with a homogenous pattern are usually reflective of a transient and self-limiting case of lichen planus. In contrast, persistent lesions tend to manifest a granular pattern, clinically resembling ashy dermatitis (Fig. 11.10).

Psoriasis

Although the clinical diagnosis of psoriasis is usually straightforward, atypical presentations, such as when only a few plaques are present or when the psoriasis presents as guttata lesions, can make the certainty of diagnosis of psoriasis more challenging. In such cases, the dermoscopic patterns of regularly distributed and shaped, dotted vessels along with the presence of surface scale can help confirm the diagnosis of psoriasis (Vázquez-López et al., 2003; Vázquez-López et al., 2004; Zalaudek et al., 2006a).

▲ **Figure 11.7a** Clinical image of a lesion of lichen planus.

◀ **Figure 11.7b** Dermoscopy reveals Wickham striae and a few vessels surrounding the white Wickham striae. The presence of erythema, vessels, and striae is indicative of active lichen planus.

Figure 11.8 The dermoscopic hallmark of lichen planus in its active phase of inflammation with whitish striae (Wickham striae) on a purple background surrounded by dotted or linear vessels. Sometimes some central keratin plugs as seen in this case can also be present. The latter increase in number and size in hyperkeratotic variants.

Figure 11.10 Dermoscopy of lichen planus in its regressing phase reveals multiple gray dots or blotches, which correspond histopathologically to pigment-laden melanophages in the upper dermis. This pattern indicates a clinically persisting course of discoloration, also known as ashy dermatitis (insert).

Figure 11.9 Dermoscopic image of lichen planus with dotted vessels and Wickham striae.

Pityriasis Rosea

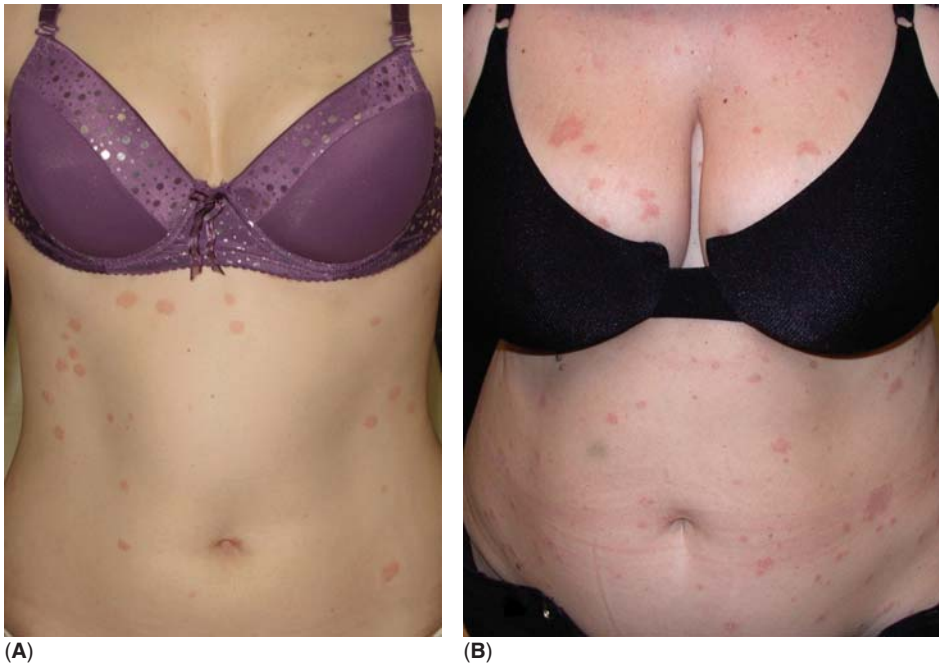
Pityriasis rosea may clinically mimic psoriasis of the guttate type (Fig. 11.11). However, in contrast to the homogenously distributed dotted vessels typically seen in psoriasis, pityriasis rosea consists of a brownish to reddish homogenous pigmented patch that is surrounded by the characteristic "colarette" of scale. This collaret consists of scale fragments at the border of the lesion and the scale appears to hang into the center of the lesion like a curtain. A few scattered linear or dotted vessels within the center may also be seen (Fig. 11.12) (Chuh, 2001; Chuh, 2002).

Pigmented Purpuric Dermatoses

The term benign pigmented purpuric dermatosis summarizes a group of dermatoses that are clinically characterized by yellow, orange, red, and/or brown pigmented areas. Within these areas one can usually see numerous pinpoint purpuric spots (Fig. 11.13). The five classic subtypes of benign pigmented purpura are Schamberg purpura, purpura Majocchi, eczematid-like purpura of Doucas and Kapetanakis, lichen aureus, and pigmented purpuric lichenoid dermatitis of Gougerot–Blum. Dermoscopy features of all subtypes are the same revealing multiple, red-to-purple globules or dots typically present on a yellowish to golden background. These dots and globules do not blanch when compressed (Figs. 11.13b, 11.14) (Zaballos et al., 2004; Zalaudek et al., 2006b).

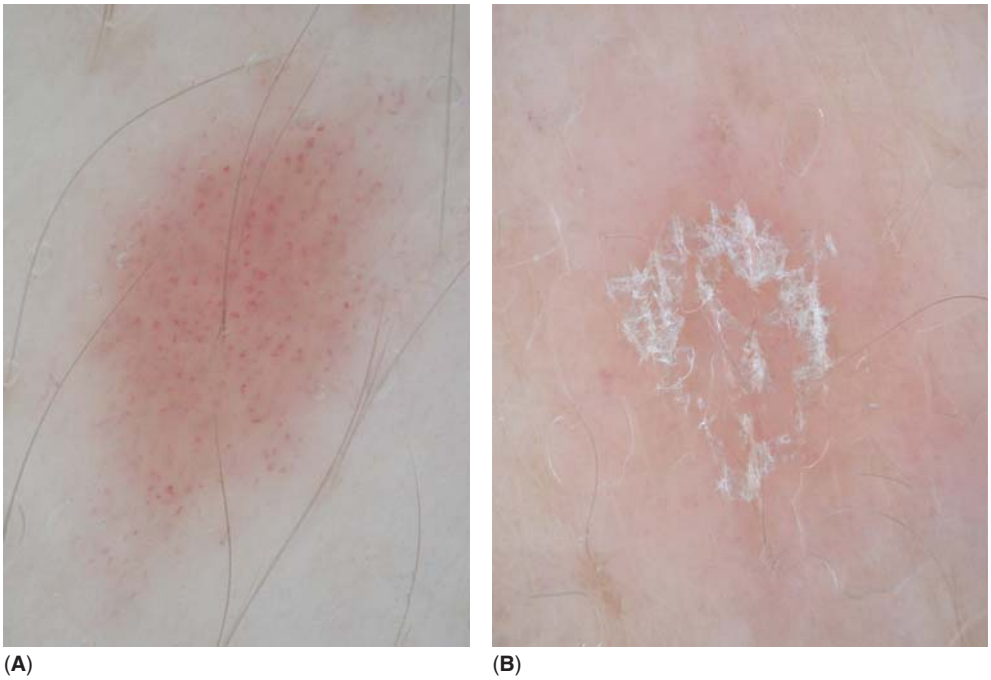
Urticarial Vasculitis

Dermoscopy can assist clinicians in differentiating common urticaria from urticarial vasculitis. Similar to pigmented purpuric dermatosis, the presence of purpuric globules in urticarial lesions suggests an underlying vasculitis (urticarial vasculitis). In contrast, lesions of common urticaria disclose red lines or avascular areas due to edema, which obscures the ability to visualize vascular structures (Fig. 11.15) (Vázquez-López et al., 2003b; Vázquez-López et al., 2004a).



(**A**) (**B**)

Figure 11.11 Clinical manifestations of psoriasis of the guttate type (**A**) and pityriasis rosea (**B**).



(**A**) (**B**)

Figure 11.12 Psoriasis reveals dermoscopically regularly distributed dotted vessels (**A**). In contrast, pityriasis rosea lacks vascular pattern and is characterized by the typical colarette of scale (**B**).

DERMOSCOPY OF HAIR DISORDERS (TRICHOSCOPY)

The clinical diagnosis of hair and scalp disorders is often clinically challenging. Evaluating these disorders with dermoscopy can provide information that helps the clinician in rendering the correct diagnosis (Inui et al., 2008; Inui et al., 2008; Liu et al., 2008; Olszewska et al., 2008; Radowska et al., 2007; Rudnicka et al., 2008; Ross et al., 2006; Tosti et al., 2005).

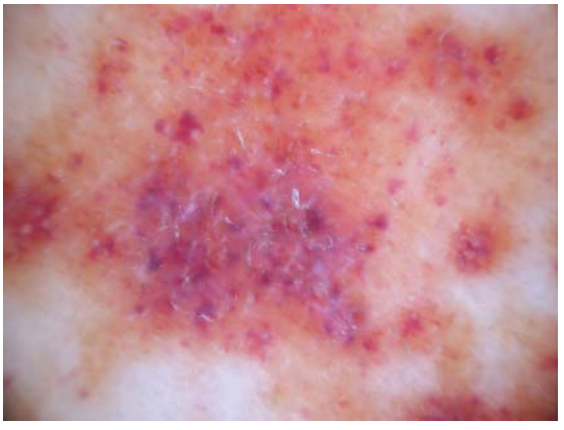
Sebopsoriasis

Similar to psoriasis of the trunk, psoriasis and to lesser extent seborrheic dermatitis of the scalp are dermoscopically characterized by twisted loops or dotted vessels that are regularly distributed around the hair follicles and the scalp (sebopsoriasis) (Ross et al., 2006).

Cicatricial Alopecia–Lichen Planopilaris

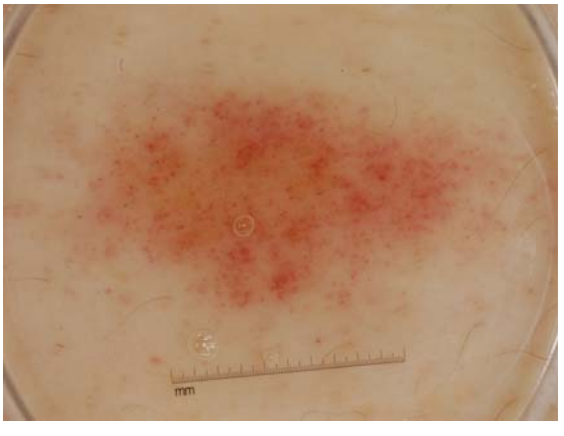
The loss of hair follicle orifices, perifollicular erythema, and/or scale surrounding the hair follicles is highly suggestive for lichen planopilaris. Occasionally, white dots, corresponding to empty fibrotic hair follicle orifices, may be present. These white dots need to be differentiated from the yellow dots, which correspond with hyperkeratotic hair follicle openings, and are typically seen in alopecia areata (Inui et al., 2008c).

▲ **Figure 11.13a** Clinical manifestation of pigmented purpuric dermatosis, type lichen aureus.



◀ **Figure 11.13b** Pigmented purpuric dermatosis, irrespective of subtype, reveals on dermoscopy red–to-purple dots or globules (petechiae) on a typically orange to golden background and this color does not blanch under compression (i.e., diascopy).

▲ **Figure 11.14a** Clinical image of lichen aureus.



◀ **Figure 11.14b** Dermoscopy reveals a golden background color with numerous petechiae.

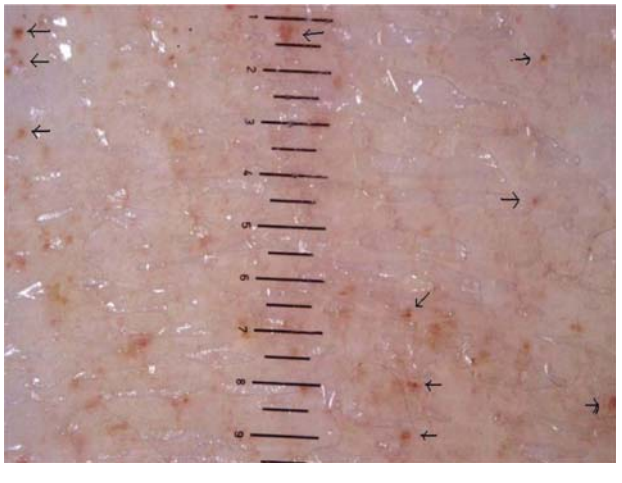


Figure 11.15 Urticarial vasculitis. Erythematous papules revealing purpuric dots and globules under dermoscopy. Purpuric globules in this case correspond histologically with vasculitis. Common urticaria and urticarial vasculitis can thus be differentiated with dermoscopy by the presence or absence of purpuric globules. Their presence is indicative of underlying vasculitis and their absence is suggestive of common urticaria.

Alopecia Areata

Yellow dots are a common finding in alopecia areata. Their presence can help confirm a diagnosis of alopecia areata and can help differentiate it from trichotillomania and telogen effluvium. Although yellow dots may also occur in some cases of androgenetic alopecia, the additional presence of hair shaft abnormalities typically associated with alopecia areata, such as exclamation point hairs, cadaverized hairs, and dystrophic hairs, leave little doubt in the diagnosis (Fig. 11.16) (Inui et al., 2008a; Inui et al., 2008b; Rudnicka et al., 2008; Tosti et al., 2005). The latter hair shaft abnormalities are particularly helpful in differentiating acute and diffuse alopecia areata of the female scalp from female pattern alopecia, which reveals only variations of the hair shaft diameter (Inui et al., 2008c; Rakowska et al., 2007).

DERMOSCOPY OF THE NAILFOLD (CAPILLAROSCOPY)

Autoimmune diseases, such scleroderma, lupus, dermatomyositis, and/or mixed connective tissue disease are commonly associated with changes of the nailfold capillaries. Although dermoscopy cannot replace laboratory or radiographic investigations, dermoscopy does allow for the rapid evaluation of the nail folds for the presence or absence of vascular abnormalities, such as dilated tortuous capillary loops (Fig. 11.17), megacapillaries, and microhemorrhages (Fig. 11.18).These irregular nailfold vascular structures are collectively referred to as the scleroderma pattern (SD pattern) of vessels because they can all be clearly visualized in patients with scleroderma. The presence of SD pattern of vessels in the nail folds can help in confirming the clinical suspicion of one of the autoimmune diseases mentioned above. Table 11.3 summarizes the dermoscopic nailfold vascular features and their diagnostic significance in different autoimmune diseases (Baron et al., 2007; Beltràn et al., 2007; Bergmann et al., 2003; Park et al., 2008; Sontheimer, 2004). Notably, the lack of vascular abnormalities in the nail folds is a reliable sign that can be used to exclude the diagnosis of one of the autoimmune disorders mentioned above. On the other hand, the presence of vascular abnormalities in the nail fold is not sufficient "per se" to diagnose an autoimmune disorder; however, their presence can be used to confirm

Figure 11.16 (**A**) Clinical features of alopecia areata. (**B**) Dermoscopically one can see yellow dots within the hair follicle ostia (*arrows*). (**C**) Cadaverized hairs, and other hair abnormalities such as exclamation and dystrophic hairs, are pathognomonic for alopecia areata.

Figure 11.17 Nailfold "hairpin-like" capillaries of the finger can be seen. Large capillaries and avascular areas have been used for the screening of scleroderma and patients with Raynaud's phenomenon. In this image, hemorrhagic areas are also shown, which may be related to angiopathy or minor trauma.

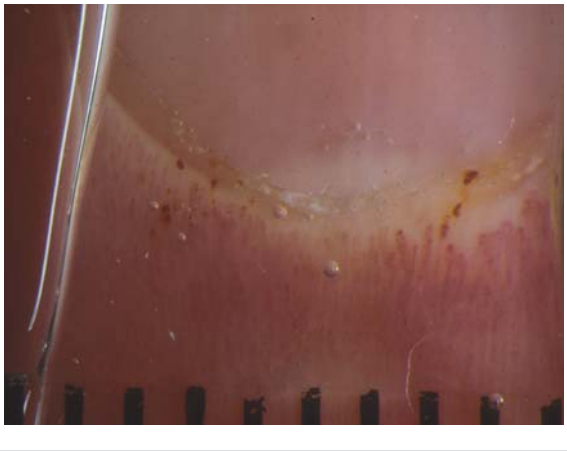


Figure 11.18 Capillaroscopy in dermatomyositis. The vessels are arranged densely, they are elongated and there is hemorrhage, which is reflective of the vasculitic process.

Table 11.3 Dermoscopy Patterns of Vascular Abnormalities Associated with Different Autoimmune Diseases

Diagnosis	Definition/diagnostic significance
SD pattern	Two or more of the following patterns in at least two nail folds: Enlargement of the capillary loops Loss of capillaries Disorganization of the distribution of the capillaries Budding capillaries Twisted capillaries and capillary hemorrhages (extravasates)
Dermatomyositis	SD pattern
Lupus erythematosus	SD pattern/mixed vascular pattern including giant capillaries or loss of capillaries
MCTD	SD pattern
Raynaud phenomenon without evidence of underlying CTD	SD pattern/twisted capillaries and extravasates of erythrocytes
Scleroderma	SD pattern

Abbreviations: CTD, connective tissue disease; MCTD, mixed connective tissue disease; SD, scleroderma.

the diagnosis. To be able to effortlessly recognize SD pattern vessels requires knowing what normal nailfold capillaries look like. We recommend that novices examine healthy nail folds so as to acquaint themselves with the range of normal vessel morphologies. This training of the eye to recognize normal features helps in the easy recognition of any pathologic vascular changes, should they occur.

DERMOSCOPY IN TREATMENT DECISION AND MONITORING

Besides utilizing dermoscopy for the purpose of rendering a more precise diagnosis, it can also be used for monitoring skin reactions to treatment and/or treatment response.

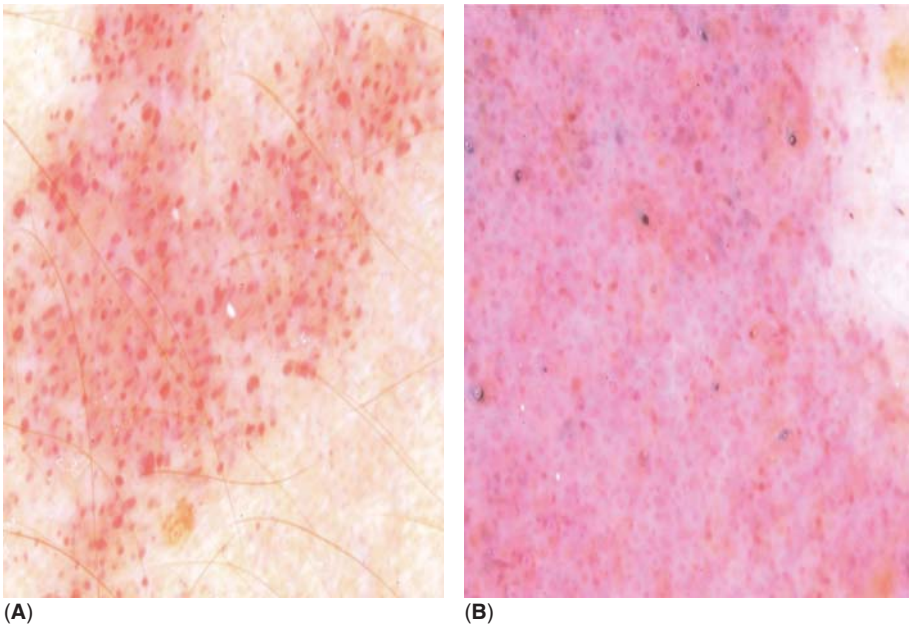


Figure 11.19 Dermoscopy of port-wine stains with superficial pattern (**A**) and deep pattern (**B**). In the former only bright red globules can be seen, which are predictive for a good response to laser treatment. By contrast, the presence of a gray veil as seen in (**B**) is due to a vascular plexus in the deeper parts of the skin and is indicative of a poor response to laser treatment.

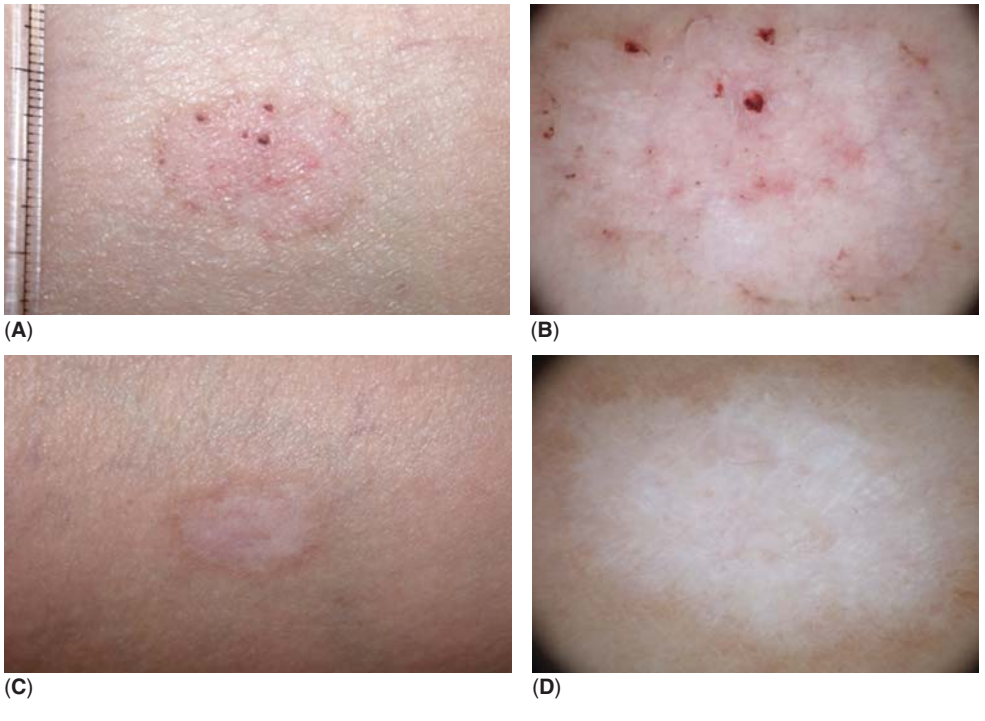


Figure 11.20 Clinical and dermoscopic images of a superficial BCC before (**A, B**) and after (**C, D**) topical treatment. A and C are the respective clinical images corresponding to the the dermoscopic images B and D.Dermoscopy aids not only in the diagnosis of superficial BCC by revealing shiny red-to-white structureless central areas and multiple small brown erosions, but also for treatment monitoring. As seen in (**D**), after successful treatment with topical imiquimod no dermoscopic features suggestive of persistent BCC are present. There are only white scar-like areas, which correspond to postinflammatory fibrosis.

In patients with port-wine stains (PWS), the pretreatment dermoscopic evaluation enables clinicians to estimate and predict the response to laser treatment. It has been shown that the venous plexus of PWS revealing dotted and/or globular patterns without a gray-whitish veil on dermoscopy is located superficially in the upper dermis. PWS with this dermoscopy pattern respond well to laser treatment (Procaccini et al., 2001; Sevila et al., 2004; Vázquez-López et al., 2005; Vázquez-López et al., 2004a; Vázquez-López et al., 2007a). In contrast, the presence of a gray-whitish veil and/or linear red-lined vessels indicates that the venous malformation is located deeper in the dermis, and successful treatment with lasers of such lesions can be more challenging (Fig. 11.19).

Dermoscopy has also been used in monitoring the response to the nonsurgical topical treatment of basal cell carcinomas (BCCs) (Fig. 11.20) as well as in the early recognition of unwanted side effects to topical treatments

▲ **Figure 11.21a** Clinical image of porokeratosis.

◀ **Figure 11.21b** Dermoscopy of porokeratosis reveals a double rim of scale. The center of the porokeratosis is usually hypopigmented and reveals numerous dotted vessels.

(Bianchi et al., 2004; Diluvio et al., 2008; Micantonio et al., 2006; Vázquez-López et al., 2004a). Many superficial BCCs are amenable to treatment with topical therapies, such as with imiquimod. Dermoscopy can be used to initially diagnose the superficial BCC and then it can be used to document the successful (or unsuccessful) clearance of the cancer (Fig. 11.20). Dermoscopy can also be used to follow the apparent successfully treated site for any evidence of recurrence. Another example for the use of dermoscopy is in monitoring skin for the development of potential adverse side effects from topical therapy with steroids. The dermoscopic appearance of clinically unapparent red lines (telangiectasias) on the skin treated with topical steroid has been reported as an early sign of impending steroid-induced skin atrophy. If the topical steroids are discontinued during this early stage, the skin will not manifest clinically visible signs of atrophy.

CONCLUSION

Dermoscopy patterns have been described for numerous inflammatory and infectious skin conditions. As the new generation of hand-held dermoscopes are quite compact and can easily be placed in the clinician's pocket, it can be anticipated that the use of dermoscopy will become common place and will be utilized as an adjunct to naked-eye diagnosis in the assessment of a multitude of skin, hair, and nail diseases.

Key Points

The five key indications of dermoscopy in general dermatology:

1. Entodermoscopy
2. Inflammoscopy
3. Trichoscopy
4. Capillaroscopy
5. Dermoscopy for treatment decisions and monitoring

Specific dermoscopic patterns:

- Scabies: Jet with contrail features
- Mulloscum contagiosum: Central polylobular structureless areas surrounded by crown vessels
- Tinea nigra: Wispy brown pigmented strands that do not respect the furrows or ridges on the palms/soles
- Lice nits: ovoid if vital, plane end if empty
- Verruca vulgaris: Verrucous papule with thrombosed vessels.
- Lichen planus: Whitish striae on a purple background
- Psoriasis: Regularly distributed dotted vessels and scales
- Pityriasis rosea: Colarette scaling
- Pigmented purpuric dermatosis and urticarial vasculitis: red-to-purple dots and globules that do not blanch under compression
- Alopecia areata: Yellow dots and hair abnormalities
- Nailfold capillaries: Megacapillaries, tortuous capillaries, hemorrhages.

REFERENCES

Argenziano, G., Fabbrocini, G. & Delfino, M., 1997, Epiluminescence microscopy. a new approach to in vivo detection of Sarcoptes scabiei. *Arch Dermatol*, 133, 751–3.

Bae, J., Kang, H., Kim, H., Park, Y., 2008, Differential diagnosis of plantar wart from corn, callus and healed wart with the aid of dermoscopy. *Br J Dermatol*, 160, 220–2.

Bae, J.M., Kang, H., Kim, H.O., Park, Y.M., 2009, Differential diagnosis of plantar wart from corn, callus and healed wart with the aid of dermoscopy. *Br J Dermatol*, 160, 220–2.

Bakos, R.M. & Bakos, L., 2007a, Dermoscopic diagnosis of furuncular myiasis. *Arch Dermatol*, 143, 123–4.

Bakos, R.M. & Bakos, L., 2007b, Dermoscopy for diagnosis of pediculosis capitis. *J Am Acad Dermatol*, 57, 727–8.

Bakos, R.M. & Bakos, L., 2008, 'Whitish chains': a remarkable in vivo dermoscopic finding of tungiasis. *Br J Dermatol* [Epub ahead of print].

Baron, M., Bell, M., Bookman, A., et al., 2007, Office capillaroscopy in systemic sclerosis. *Clin Rheumatol*, 26, 1268–74.

Bauer, J., Blum, A., Sonnichsen, K., et al., 2001, Nodular scabies detected by computed dermatoscopy. *Dermatology*, 203, 190–1.

Bauer, J., Forschner, A., Garbe, C. & Rocken, M., 2004, Dermoscopy of tungiasis. *Arch Dermatol*, 140, 761–3.

Bauer, J., Forschner, A., Garbe, C. & Rocken, M., 2005, Variability of dermoscopic features of tungiasis. *Arch Dermatol*, 141, 643–4.

Bergman, R., Sharony, L., Schapira, D., et al., 2003, The handheld dermatoscope as a nail fold capillaroscopic instrument. *Arch Dermatol*, 139, 1027–30.

Beltrán, E., Toll, A., Pros, A., Carbonell, J. & Pujol, R.M., 2007, Assessment of nailfold capillaroscopy by x 30 digital epiluminescence (dermoscopy) in patients with Raynaud phenomenon. *Br J Dermatol*, 156, 892–8.

Bianchi, L., Orlandi, A., Campione, E., et al., 2004, Topical treatment of basal cell carcinoma with tazarotene: a clinicopathological study on a large series of cases. *Br J Dermatol*, 151, 148–56.

Blum, A., Metzler, G., Bauer, J., et al., 2001, The dermatoscopic pattern of clear-cell acanthoma resembles psoriasis vulgaris. *Dermatology*, 203, 50–2.

Brasiello, M., Zalaudek, I., Ferrara, G., et al., 2008, Lupus vulgaris: a new look at an old symptom: the lupoma observed with dermoscopy. *Dermatology* [Epub ahead of print].

Brunetti, B., Vitiello, A., Delfino, S. & Sammarco, E., 1998, Findings in vivo of Sarcoptes scabiei with incident light microscopy. *Eur J Dermatol*, 8, 266–7.

Bugatti, L., Filosa, G., Broganelli, P., et al., 2003, Psoriasis-like dermoscopic pattern of clear cell acanthoma. *J Eur Acad Dermatol Venereol*, 17, 452–5.

Cabrera, R. & Daza, F., 2008, Tungiasis: eggs seen with dermoscopy. *Br J Dermatol*, 158, 635–6.

Chuh, A.A., 2001, Collarette scaling in pityriasis rosea demonstrated by digital epiluminescence dermatoscopy. *Australas J Dermatol*, 42, 288–90.

Chuh, A.A., 2002, The use of digital epiluminescence dermatoscopy to identify peripheral scaling in pityriasis rosea. *Comput Med Imaging Graph*, 26, 129–34.

Dalmau, J., Abellaneda, C., Puig, S., Zaballos, P. & Malvehy, J., 2006, Acral melanoma simulating warts: dermoscopic clues to prevent missing a melanoma. *Dermatol Surg*, 32, 1072–8.

Delfino, M., Argenziano, G. & Nino, M., 2004, Dermoscopy for the diagnosis of porokeratosis. *J Eur Acad Dermatol Venereol*, 18, 194–5.

Diluvio, L., Campione, E., Paterno, E.J., et al., 2008, Peculiar clinical and dermoscopic remission pattern following imiquimod therapy of basal cell carcinoma in seborrhoeic areas of the face. *J Dermatolog Treat*, 7, 1–5.

Di Stefani, A., Hofmann-Wellenhof, R. & Zalaudek, I., 2006a, Dermoscopy for diagnosis and treatment monitoring of pediculosis capitis. *J Am Acad Dermatol*, 54, 909–11.

Di Stefani, A., Hofmann-Wellenhof, R., Zalaudek, I., et al., 2006b, Usefulness of dermoscopy in louse infestations. *Dermatology*, 212, 302

Di Stefani, A., Rudolph, C.M., Hofmann-Wellenhof, R. & Mullegger, R.R., 2005, An additional dermoscopic feature of tungiasis. *Arch Dermatol*, 141, 1045–6.

Dupuy, A., Dehen, L., Bourrat, E., et al., 2007, Accuracy of standard dermoscopy for diagnosing scabies. *J Am Acad Dermatol*, 56, 53–62.

Elsner, E., Thewes, M. & Worret, W.I., 1997, Cutaneous larva migrans detected by epiluminescent microscopy. *Acta Derm Venereol*, 77, 487–8.

Inui, S., Nakajima, T., Nakagawa, K. & Itami, S., 2008a, Clinical significance of dermoscopy in alopecia areata: analysis of 300 cases. *Int J Dermatol*, 47, 688–93.

Inui, S., Nakajima, T. & Itami, S., 2008b, Significance of dermoscopy in acute diffuse and total alopecia of the female scalp: review of twenty cases. *Dermatology*, 217, 333–6.

Inui, S., Nakajima, T., Shono, F. & Itami, S., 2008c, Dermoscopic findings in frontal fibrosing alopecia: report of four cases. *Int J Dermatol*, 47, 796–9.

Kim, H.O., Bae, J.M., Kim, Y.Y., et al. 2006, Differential diagnosis of wart from callus and healed wart with aid of dermoscopy. *Dermatology*, 212, 307.

Lallas, A., Kyrgidis, A., Tzellos, T.G., et a. 2012, Accuracy of dermoscopic criteria for the diagnosis of psoriasis, dermatitis, lichen planus and pityriasis rosea. *Br J Dermatol*, 166, 1198–205.

Liu, C.I. & Hsu, C.H., 2008, Rapid diagnosis of monilethrix using dermoscopy. *Br J Dermatol*, 159, 741–3.

Micantonio, T., Fargnoli, M.C. & Peris, K., 2006, Usefulness of dermoscopy to monitor clinical efficacy of imiquimod treatment for lentigo maligna. *Arch Dermatol*, 142, 530–1.

Morales, A., Puig, S., Malvehy, J. & Zaballos, P., 2005, Dermoscopy of molluscum contagiosum. *Arch Dermatol*, 141, 1644.

Pagliarello, C., Fossati, B., Landi, F., et al., 2006, Dermoscopy of a tick bite: a case report. *Dermatology*, 212, 31.

Olszewska, M., Rudnicka, L., Rakowska, A., Kowalska-Oledzka, E. & Slowinska, M., 2008, Trichoscopy. *Arch Dermatol*, 144, 1007.

Park, J.H., Lee, D.Y., Cha, H.S. & Koh, E.M., 2008, Handheld portable digital dermoscopy: routine outpatient use for evaluating nail-fold capillary changes in autoimmune connective tissue diseases. *J Eur Acad Dermatol Venereol* [Epub ahead of print].

Prins, C., Stucki, L., French, L., Saurat, J.H. & Braun, R.P., 2004, Dermoscopy for the in vivo detection of sarcoptes scabiei. *Dermatology*, 208, 241–3.

Procaccini, E.M., Argenziano, G., Staibano, S., et al., 2001, Epiluminescence microscopy for port-wine stains: pretreatment evaluation. *Dermatology*, 203, 329–32.

Rakowska, A., Slowinska, M., Czuwara, J., Olszewska, M. & Rudnicka, L., 2007, Dermoscopy as a tool for rapid diagnosis of monilethrix. *J Drugs Dermatol*, 6, 222–4.

Ross, E.K., Vincenzi, C. & Tosti, A., 2006, Videodermoscopy in the evaluation of hair and scalp disorders. *J Am Acad Dermatol*, 55, 799–806.

Rudnicka, L., Olszewska, M., Rakowska, A., Kowalska-Oledzka, E. & Slowinska, M., 2008, Trichoscopy: a new method for diagnosing hair loss. *J Drugs Dermatol*, 7, 651–4.

Smith, S.B., Beals, S.L., Elston, D.M. & Meffert, J.J., 2001, Dermoscopy in the diagnosis of tinea nigra plantaris. *Cutis*, 68, 377–80.

Scanni, G. & Bonifazi, E., 2006, Viability of the head louse eggs in pediculosis capitis. A dermoscopy study. *Eur J Pediat Dermatol*, 16, 201–4.

Sevila, A., Nagore, E., Botella-Estrada, R., et al., 2004, Videomicroscopy of venular malformations (port-wine stain type): prediction of response to pulsed dye laser. *Pediatr Dermatol*, 21, 589–96.

Sontheimer, R.D., 2004, A portable digital microphotography unit for rapid documentation of periungual nailfold capillary changes in autoimmune connective tissue diseases. *J Rheumatol*, 31, 539–44.

Teoli, M., Di Stefani, A., Botti, E., Mio, G. & Chimenti, S., 2006, Dermoscopy for treatment monitoring of viral warts. *Dermatology*, 212, 318.

Tosti, A., Iorizzo, M. & Piraccini, B.M., 2005, Androgenetic alopecia in children: report of 20 cases. *Br J Dermatol*, 152, 556–9.

Vázquez-López, F., Coto-Segura, P., Fueyo-Casado, A. & Pérez-Oliva, N., 2007a, Dermoscopy of port-wine stains. *Arch Dermatol*, 143, 962.

Vázquez-López, F., Gómez-Díez, S., Sánchez, J. & Pérez-Oliva, N., 2007b, Dermoscopy of active lichen planus. *Arch Dermatol*, 143, 1092.

Vázquez-López, F., Kreusch, J. & Marghoob, A.A., 2004a, Dermoscopic semiology: further insights into vascular features by screening a large spectrum of nontumoral skin lesions. *Br J Dermatol*, 150, 226–31.

Vázquez-López, F., Lopez-Escobar, M., Maldonado-Seral, C., et al., 2004b, The handheld dermoscope improves the recognition of giant pseudocomedones in Darier's disease. *J Am Acad Dermatol*, 50, 454–5.

Vázquez-López, F., Maldonado-Seral, C., López-Escobar, M. & Pérez-Oliva, N., 2003a, Dermoscopy of pigmented lichen planus lesions. *Clin Exp Dermatol*, 28, 554–5.

Vázquez-López, F., Maldonado-Seral, C., Soler-Sanchez, T., et al., 2003b, Surface microscopy for discriminating between common urticaria and urticarial vasculitis. *Rheumatology (Oxford)*, 42, 1079–82.

Vázquez-López, F., Manjón-Haces, J.A., Maldonado-Seral, C., et al., 2003c, Dermoscopic features of plaque psoriasis and lichen planus: new observations. *Dermatology*, 207, 151–6.

Vázquez-López, F., Manjon-Haces, J.A., Vazquez-Lopez, A.C., et al., 2003d, The hand-held dermatoscope improves the clinical evaluation of port-wine stains. *J Am Acad Dermatol*, 48, 984–5.

Vázquez-López, F. & Marghoob, A.A., 2004c, Dermoscopic assessment of long-term topical therapies with potent steroids in chronic psoriasis. *J Am Acad Dermatol*, 51, 811–13.

Vázquez-López, F. & Pérez-Oliva, N., 2005, Usefulness of the dermoscope for evaluating the depth of venular malformations. *Pediatr Dermatol*, 22, 283.

Weinstock, M.A. & Kempton, S.A., 2000, Case report: teledermatology and epiluminescence microscopy for the diagnosis of scabies. *Cutis*, 66, 61–2.

Xavier, M.H., Ribeiro. L.H., Duarte, H., Saraça, G. & Souza, A.C., 2008, Dermatoscopy in the diagnosis of tinea nigra. *Dermatol Online J*, 14, 15.

Zaballos, P., Ara, M., Puig, S. & Malvehy, J., 2006, Dermoscopy of molluscum contagiosum: a useful tool for clinical diagnosis in adulthood. *J Eur Acad Dermatol Venereol*, 20, 482–3.

Zaballos, P., Puig, S. & Malvehy, J., 2004, Dermoscopy of pigmented purpuric dermatoses (lichen aureus): a useful tool for clinical diagnosis. *Arch Dermatol*, 140, 1290–1.

Zalaudek, I., Argenziano, G., Di Stefani, A., et al., 2006a, Dermoscopy in general dermatology. *Dermatology*, 212, 7–18.

Zalaudek, I., Ferrara, G., Brongo, S., Giorgio, C.M. & Argenziano, G., 2006b, Atypical clinical presentation of pigmented purpuric dermatosis. *J Dtsch Dermatol Ges*, 4, 138–40.

Zalaudek, I., Giacomel, J., Cabo, H., et al., 2008, Entodermoscopy: a new tool for diagnosing skin infections and infestations. *Dermatology*, 216, 14–23.

Zalaudek, I., Hofmann-Wellenhof, R. & Argenziano, G., 2003, Dermoscopy of clear-cell acanthoma differs from dermoscopy of psoriasis. *Dermatology*, 207, 428; author reply 9.

12 Vascular structures

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Blood vessels are critical to the survival and growth of cells and tissues. The rate of growth and ultimate tumor size, whether benign or malignant, is governed at least in part by the tumor's ability to derive ample blood flow to support the metabolic demands of its cells. Therefore, tumors may manifest signs of an increase in blood vessels and flow. This is readily observed in many basal cell carcinomas (BCCs) in which the clinical morphology often reveals telangiectasias. Although other tumors may not clinically manifest vasculature, vessels are indeed present but may be of small caliber or situated deeper within the skin. Dermoscopy, by providing magnification and visual access to subepidermal structures, has permitted clinicians to observe many of these vessels (Tables 12.1–12.4) (Argenziano et al., 2004).

Anatomy of normal skin vasculature: The skin receives vascular supply through superficial and deep vascular plexuses in the dermis (Fig. 12.1). These plexuses constitute anatomic landmarks in skin histology—the superficial vascular plexus marks the junction between the papillary and reticular dermis, whereas the deep vascular plexus separates the reticular dermis from subcutaneous fat (Lever). The superficial plexus is made up of anastomosing small-caliber arterioles that branch into capillaries, which extend into dermal papillae to supply the overlying epidermis, as well as envelop adnexal structures. The deep plexus is made up of medium-caliber vessels, which emanate from larger vessels that traverse the adipose septae of the subcutis. Additionally, the deep plexus connects with the superficial vascular plexus through vertically oriented vessels.

Tumor microenvironment: The architecture and distribution of vascular structures, determined in part by neoangiogenic factors, angiogenic inhibitors, and tumor–stromal interactions, differ with tumor type (Argenziano et al., 2004). Oncogene activation in tumors drives angiogenesis by the expression of angiogenic factors, such as vascular endothelial growth factor (VEGF) and by inhibiting antiangiogenic factors, such as thrombospondin-1. Fibroblasts and endothelial cells are among the many stromal cells involved in the metastatic process, especially those adjacent to the tumor, that is, on the "tumor front." The tumor microenvironment refers to tumor cells themselves and the surrounding stromal cells and components, such as cytokines, chemokines, collagen, elastin, and growth factors (Labrousse et al., 2004). The interaction of all microenvironment components play an important role in tumor growth and progression. For example, melanoma cells interact with the stroma by way of cytokines, growth factors, and direct cell–cell contact (Labrousse et al., 2004; Flach et al., 2011). Melanoma cells release autocrine growth factors, which stimulate proliferation of melanoma cells, as well as paracrine growth factors, including VEGF and platelet-derived growth factor (PDGF), which are involved in angiogenesis and invasion. VEGF has been detected in vertical growth phase melanoma and melanoma metastases, in contrast to benign melanocytic lesions that show no immunoreactivity for VEGF (Labrousse et al., 2004).

Appropriate dermoscopic technique for the visualization of vascular structures: Care must be exercised to insure that blood vessels, if present, are adequately visualized using dermoscopy. Cutaneous blood vessels can readily be blanched by even slight pressure on the skin surface. Thus, nonpolarized dermoscopy utilizing alcohol as the fluid interface, where the glass plate of the dermoscope is pressed firmly against the skin surface, has the tendency to blanch out much of the cutaneous vasculature. To prevent this blanching effect, it is advised that the fluid interface (oil or alcohol) be replaced with ultrasound gel. The high viscosity of gel allows one to place the dermoscope onto the lesion with minimal pressure while maintaining

Table 12.1 Morphological Description of Vascular Structures

Name of vascular feature	Description of morphology
Primary vascular structure	
Arborizing vessels	Bright red, thick vessels with a large diameter, of 0.2 mm or more, that branch into fine terminal capillaries with an approximate diameter of 10 μm
Short fine telangiectasias	Thin, in-focus vessels, with some branching
Comma vessels	Vessels that are slightly curved or bent with rare branching, often appear blurry
Dotted vessels	Clusters of tiny red dots (diameter 0.01–0.02 mm), similar to that of a pinhead. May occupy the periphery of the lesion, may be evenly distributed, or may be organized as a "string of pearls."
Glomerular vessels	Tightly coiled, tortuous vessels shaped like the glomerulus of the kidney, larger than dotted vessels, and are often distributed in clusters
Hairpin vessels	Vessels with a U-shaped loop, may be fine, thick, or irregular with twists or kinks. Often surrounded by a whitish halo in keratinocytic tumors or completely surrounded in a background of pink color in melanoma.
Milky red area (vascular blush)	Large areas of fuzzy or unfocused milky red or pink color of increased vascularity; other dermoscopic structures may be seen within this area
Milky red globules	Globules with milky red coloring
Polymorphous vessels	The combination of two or more different vascular structures in one lesion
Linear–irregular vessels	Short vessels that are linear in shape, but vary in thickness and length. May contain twists or kinks
Corkscrew vessels	Coiled or winding vessels
Lagoons/lacunas	Large red or maroon or bluish colored globules that are often separated from each other by blue-white colored septae.
Vascular pattern	
Crown vessels	Groups of orderly, bending vessels with rare branching, located at the periphery of the lesion, extending toward, but not crossing, the center
String of pearls	Dotted, globular or glomerular vessels in a serpiginous distribution like a "string of pearls"
Strawberry pattern	Pink/red pseudonetwork with blurry vessels coursing between hair follicle openings, and presence of central keratotic plugs create a pattern reminiscent of a strawberry
Follicular red dots	Red dots regularly distributed among and around hair follicle openings, in a region of alopecia

Table 12.2 Features of Vascular Structures

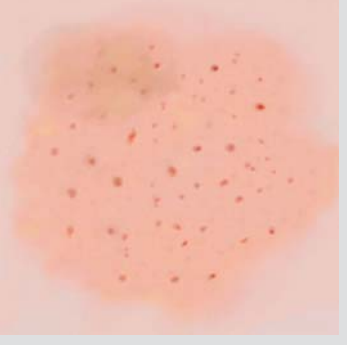
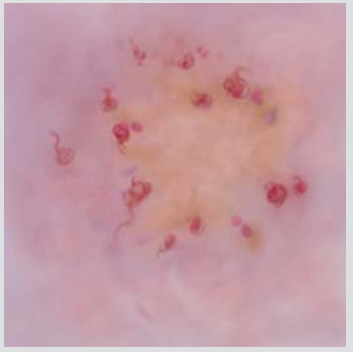
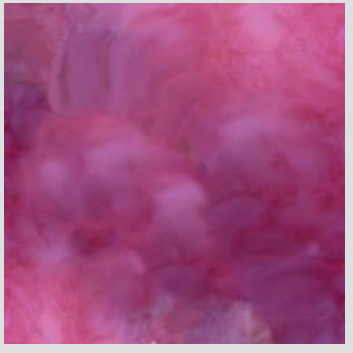
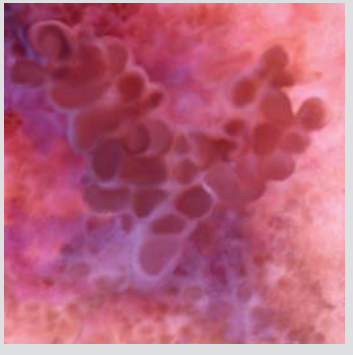
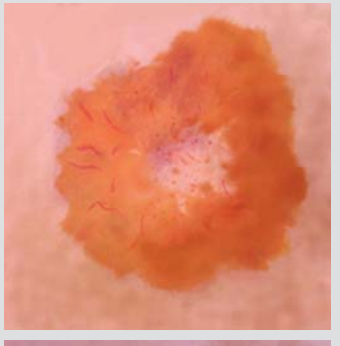
Name	Alternative name	Most commonly associated with	Positive predictive value[a]	Other entities to consider	Vessel image
Arborizing	Linear straight, linear serpentine (large caliber)[b]	Basal cell carcinoma	94.1% for BCC[a]	Melanocytic lesion	
Short fine telangiectasias	Linear straight, linear serpentine (small caliber)[b]	Superficial basal cell carcinoma Fibroepithelioma of pinkus		—	
Hairpin	Linear looped[b]	Seborrheic keratosis (vessels surrounded by a white halo) Keratoacanthoma (peripheral) Melanoma (thick; surrounded by pink color) Warts	70% for SK[a]	Squamous cell carcinoma Basal cell carcinoma Dermal nevi Spitz nevi	
Dotted	Red dots[b]	Melanoma Melanocytic lesion	37.8% for melanoma[a] 90% for melanocytic lesion[a]	Congenital nevi Spitz nevi Dermal nevi Dysplastic nevi Psoriasis Clear cell acanthoma Squamous cell carcinoma	

Table 12.2 (cont.) Features of Vascular Structures

Name	Alternative name	Most commonly associated with	Other entities to consider	Other entities to consider	Vessel image
Glomerular	Linear coiled[b]	Bowen's disease Squamous cell carcinoma Intraepidermal carcinoma	61.9% for Bowen's[a]	Melanoma Seborrheic keratosis Stasis dermatitis	
Vascular blush	—	Melanoma		Dysplastic nevi Basal cell carcinoma Squamous cell carcinoma	
Milky red globules and Red clods[b]	—	Melanoma	77.8%[a]	—	

(*Continued*)

Comma	Linear curved[b]	Dermal nevi	94%[a]	Compound nevi	
Linear irregular	Linear straight, linear serpentine[b]	Melanoma	67.6%[a]	Dysplastic nevi Basal cell carcinoma	
Polymorphous	—	Melanoma (dotted and linear)	52.6%[a]	Melanocytic nevi Eccrine poromas	
Corkscrew	Linear helical[b]	Melanoma		—	

[a]From Argenziano et al. (2004).
[b]From Kittler et al.

Table 12.3 Diagnosis with Most Commonly Associated Vascular Structures

Disease entity	Vascular structures	Details/distribution
BCC	Arborizing vessels	Thick vessels
Bowen's disease	Glomerular vessels	Scaly surface
Clear cell acanthoma	Dotted vessels	"String of pearls"
Congenital melanocytic nevus	Comma vessels	Blurry vessels
Cutaneous melanoma metastasis	Corkscrew vessels	—
Dermal nevi	Comma vessels	—
Desmoplastic melanoma	Corkscrew vessels Milky red areas Linear irregular vessels Polymorphous vessels	—
Dysplastic nevi	Comma vessels Dotted vessels	—
Discoid lupus erythematous	Follicular red dots	—
Eccrine poroma	Glomerular vessels Hairpin vessels Linear–irregular vessels Flower-like shaped vessels (Shalom et al., 2012) Polymorphous vessels	White-pink halo around vessels
Facial actinic keratosis	Strawberry pattern	—
Hemangioma	Lagoons/lacunas	—
Keratoacanthoma	Hairpin vessels	White halo, peripherally distributed, yellow keratin plug at center
Melanoma	Dotted vessels Serpentine vessels Milky red globules Polymorphous vessels	Focally distributed Surrounding pink area
Molluscum contagiosum	Crown vessels	—
Nodular melanoma	Corkscrew vessels	—
Psoriasis	Dotted vessels	Homogenous distribution, light red background
Pyogenic granuloma	Red-white or pink homogeneous areas	With white collarette and white rail lines
Sebaceous hyperplasia	Crown vessels	—
SK	Thin hairpin vessels Irregular hairpin (irritated SK)	White halo around vessels
Spitz nevus	Dotted vessels	—
Squamous cell carcinoma	Glomerular vessels Dotted vessels	Peripherally distributed
Superficial BCC	Short fine telangiectasias	Irregularly distributed
Venous stasis dermatitis	Dotted vessels Glomerular vessels	Similar to nearby lesions
Warts	Thin hairpin vessels	Evenly distributed, often thrombosed

Abbreviations: BCC, basal cell carcinoma; SK, seborrheic keratosis.

full contact between the glass plate and the skin. Fortunately, polarized noncontact dermoscopes have eliminated the need for direct contact between the glass plate and skin, thereby eliminating the need for a liquid interface. Utilizing noncontact polarized dermoscopy has given us the ability to not only observe blood vessels, but also to indirectly assess the vascular volume within skin lesions. An increased vascular volume can be appreciated as a vascular blush (milky red area, pink veil) (Fig. 12.2A–C).

VASCULAR PRIMARY MORPHOLOGY (TABLES 12.1, 12.2)

Arborizing Blood Vessels

Arborizing vessels appear under dermoscopy as bright red, thick diameter vessels (0.2 mm or more) from which emanate branching vessels with progressively thinner diameters (Braun et al., 2009b). The arborizing vessels are sharply in focus due to their superficial location, situated slightly below the epidermis, and exhibit irregular branching into fine terminal capillaries of small diameter (10 μm) (Argenziano et al., 2004; Kreusch, 2002; Malvehy et al., 2006). These "tree-like vessels" are present in more than 80% of BCCs, yielding a positive predictive value (PPV) of 94%, and sensitivity and specificity of 96.1% and 90.9%, respectively (Figs. 12.3 and 12.4). (Kreusch, 2002; Argenziano et al., 2004) Adnexal tumors can sometimes appear similar to BCCs and may display arborizing vessels. (Sgambato et al., 2008) Although uncommon, arborizing vessels may be seen in benign lesions, such as fibrous papules, intradermal nevi, and epidermoid cysts; however, in these lesions the vessels are usually not in sharp focus. In addition, arborizing vessels can, on rare occasions, be seen in invasive cancers, including melanoma and Merkel cell carcinoma (Stoecker & Stolz, 2008).

There are several histologic variants of BCC, including nodular, superficial, and infiltrative. Each of these BCC subtypes can present as amelanotic lesions or they can present with pigment. BCCs that are amelanotic can be identified based on the presence of arborizing vessels, shiny white areas, crystalline structures, and/or ulceration. Pigmented BCCs (pBCC), which may clinically mimic melanoma, contain specific dermoscopic structures that aid in their proper diagnosis (see chap. 5a, "Basal cell carcinoma"). Menzies model for dermoscopic diagnosis of pBCCs (sensitivity of 93% and specificity of 89–92%) includes arborizing vessels as an important diagnostic feature (Menzies, 2002; Menzies et al., 2000). Arborizing vessels were observed in 52% of pBCCs, compared with 23% of melanomas and only 8% of benign skin lesions (Menzies et al., 2000).

Table 12.4 Vascular Structures and Associated Positive Predictive Values, Sensitivity, and Specificity for Certain Diagnoses

Vascular structure	Disease entity	Positive predictive value	Sensitivity	Specificity	Odds ratio (95% confidence interval)
Arborizing vessels	Basal cell carcinoma	94.1%[a]	96.1%[b]	90.9%[b]	
	Melanoma (negative predictor)		8.6 (as predominant vessel type)[c]	82.4% (as predominant vessel type)[c]	0.44 (0.21–0.91) (as predominant vessel type)[c]
Arborizing small diameter vessels	Melanoma (negative predictor)		6.7%[c]	81.4%[c]	0.31 (0.14–0.70)[c]
Comma vessels	Dermal nevus	94%[a]			
	Melanoma (negative predictor)		1.0% (regular distribution)	90.8% (regular distribution)[c]	0.10 (0.01–0.70) (regular distribution)[c]
			[c] 2.9% (as predominant vessel type)[c]	84.4% (as predominant vessel type)[c]	0.16 (0.05–0.52) (as predominant vessel type)[c]
Dotted vessels	Melanoma	37.8%[a]	33.3% (as predominant vessel type)[c]	79.8% (as predominant vessel type)[c]	2.0 (1.2–3.2) (as predominant vessel type)[c]
	Dermal/congenital nevus	15.6%[a]			
	Clark nevus	21.1%[a]			
	Spitz nevus	15.6%[a]			
	Basal cell carcinoma	1.1[a]			
Glomerular vessels	Bowen's disease	61.9%[a]			
	Squamous cell carcinoma	4.8%[a]			
Hairpin vessels	Seborrheic keratosis	70%[a]			
	Melanoma		21.0%[c]	90.6%[c]	2.5 (1.4–4.5)%[c]
	Squamous cell carcinoma	13.3%[a]			
Linear irregular vessels	Melanoma	67.6%[a]	40.0%[c]	70.9%[c]	1.6 (1.0–2.5)%[c]
			34.3% (as predominant vessel type)[c]	79.8% (as predominant vessel type)[c]	2.1 (1.3–3.3) (as predominant vessel type)[c]
Milky red globules	Melanoma		21.0%[c]	88.3%[c]	2.0 (1.1–3.5)%[c]
Milky red pink areas	Melanoma		50.5%[c]	71.2%[c]	2.5 (1.6–3.9)[c]
Milky red globules/areas	Melanoma	77.8%[a]	21.0% (melanoma)[c]	88.3% (melanoma)[c]	
	Basal cell carcinoma	11.1%[a]			
Polymorphous vessels	Melanoma	52.6%[a]	29.5% (dotted and linear irregular)[c]	84.7%[c]	2.3 (1.4–3.8)[c]
	Basal cell carcinoma	10.5%[a]			
Predominant central vessels	Melanoma		16.2%[c]	94.1%[c]	3.1 (1.6–6.0)[c]
Vessels of irregular shape and size	Melanoma		62.9%[c]	53.8%[c]	2.0 (1.3–3.1)[c]
More than one shade of pink	Melanoma		32.4%[c]	82.9%[c]	2.3 (1.4–3.8)[c]
Crown vessels	Sebaceous hyperplasia	83.3%[a]			

[a]From Argenziano et al. (2004).
[b]From Kreusch (2002).
[c]From Menzies et al. (2008).
[d]From Pizzichetta et al. (2004).

While arborizing vessels are often quite prominent in nodular BCC, they tend to be less conspicuous in superficial BCCs (sBCC) and in fibroepithelioma of Pinkus, a rare BCC subtype (Giacomel & Zalaudek, 2005; Zalaudek et al., 2006a).

In sBCC it is common to see short fine telangiectasias, which are sharply in focus and arranged irregularly throughout the lesion. Additional presence of shiny white-to-red areas and multiple small ulcerations or erosions can provide reassurance that the lesion under investigation is a superficial BCC (Giacomel & Zalaudek, 2005; Scalvenzi et al., 2008). These fine arborizing vessels, which are described as smaller in diameter than typical arborizing vessels and with less branching, have also been noted in fibroepithelioma of Pinkus. In addition, Pinkus tumors are often accompanied by dotted vessels at the lesion's periphery (Zalaudek et al., 2006a).

Hairpin Vessels

Hairpin vessels are characterized by vessels that resemble hairpins, consisting of a U-shape with a sharp bend at one end. These looped hairpin vessels can appear distorted when the hairpin configuration twists around its own axis (Braun et al., 2009a). Hairpin vessels are found in melanocytic and nonmelanocytic tumors (Malvehy et al., 2006; Braun et al., 2002). Relatively thin, uniform hairpin vessels are often seen in keratinizing tumors, such as seborrheic keratoses (SKs) (Fig. 12.5) (Malvehy et al., 2007). In these benign keratinizing tumors, a whitish halo often surrounds the vessels (Argenziano

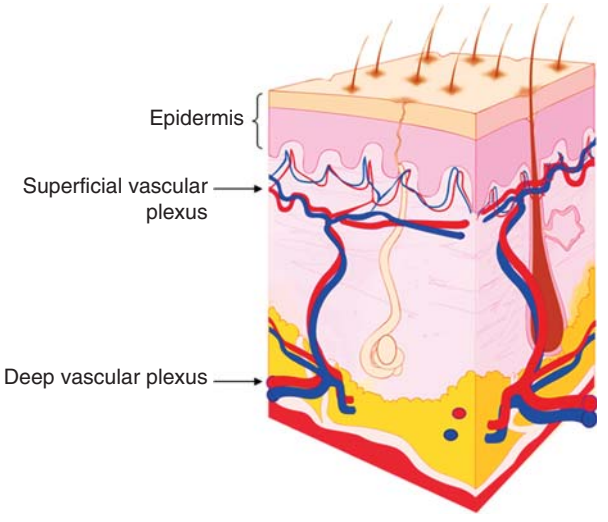


Figure 12.1 Schematic image demonstrating the deep and superficial vascular plexuses that provide blood flow to the skin.

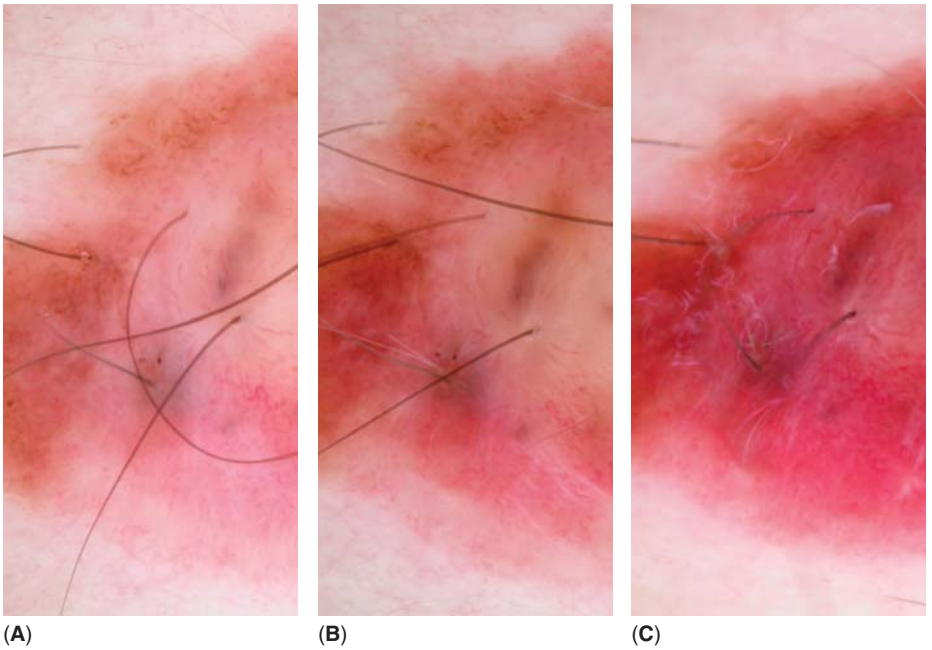
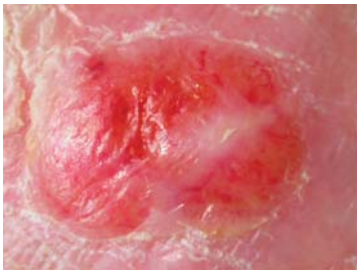


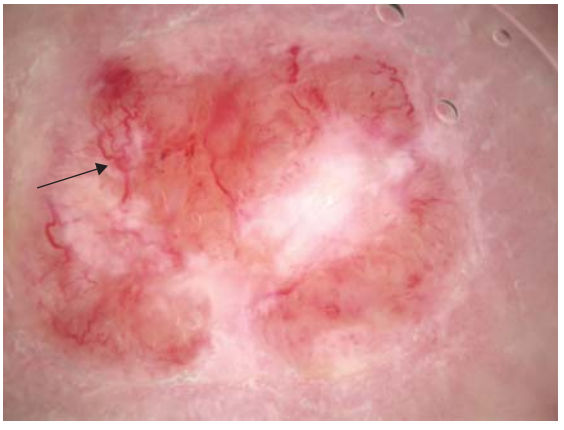
Figure 12.2 Nonpolarized contact dermoscopy with alcohol interface (**A**), nonpolarized contact dermoscopy with gel interface (**B**) and polarized noncontact dermoscopy (**C**). The images demonstrate the difference in appearance of vascular features as seen using different dermoscopic modalities. If alcohol is used as the liquid interface, more pressure needs to be applied to eliminate air bubbles. This is turn has a tendency to blanch out the vessels (**A**). Applying a gel acts as a cushion and decreases the amount of pressure required to adequately inspect the lesion dermoscopically (**B**). The decreased pressure applied to the skin prevents blanching of vessels (**B**). The device that provides the best visualization of the skin vessels and vascular blush is the non-contact polarized dermatoscope (**C**).

▲ **Figure 12.3a** Clinical image.

◀ **Figure 12.3b** Polarized noncontact dermoscopy image of a basal cell carcinoma demonstrating arborizing vessels (*arrow*) and a blue ovoid nest (*arrowhead*).

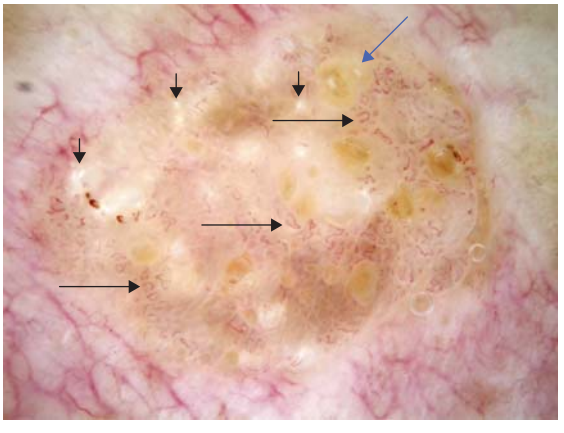


▲ **Figure 12.4a** Clinical image.



◀ **Figure 12.4b** Polarized contact dermoscopy image of a basal cell carcinoma demonstrating arborizing vessels (*arrow*).

▲ **Figure 12.5a** Clinical image.



◀ **Figure 12.5b** Polarized contact dermoscopy image of a seborrheic keratosis demonstrating hairpin vessels (*black arrows*), milia-like cysts (*arrowheads*) and comedo-like openings (*blue arrow*).

et al., 2004). This whitish halo probably represents viable tumor keratinocytes surrounding the dermal papilla, which contains the hairpin vessel. In a study of pigmented SKs, hairpin vessels were seen in 63% of lesions; more specifically, these vessels were seen in 50% of plaque-type SKs and 43% of papular/nodular SKs but were only seen in 6% of patch type SKs (Braun et al., 2002). In another study looking at lesions with vascular dermoscopic structures, 51.2% of SKs contained hairpin vessels, conferring a PPV of 70% (Argenziano et al., 2004). In keratoacanthomas, hairpin vessels are located peripherally, with a yellow keratotic center (Fig. 12.6) (Kreusch, 2002). In contrast, hairpin vessels in melanomas are often surrounded by a pink halo (Fig. 12.7) (Malvehy et al., 2007; Stoecker & Stolz, 2008; Ka et al., 2004). Hairpin vessels may also be observed in warts, SCCs, BCCs, dermal nevi, and Spitz nevi (Kreusch, 2002; Argenziano et al., 2004; Zell et al., 2008; Suwattee et al., 2007; Ahlgrimm-Siess et al., 2010).

Dotted Vessels

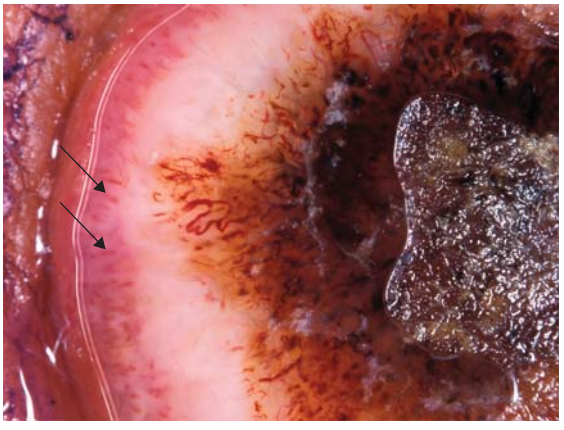
Dotted vessels appear as small red dots with a diameter of 0.01–0.02 mm, and they represent vessels aligned perpendicular to the skin surface (Kreusch, 2002; Stoecker & Stolz, 2008). They can be seen in inflamed skin, traumatized skin, or in skin overlying stasis. However, they can also be seen in cutaneous tumors. The presence of dotted vessels often implies that a lesion is melanocytic; in one study, 90% of the lesions with dotted vessels were melanocytic (Fig. 12.8) (Argenziano et al., 2004). In melanocytic tumors, dotted vessels confer a PPV of 38% for melanoma, 16% for dermal/congenital nevi, 21% for Clark nevi, and 16% for Spitz nevi. (Argenziano et al., 2004) In benign nevi, dotted vessels correspond to vessels at the tips of the dermal papillae and dermoscopically often appear to be situated within the holes of the pigment network. In melanoma, dotted vessels, which are frequently found in conjunction with other vessel types, can be seen anywhere within the lesion but tend to be present at a higher concentration toward the center of the lesion (Zell et al., 2008). In a study of amelanotic and hypomelanotic melanomas (AHM), dotted vessels were more commonly seen in melanomas ≤1 mm in thickness (27.6%) when compared with those >1 mm in thickness (20.0%); when evaluating purely amelanotic melanomas, dotted vessels were seen in 60% of cases (Fig. 12.9) (Pizzichetta et al., 2004). In another study, Bono and colleagues reported the presence of dotted vessels in 100% of thin amelanotic melanomas (<1 mm) (n = 9) (Bono et al., 2001). The aforementioned data suggests that dotted vessels may be one of the first morphologic types of neoangiogenic vessels visible in melanoma because they appear to be more prevalent in thinner tumors.

In a study analyzing amelanotic/hypomelanotic benign melanocytic lesions (AHBML) and amelanotic/hypomelanotic nonmelanocytic lesions (AHNML) (tumors), dotted vessels were observed in 32.7% and 21.8% of lesions, respectively (Pizzichetta et al., 2004). In nonmelanocytic lesions, dotted vessels are commonly seen in psoriasis, clear cell acanthomas (CCA), and squamous cell carcinoma (SCC) (Bugatti et al., 2003). The distribution and arrangement of dotted vessels within the aforementioned lesions can be very helpful in diagnosis. Dotted vessels in psoriasis are relatively uniform in size and are distributed homogenously throughout the plaque (Vazquez-Lopez et al., 2003; Pan et al., 2008; Vazquez-Lopez et al., 2007). When dotted vessels are arranged in a "string of pearls" or serpiginous distribution, then the diagnosis of CCA is almost certain (Fig. 12.10) (Marghoob & Braun, 2010; Bugatti et al., 2003). Dotted vessels present focally at the periphery or throughout the entire lesion and in association with adherent scale is suggestive of SCC (Zell et al., 2008).

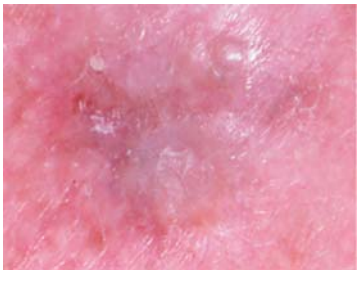
Milky Red Globules/Areas

Milky red globules are, as their name suggests, globules with a milky reddish coloring (Fig. 12.11). These vascular structures may be observed

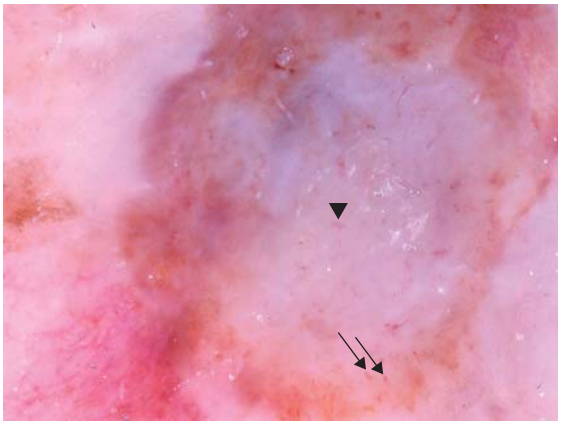
▲ **Figure 12.6a** Clinical image.



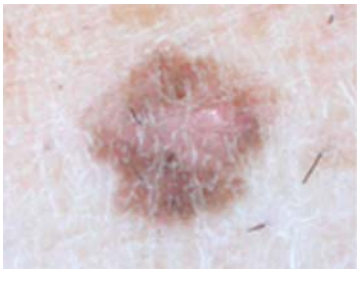
◀ **Figure 12.6b** Polarized contact dermoscopy image of a keratoacanthoma demonstrating hairpin vessels at the periphery (*arrows*).



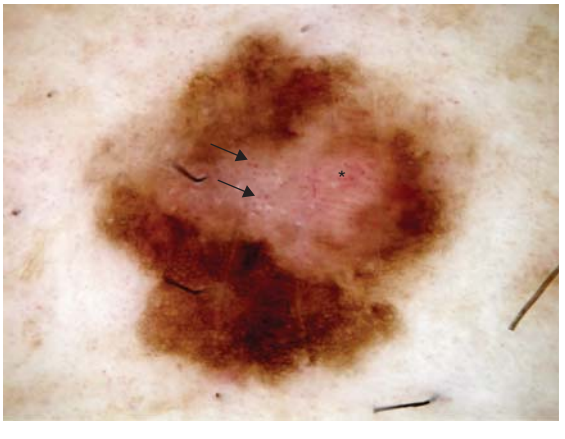
▲ **Figure 12.7a** Clinical image.



◀ **Figure 12.7b** Polarized contact dermoscopy image of a 5.6 mm desmoplastic melanoma demonstrating hairpin vessels (*arrow*) and a corkscrew vessel (*arrowhead*).

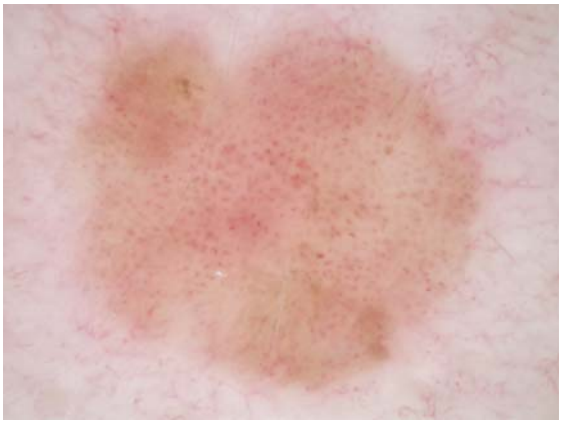


▲ **Figure 12.8a** Clinical image.



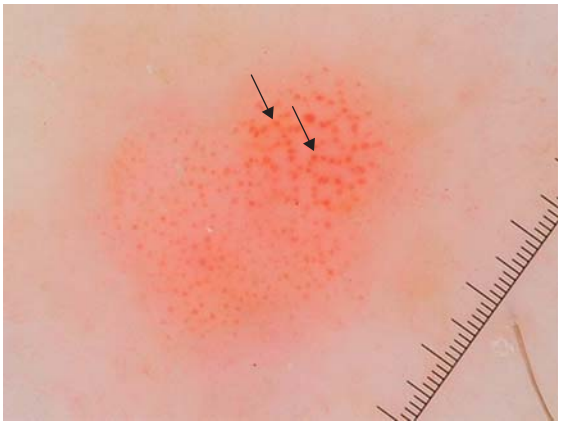
◀ **Figure 12.8b** Polarized contact dermoscopy image of a 0.45 mm melanoma demonstrating dotted vessels (*arrow*) and vascular blush (*asterisk*).

▲ **Figure 12.9a** Clinical image.



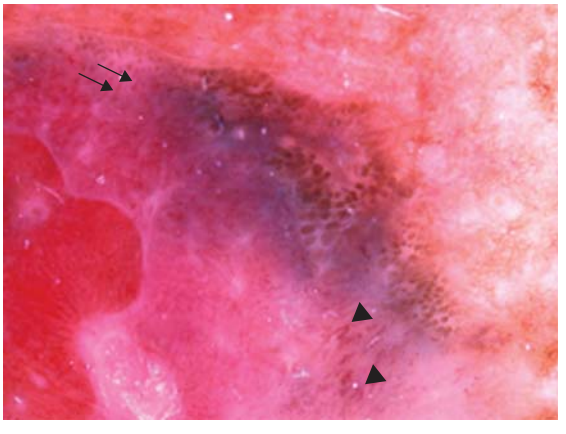
◀ **Figure 12.9b** Polarized noncontact dermoscopy image of an amelanotic melanoma demonstrating dotted vessels.

▲ **Figure 12.10a** Clinical image.



◀ **Figure 12.10b** Polarized noncontact dermoscopy image of a clear cell acanthoma demonstrating dotted vessels in a "string of pearls" arrangement (*arrows*).

▲ **Figure 12.11a** Clinical image.



◀ **Figure 12.11b** Polarized noncontact dermoscopy image of a melanoma demonstrating polymorphous vessels, including irregular linear vessels (*arrows*), milky red globules, and hairpin vessels (*arrowheads*).

within or near areas with a milky red color (Argenziano et al., 2004). Although milky red globules are not seen frequently, when present, they are highly suggestive of invasive melanoma (Braun et al., 2009a). They may be valuable in the recognition of thicker AHM, which often do not have many noticeable or identifying features (Cavicchini et al., 2007). In AHM, milky red globules/red areas were reported in 31% of thin melanomas (≤1 mm) and in 93.3% of thick melanomas (>1 mm), as compared with 17.3% and 9.1% of AHBML and AHNML, respectively (Pizzichetta et al., 2004). In another study, 4.7% of melanomas with vascular structures on dermoscopy contained milky red globules/areas, correlating with a PPV of 77.8%; only 0.5% of nonmelanoma lesions had these structures (Argenziano et al., 2004).

Vascular blush, also known as erythematous blush, pink veil, or milky red areas, represents a red or pink region that corresponds to an area with increased vascularity (Fig. 12.12) (Marghoob & Braun, 2010). Thus, vascular blush can be seen in lesions, such as dermatofibromas, vascular tumors, such as pyogenic granulomas, inflammatory lesions, and both melanoma and nonmelanoma skin cancers. Although vascular blush can be seen in nevi, it tends to be more common and conspicuous in melanoma (Stoecker & Stolz, 2008; Marghoob & Braun, 2010; Phan et al., 2010).

Glomerular Vessels

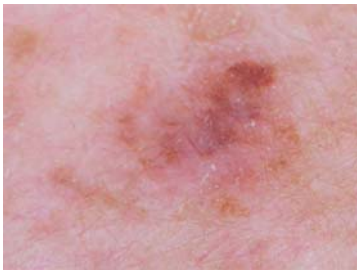
Glomerular vessels are the dermoscopic manifestations of tortuous, dilated capillaries (Braun et al., 2009a; Minagawa et al., 2009). They are named as such because their morphology is reminiscent of the convoluted capillaries that comprise the glomerular apparatus of the kidney (Figs. 12.13) (Argenziano et al., 2004). Glomerular vessels are larger than dotted vessels and can be positioned in clusters throughout the lesion. Histologically these vessels correlate to dilated capillaries in the dermal papillae and papillary dermis (Felder et al., 2006). Most commonly, glomerular vessels are associated with SCCs, in which the glomerular vessels are principally distributed focally in clusters and at the periphery of the lesion together with hyperkeratosis (i.e., scaly surface) (Pan et al., 2008; Zalaudek et al., 2004; Bugatti et al., 2004). In a study of Bowen's disease (BD), 80% of pigmented BD and 100% of nonpigmented BD displayed glomerular vessels (Zalaudek et al., 2004). In another study, glomerular vessels were seen in 81.2% of BD cases with a PPV of 61.9%. In contrast, glomerular vessels were seen in only 1.3% of melanomas (Figure 12.14), 12.2% of SKs, and 7.1% of invasive SCCs (Argenziano et al., 2004). Glomerular vessels can also be seen in CCA where the vessels will be arranged in a string of pearls distribution, in psoriasis (Fig. 12.15) where the vessels are distributed throughout the lesion in an organized pattern, and in stasis dermatitis where these vessels will be visible in normal appearing skin (Zaballos et al., 2006). Lastly, glomerular vessels can also be seen in melanoma, especially within metastatic foci (Minagawa et al., 2009).

Comma Vessels

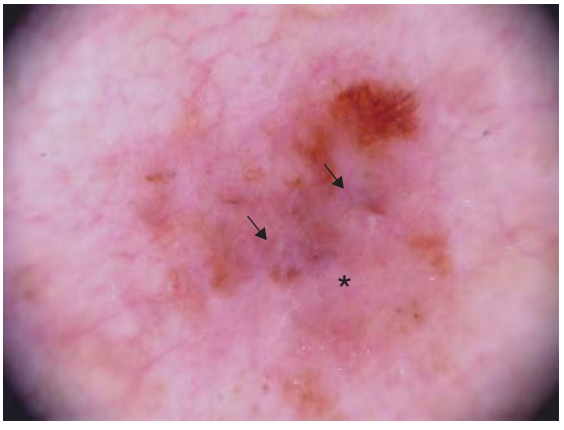
Comma vessels are slightly curved vessels that appear to take the shape of a comma (Figs. 12.16 and 12.17) (Braun et al., 2009a; Zell et al., 2008). These vessels tend to appear slightly out of focus, as their deeper location within the dermis does not allow for sharp visualization under dermoscopy (Braun et al., 2009a; Stoecker & Stolz, 2008; Kreusch, 2002) Comma vessels are most commonly associated with dermal nevi (Malvehy et al., 2007; Marghoob & Braun, 2010; Suwattee et al., 2007). In a study of dermal/congenital nevi, 66.3% exhibited this vascular pattern, with a PPV of 94% (Argenziano et al., 2004). In another study, comma vessels, when distributed in an organized fashion and when they comprise the predominant observed vessel morphology, are predictive that the lesion in question is not a melanoma (Menzies et al., 2008). In other words, comma vessels are highly suggestive of benign nevi with dermal nevi being the most common, but they can also be seen in compound nevi (Braun et al., 2009a).

Linear Irregular Vessels

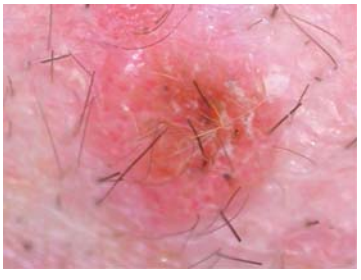
Linear irregular or serpentine vessels are red vascular structures with a range of size, shape, and distribution (Argenziano et al., 2004). They can be identified in melanoma (Fig. 12.18), BCCs, and dysplastic nevi (Zell et al.,



▲ **Figure 12.12a** Clinical image.



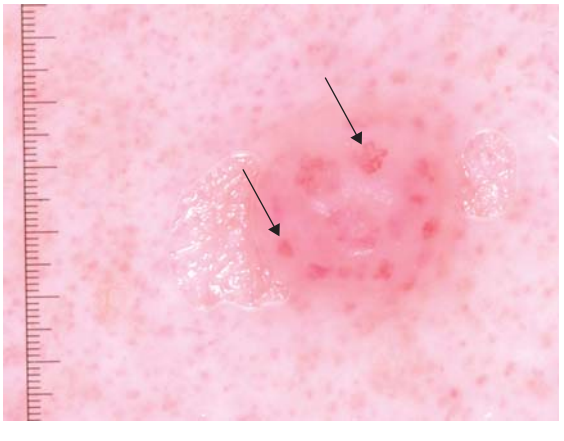
◀ **Figure 12.12b** Polarized noncontact dermoscopy image of a melanoma demonstrating milky red areas (*arrows*) and vascular blush (*asterisk*).



▲ **Figure 12.13a** Clinical images.

◀ **Figure 12.13b** Polarized contact dermoscopy image of a squamous cell carcinoma demonstrating glomerular vessels (*arrows*).

▲ **Figure 12.14a** Clinical image.



◀ **Figure 12.14b** Polarized contact dermoscopy image of a metastatic focus of melanoma with tortuous vessels resembling glomerular vessels. True glomerular vessels are more tightly coiled. In melanoma the vessels take on a more tortuous or corkscrew like appearance. (*arrows*).

▲ **Figure 12.15a** Clinical image.

◀ **Figure 12.15b** Polarized noncontact dermoscopy image of a psoriatic plaque demonstrating dotted and glomerular vessels.

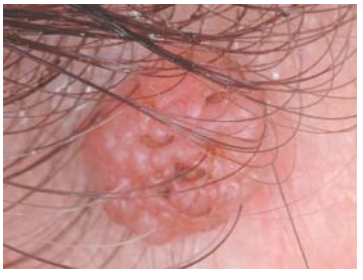
2008; Braun et al., 2009a). In one study, 33.3% of melanomas had these vessels, with a PPV of 67.6% (Argenziano et al., 2004). In another study of AHM, linear–irregular vessels were seen in 10.3% of thin AHM (<1 mm), in 0% of thick AHM (>1 mm), and 0% in amelanotic/hypomelanotic benign melanocytic lesions (Pizzichetta et al., 2004). Thus, similar to dotted vessels, the presence of these vessels suggests that the melanoma is still relatively thin.

Polymorphous Vessels

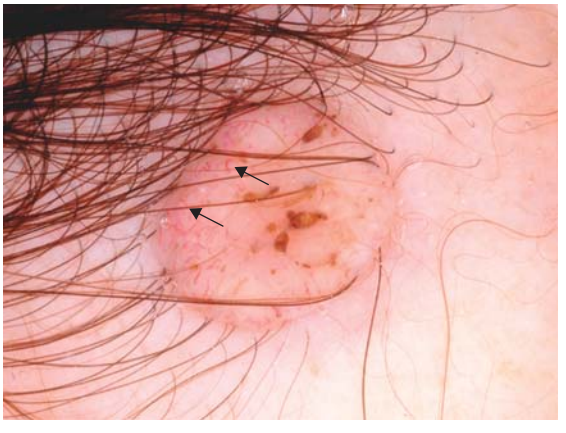
Polymorphous vessels are used to describe the vasculature of lesions in which two or more types of vessel morphologies are detected (Marghoob & Braun, 2010). The presence of polymorphous vessels may suggest a diagnosis of melanoma (Fig. 12.18) (Braun et al., 2009a). The most common combination of vessel types seen in melanoma is the presence of both dotted vessels and linear–irregular vessels (Argenziano et al., 2004; Stoecker & Stolz, 2008). In a study of lesions with vascular features seen on dermoscopy, only 20% of the lesions contained polymorphous structures, which correlated with a PPV of 52.6% for melanoma (Argenziano et al., 2004). More specifically, the combination of dotted and linear–irregular vessels was found in 18% of AHM but only extremely rarely in other nonmelanoma amelanotic/hypomelanotic lesions (1.8% of AHNML and 0% of AHBML) (Pizzichetta et al., 2004). Polymorphous vessels in combinations other than dotted vessels and linear–irregular vessels may be observed in cutaneous melanoma metastases (Minagawa et al., 2009). They can also be seen in papillomatous melanocytic nevi and other tumors, such as eccrine poromas (Niederkorn et al., 2009; Ferrari et al., 2009).

Corkscrew or Tortuous Vessels

Corkscrew vessels appear as tightly coiled or tortuous vessels and have been observed in nodular melanoma, desmoplastic melanoma, and cutaneous melanoma metastases (Figs. 12.7 and 12.19) (Bono et al., 2004).



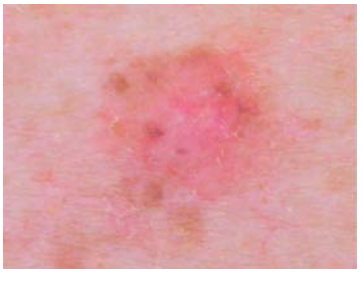
▲ **Figure 12.16a** Clinical image.



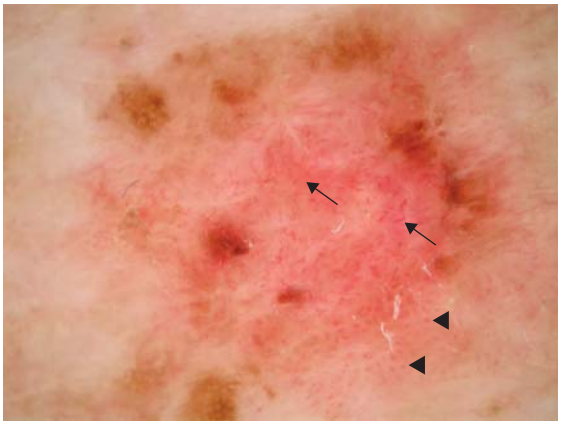
◀ **Figure 12.16b** Nonpolarized contact dermoscopy image of a dermal nevus demonstrating comma vessels (*arrows*).

▲ **Figure 12.17a** Clinical image.

◀ **Figure 12.17b** Polarized noncontact dermoscopy image of a congenital nevus demonstrating numerous vessels of various morphologies.



▲ **Figure 12.18a** Clinical image.



◀ **Figure 12.18b** Polarized noncontact dermoscopy image of a microinvasive melanoma demonstrating polymorphous vessels, including irregular–linear vessels (*arrows*) and dotted vessels (*arrowheads*).

VASCULAR PATTERNS

Crown Vessels

Crown vessels comprise linear, curved vessels with minimal branching, situated along the periphery and extending toward the center without crossing it, giving the appearance of a crown (Argenziano et al., 2004; Zell et al., 2008). Crown vessels are characteristic of sebaceous hyperplasia; this pattern was seen in 83.3% of sebaceous hyperplasia with a PPV of 83.3% (Fig. 12.20). (Zaballos et al., 2005; Argenziano et al., 2004). Crown vessels may also be seen in molluscum contagiosum (Morales et al., 2005).

Strawberry Pattern

The term "strawberry pattern" refers to the distinctive dermoscopic appearance of facial actinic keratoses, consisting of a pink/red pseudonetwork with blurry vessels coursing between hair follicle openings filled with keratotic plugs (Zalaudek et al., 2006b). See also chapter 5b (Fig. 5b.1).

String of Pearls Pattern

This pattern represents the unique appearance of dotted or glomerular vessels arranged in a serpiginous distribution that may appear like a "string of pearls." This pattern is highly suggestive of a diagnosis of clear cell acanthoma (Fig. 12.10) (Marghoob & Braun, 2010, Bugatti et al., 2003).

Follicular Red Dots

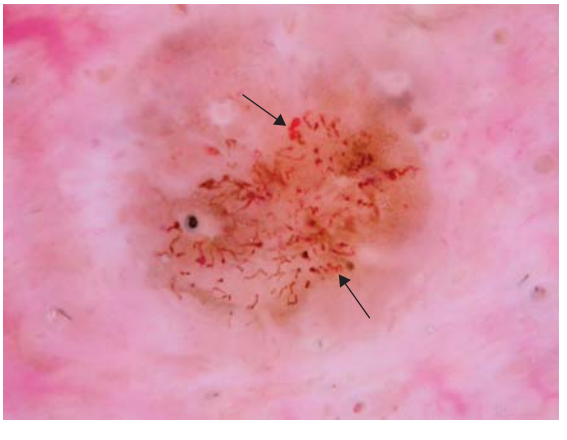
Another more recently described vascular feature is the pattern of follicular red dots, which have been described in active discoid lupus erythematosus (Tosti et al., 2009). The follicular red dots are seen surrounding the hair follicle openings and consist of regularly distributed, concentric reddish dots in a region of alopecia. This may represent dilation of blood vessels with extravasation of red blood cells surrounding the widened infundibula (Tosti et al., 2009).

CONCLUSION

The recognition of vascular structures under dermoscopy has become increasingly important for a range of diagnoses (Tables 12.3 and 12.4). The identification of specific vascular characteristics is an important element of the two-step dermoscopic algorithm. When the lesion is categorized as a nonmelanocytic lesion, vascular features can help to diagnose the lesion more specifically, and hence guide management (Level 5 of the revised two-step dermoscopic algorithm). If the lesion is clearly recognized as a melanocytic tumor, then the identification of vessel type and distribution may facilitate the differentiation between benign and malignant diagnoses (Level 6 of the revised two-step dermoscopic algorithm) (Marghoob & Braun, 2010). For more ambiguous cases in which the lesion cannot be easily classified as melanocytic or nonmelanocytic, the clinician may need to rely on vascular structures as the only recognizable features that can assist in the diagnosis.

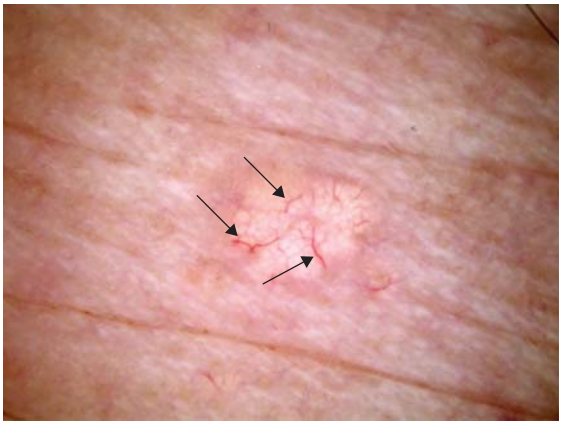
In conclusion, it has become apparent that a finite number of morphologically distinct blood vessels can be visualized under dermoscopy. The vessel morphology and distribution along with other accompanying features can assist the clinician in correctly identifying many benign and malignant lesions. In general, vessels in melanocytic lesions include dotted vessels, comma vessels, linear irregular vessels/serpentine vessels, milky red globules, vascular blush, and polymorphous vessels. Vessels suggestive of nonmelanocytic lesions include arborizing vessels, hairpin vessels, glomerular vessels, crown vessels, and dotted vessels in a string of pearls pattern.

▲ **Figure 12.19a** Clinical image.



◀ **Figure 12.19b** Polarized noncontact dermoscopy image of an epidermotropic melanoma metastasis demonstrating corkscrew vessels (*arrows*).

▲ **Figure 12.20a** Clinical image.



◀ **Figure 12.20b** Polarized noncontact dermoscopy image of a sebaceous hyperplasia demonstrating crown vessels (*arrow*).

Key Points

1. Vessel morphology, distribution and arrangement can help in diagnosing some lesions.
2. The vessel morphologies with the highest predictive value include arborizing vessels for BCC, glomerular vessels for SCC, comma vessels for dermal nevi, dotted vessels for melanocytic lesions, and hairpin vessels with a white halo for keratonizing tumors.
3. Dotted and serpentine vessels can be seen in melanocytic lesions. If both dotted and serpentine vessels are present in an acquired melanocytic lesion, melanoma needs to be ruled out.
4. The vascular patterns with the highest diagnostic significance include serpentine or string of pearls pattern associated with clear cell acanthoma, and crown vessels seen in sebaceous hyperplasia.

REFERENCES

Ahlgrimm-Siess, V., Cao, T., Oliviero, M., et al., 2010, The vasculature of nonmelanocytic skin tumors in reflectance confocal microscopy, II: Vascular features of seborrheic keratosis. *Arch Dermatol*, 146, 694–5.

Argenziano, G., Zalaudek, I., Corona, R., et al., 2004, Vascular structures in skin tumors: a dermoscopy study. *Arch Dermatol*, 140, 1485–9.

Bono, A., Maurichi, A., Moglia, D., et al., 2001, Clinical and dermatoscopic diagnosis of early amelanotic melanoma. *Melanoma Res*, 11, 491–4.

Bono, R., Giampetruzzi, A.R., Concolino, F., et al., 2004, Dermoscopic patterns of cutaneous melanoma metastases. *Melanoma Res*, 14, 367–73.

Braun, R.P., Oliviero, M., Kolm, I., et al., 2009a, Dermoscopy: what's new? *Clin Dermatol*, 27, 26–34.

Braun, R.P., Rabinovitz, H., Tzu, J.E. & Marghoob, A.A., 2009b, Dermoscopy research–an update. *Semin Cutan Med Surg*, 28, 165–71.

Braun, R.P., Rabinovitz, H.S., Krischer, J., et al., 2002, Dermoscopy of pigmented seborrheic keratosis: a morphological study. *Arch Dermatol*, 138, 1556–60.

Bugatti, L., Filosa, G., Broganelli, P. & Tomasini, C., 2003, Psoriasis-like dermoscopic pattern of clear cell acanthoma. *J Eur Acad Dermatol Venereol*, 17, 452–5.

Bugatti, L., Filosa, G. & De Angelis, R., 2004. Dermoscopic observation of Bowen's disease. *J Eur Acad Dermatol Venereol*, 18, 572–4.

Cavicchini, S., Tourlaki, A. & Bottini, S., 2007, Dermoscopic vascular patterns in nodular "pure" amelanotic melanoma. *Arch Dermatol*, 143, 556.

Felder, S., Rabinovitz, H., Oliviero, M. & Kopf, A., 2006, Dermoscopic differentiation of a superficial basal cell carcinoma and squamous cell carcinoma in situ. *Dermatol Surg*, 32, 423–5.

Ferrari, A., Buccini, P., Silipo, V., et al., 2009, Eccrine poroma: a clinical-dermoscopic study of seven cases. *Acta Derm Venereol*, 89, 160–4.

Flach E.H., Rebecca V.W., Herlyn M., Smalley K.S. & Anderson A.R., 2011, Fibroblasts contribute to melanoma tumor growth and drug resistance. *Mol Pharm*, 8, 2039–49.

Giacomel, J. & Zalaudek, I., 2005, Dermoscopy of superficial basal cell carcinoma. *Dermatol Surg*, 31, 1710–13.

Ka, V.S., Clark-Loeser, L. & Marghoob, A.A., 2004, Vascular pattern in seborrheic keratoses and melanoma. *Dermatol Surg*, 30, 75–7.

Kittler, H., Riedl, E., Rosendahl, C. & Cameron, A. Dermatoscopy of unpigmented lesions of the skin: a new classification of vessel morphology based on pattern analysis. Available from: http://www.derm101.com, Accessed 2012.

Kreusch, J.F., 2002, Vascular patterns in skin tumors. *Clin Dermatol*, 20, 248–54.

Labrousse, A.L., Ntayi, C., Hornebeck, W. & Bernard, P., 2004, Stromal reaction in cutaneous melanoma. *Crit Rev Oncol Hematol*, 49, 269–75.

Lever W.F. and David E.E., 2009, *Lever's Histopathology of the Skin*. Philadelphia: Lippincott Williams & Wilkins.

Malvehy, J., Puig, S., Argenziano, G., Marghoob, A.A. & Soyer, H.P., 2007, Dermoscopy report: proposal for standardization. Results of a consensus meeting of the International Dermoscopy Society. *J Am Acad Dermatol*, 57, 84–95.

Malvehy, J., Puig, S., Braun, R.P., Marghoob, A.A., Kopf, A.W., 2006, *Handbook of Dermoscopy*. London: Taylor & Francis.

Marghoob, A.A. & Braun, R., 2010, Proposal for a revised 2-step algorithm for the classification of lesions of the skin using dermoscopy. *Arch Dermatol*, 146, 426–8.

Menzies, S.W., 2002, Dermoscopy of pigmented basal cell carcinoma. *Clin Dermatol*, 20, 268–9.

Menzies, S.W., Kreusch, J., Byth, K., et al., 2008, Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1120–7.

Menzies, S.W., Westerhoff, K., Rabinovitz, H., et al., 2000, Surface microscopy of pigmented basal cell carcinoma. *Arch Dermatol*, 136, 1012–16.

Minagawa, A., Koga, H., Sakaizawa, K., Sano, K. & Saida, T., 2009, Dermoscopic and histopathological findings of polymorphous vessels in amelanotic cutaneous metastasis of pigmented cutaneous melanoma. *Br J Dermatol*, 160, 1134–6.

Morales, A., Puig, S., Malvehy, J. & Zaballos, P., 2005, Dermoscopy of molluscum contagiosum. *Arch Dermatol*, 141, 1644.

Niederkorn, A., Ahlgrimm-Siess, V., Fink-Puches, R., et al., 2009, Frequency, clinical and dermoscopic features of benign papillomatous melanocytic naevi (Unna type). *Br J Dermatol*, 161, 510–14.

Pan, Y., Chamberlain, A.J., Bailey, M., et al., 2008, Dermatoscopy aids in the diagnosis of the solitary red scaly patch or plaque-features distinguishing superficial basal cell carcinoma, intraepidermal carcinoma, and psoriasis. *J Am Acad Dermatol*, 59, 268–74.

Phan, A., Dalle, S., Touzet, S., et al., 2010, Dermoscopic features of acral lentiginous melanoma in a large series of 110 cases in a white population. *Br J Dermatol*, 162, 765–71.

Pizzichetta, M.A., Talamini, R., Stanganelli, I., et al., 2004, Amelanotic/hypomelanotic melanoma: clinical and dermoscopic features. *Br J Dermatol*, 150, 1117–24.

Scalvenzi, M., Lembo, S., Francia, M.G. & Balato, A., 2008, Dermoscopic patterns of superficial basal cell carcinoma. *Int J Dermatol*, 47, 1015–18.

Sgambato, A., Zalaudek, I., Ferrara, G., et al., 2008, Adnexal tumors: clinical and dermoscopic mimickers of basal cell carcinoma. *Arch Dermatol*, 144, 426.

Shalom A., Schein O., Landi C., et al., 2012, Dermoscopic findings in biopsy-proven poromas. *Dermatol Surg* (in press).

Stoecker, W.V. & Stolz, W., 2008, Dermoscopy and the diagnostic challenge of amelanotic and hypomelanotic melanoma. *Arch Dermatol*, 144, 1207–10.

Suwattee, P., Schram, S.E. & Warshaw, E.M., 2007, Digital polarized light dermoscopy of clinically nonpigmented dermal nevi. *Dermatol Surg*, 33, 1120–5.

Tosti, A., Torres, F., Misciali, C., et al., 2009, Follicular red dots: a novel dermoscopic pattern observed in scalp discoid lupus erythematosus. *Arch Dermatol*, 145, 1406–9.

Vazquez-Lopez, F., Manjon-Haces, J.A., Maldonado-Seral, C., et al., 2003, Dermoscopic features of plaque psoriasis and lichen planus: new observations. *Dermatology*, 207, 151–6.

Vazquez-Lopez, F., Zaballos, P., Fueyo-Casado, A. & Sanchez-Martin, J., 2007, A dermoscopy subpattern of plaque-type psoriasis: red globular rings. *Arch Dermatol*, 143, 1612.

Zaballos, P., Ara, M., Puig, S. & Malvehy, J., 2005, Dermoscopy of sebaceous hyperplasia. *Arch Dermatol*, 141, 808.

Zaballos, P., Salsench, E., Puig, S. & Malvehy, J., 2006, Dermoscopy of venous stasis dermatitis. *Arch Dermatol*, 142, 1526.

Zalaudek, I., Argenziano, G., Leinweber, B., et al., 2004, Dermoscopy of Bowen's disease. *Br J Dermatol*, 150, 1112–6.

Zalaudek, I., Ferrara, G., Broganelli, P., et al., 2006a, Dermoscopy patterns of fibroepithelioma of Pinkus. *Arch Dermatol*, 142, 1318–22.

Zalaudek, I., Giacomel, J., Argenziano, G., et al., 2006b, Dermoscopy of facial nonpigmented actinic keratosis. *Br J Dermatol*, 155, 951–6.

Zell, D., Kim, N., Olivero, M., Elgart, G. & Rabinovitz, H., 2008, Early diagnosis of multiple primary amelanotic/hypomelanotic melanoma using dermoscopy. *Dermatol Surg*, 34, 1254–7.

13 Diagnostic accuracy of dermoscopy

Harald Kittler and Scott W. Menzies

Although there are several ways to evaluate the accuracy of a diagnostic test, the majority of studies that have evaluated the diagnostic accuracy of dermoscopy have relied on calculation of sensitivity and specificity, by comparing the diagnosis made by dermoscopy with the histopathologic diagnosis. Sensitivity is the proportion of melanomas that are correctly identified by dermoscopy, and specificity is the proportion of benign pigmented skin lesions that are correctly identified by dermoscopy. This type of analysis is simple and easy to perform, but it has several disadvantages (Vestergaard et al., 2008). One disadvantage is the fact that the diagnosis made by dermoscopy has to be divided into two groups (benign and malignant). This is surely an oversimplification of the diagnostic procedure of dermoscopy and does not accurately reflect the way in which dermoscopy is used in clinical practice. The diagnosis given by dermoscopy is hardly ever definitely benign or malignant. As with many other diagnostic techniques, dermoscopy is a tool to minimize uncertainty, but it cannot eliminate it. The diagnosis made by dermoscopy is more or less a measure of the probability that a lesion is benign or malignant. The way in which this probability is interpreted is influenced by several other variables, for example, the clinical impression of the lesion, the age of the patient, the anatomic site, and the number and appearance of other lesions in the same patient. The major task of the dermatologist who uses dermoscopy is to interpret the dermoscopic findings correctly and to decide whether the probability that the lesion is malignant is so low that a further diagnostic procedure (excision or digital monitoring) is not indicated, or whether the probability of malignancy is so high that excision of the lesion is required.

While the sensitivity and specificity remain the most important specifications when reporting the accuracy of any diagnostic instrument, calculating the sensitivity and specificity of dermoscopy has been criticized as giving answers to the wrong questions, because the question of whether a pigmented skin lesion is benign or malignant should be left to the pathologist and the primary aim of dermoscopy should be to decide whether a lesion has to be excised or not. Other disadvantages to the evaluation of diagnostic tests by their sensitivity and specificity include the prevalence of the disease of interest (in this case, melanoma) not being taken into account, and the difficulties of comparing two diagnostic tests. On the other hand, sensitivity and specificity are valid indicators of diagnostic test performance that are easily understood and, if interpreted correctly, can provide useful information. Table 13.1 summarizes the results of 13 studies that compared the diagnostic accuracy for melanoma with and without dermoscopy (with the unaided eye) (Westerhoff et al., 2000; Stanganelli et al., 1998; Stanganelli et al., 2000; Soyer et al., 1995; Nachbar et al., 1994; Lorentzen et al., 1999; Krähn et al., 1998; Dummer et al., 1993; Binder et al., 1995; Binder et al., 1997; Benelli et al., 1999; Carli et al., 1998; Carli et al., 2004a). It can be seen that the reported levels for sensitivity and specificity vary significantly between the studies. The reason for this might be that the diagnostic accuracy of dermoscopy depends on many factors, including the level of training of the dermatologists, the diagnostic difficulty of the evaluated lesions, and the type of algorithm used to evaluate the lesions. Variation in the estimates of sensitivity and specificity can also be explained by study differences in the explicit or implicit threshold used to differentiate melanoma from benign pigmented skin lesions. Shifting the threshold in one direction results in increasing the sensitivity and decreasing the specificity. Shifting the threshold in the other direction results in increasing the specificity and decreasing the sensitivity. This is the reason for the difficulties in comparing two diagnostic techniques solely by their sensitivity and specificity.

The 13 studies shown in Table 13.1 were included in a quantitative meta-analysis to answer the question of whether dermoscopy truly improves the diagnostic accuracy for melanoma in the light of the already published literature (Kittler et al., 2002). In this meta-analysis, a statistical technique was used that allowed for the comparison of diagnostic tests by calculating log odds ratios and summary receiver–operating characteristic curves, thereby circumventing the problem of differences in the threshold used to differentiate between benign skin lesions and melanoma (Fig. 13.1). The log odds ratio is a single measure of how well the test discriminates between benign skin lesions and melanoma. The mean log odds ratio achieved with dermoscopy was 4.0 [95% confidence interval (CI): 3.0–5.1], significantly higher than the log odds ratio achieved without dermoscopy (mean log odds ratio: 2.7, 95% CI: 1.9–3.4), resulting in a mean difference of 1.3 (95% CI: 0.7–2.0). This result is in line with a review published in 1997 by Mayer (Mayer, 1997), which included

Table 13.1 Results of 13 Studies, Which Directly Compared the Diagnostic Accuracy for Melanoma with and without Dermoscopy

First author and year of publication	Sample size (n)	Sensitivity (%)		Specificity (%)	
		Clinical image	Dermoscopy	Clinical image	Dermoscopy
Benelli et al., 1999	401	67	80	79	89
Binder et al., 1995	240	58	68	91	91
Binder et al., 1997	100	73	73	70	78
Carli, 1998	15	42	75	78	89
Cristofolini et al., 1994	220	85	88	75	79
Dummer et al., 1993	824	65	96	93	98
Krähn et al., 1998	80	79	90	78	93
Lorentzen et al., 1999	232	77	82	89	94
Nachbar et al., 1994	172	84	93	84	91
Soyer et al., 1995	159	94	94	82	82
Stanganelli et al., 1998	20	55	73	79	73
Stanganelli et al., 2000	3329	67	93	99	100
Westerhoff et al., 2000	100	63	76	54	58

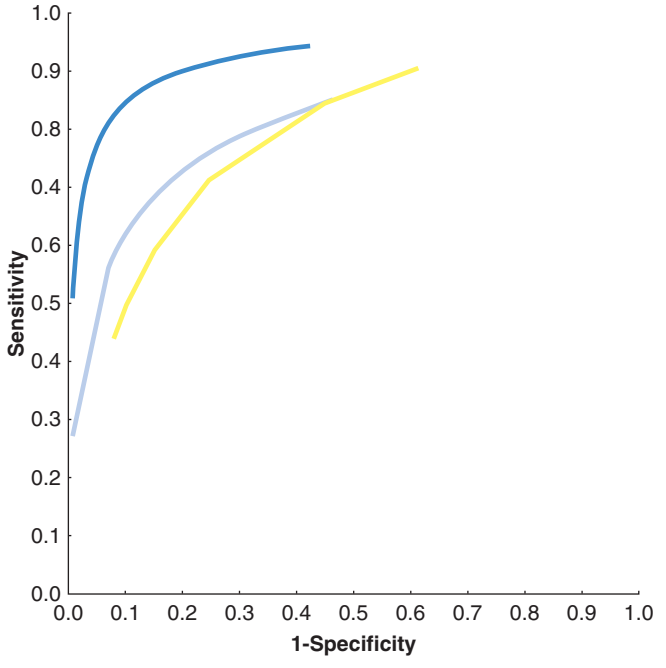


Figure 13.1 Summary receiver–operating characteristic curves for the diagnostic performance of the clinical diagnosis without dermoscopy (*light blue*), dermoscopy when performed by experts (*dark blue*) and dermoscopy when performed by nonexperts (*yellow*). These curves are summary estimates of the diagnostic accuracy of dermoscopy based on the results of 13 individual studies. The higher the curves bend up to the left upper corner, the better the diagnostic performance.

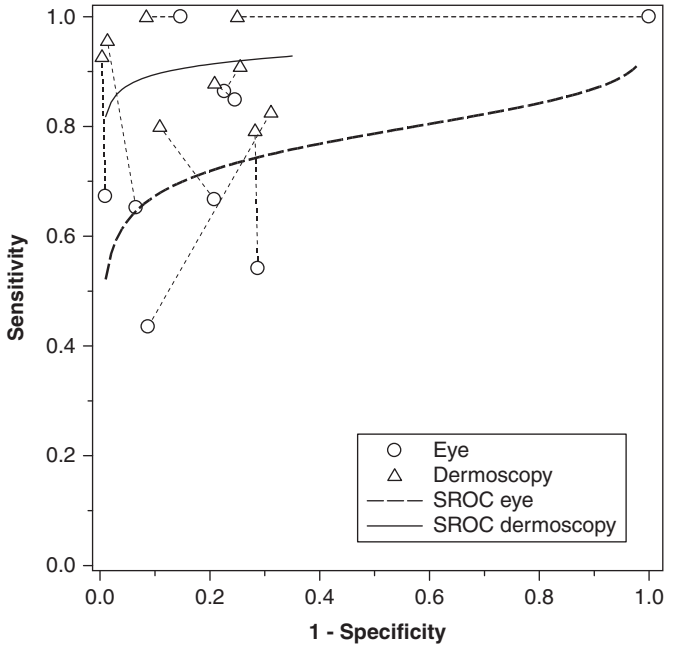


Figure 13.2 Meta-analysis was reported on 9 studies published from 1987 to January 2008, which directly compared the sensitivity and specificity of dermoscopy *versus* naked eye examination exclusively performed in a clinical setting (Vestergaard et al., 2008). Here a plot of sensitivity against 1-specificity for each study and each test with the receiver–operating characteristic curves for each test superimposed is shown. (NB: The two estimates for each study are joined by a line). The relative diagnostic odds ratio for melanoma compared with naked-eye examination was 15.6 (95% CI: 2.9–83.7, $P = 0.016$). *Source*: From Vestergaard et al. (2008) with permission.

six studies and another published meta-analysis by Bafounta et al. (2001), which included eight studies. A meta-analysis that included only studies performed in a clinical setting also confirmed the improvement of the diagnostic accuracy by dermoscopy (Vestergaard et al., 2008) (Fig. 13.2).

Although there is overwhelming evidence that dermoscopy improves the diagnostic accuracy for melanoma in comparison to inspection with the unaided eye, there are several questions that deserve further consideration. As already mentioned, the diagnostic accuracy of dermoscopy strongly depends on the level of experience of the observer. As shown by Binder and colleagues, the diagnostic accuracy achieved with dermoscopy when applied by nonexperts is not better but in fact worse than the diagnostic accuracy achieved without dermoscopy (Binder et al., 1995). This finding underscores the importance that dermoscopy cannot be recommended for untrained users. In this regard, the study by Westerhoff et al. (2000), who examined the impact of teaching dermoscopy to primary care physicians, deserves further attention. As reported in that study, the diagnostic accuracy of primary care physicians before training was only slightly better than chance. After training, there was a significant improvement in the diagnosis of melanoma using dermoscopy *versus* inspection with the unaided eye. However, the reported diagnostic accuracy after training was much lower than in comparable studies involving dermatologists.

The impact of the type of diagnostic algorithm on the diagnostic accuracy of dermoscopy has long been a matter of debate. Following the original reports by Pehamberger et al. (1987), who described the use of pattern analysis for the dermoscopic evaluation of pigmented skin lesions, a number of alternative diagnostic algorithms have been developed, including various scoring systems, for example, the ABCD rule for dermoscopy (Stolz et al., 1994), the seven-point checklist (Argenziano et al., 1998), and the algorithm developed by Menzies and associates (Menzies et al., 1996b; Menzies et al., 1996a). Pattern analysis relies on the description of a considerable number of dermoscopic features that are often difficult to recognize by nonexperts. Scoring systems can be regarded as simplified versions of pattern analysis using only a limited number of dermoscopic features. In a meta-analysis including 27 studies (Kittler et al., 2002), pattern analysis showed a slightly better diagnostic accuracy than the other algorithms, but this was not statistically significant. During the Consensus Net Meeting on dermoscopy (see www.dermoscopy.org) held in 2001, four different diagnostic algorithms for dermoscopy were compared (pattern analysis, the ABCD rule, the seven-point checklist, and the Menzies rule) (Argenziano et al., 2003). The results of the meeting indicated that pattern analysis had a higher specificity than the other algorithms. No significant differences were found with regard to sensitivity with pattern analysis compared with the other methods, although the Menzies rule had a significantly increased sensitivity compared with the ABCD rule and seven-point checklist (Argenziano et al., 2003).

The impact of an improving diagnostic specificity with dermoscopy can perhaps best be seen by comparing excision rates. In a randomized trial in a specialist setting of naked-eye examination *versus* naked eye and dermoscopy examination, there was a significant 42% reduction in patients referred to biopsy in the dermoscopy arm (Carli et al., 2004a). This is consistent with the retrospective findings of a significant reduction of the benign/malignant ratio of excised melanocytic lesions in clinicians trained in the use of dermoscopy from 18:1 (predermoscopy era) to 4:1 (postdermoscopy era) (Carli et al., 2004b). In contrast, nonusers of dermoscopy continued their diagnostic performance without improvement (from 12:1 to 14:1).

Finally, it has to be mentioned that the gold standard of diagnosis (histopathology) is not always perfect. Sometimes there is considerable disagreement among histopathologists on whether a given case is a melanoma or not. In other words, when we calculate the sensitivity and specificity, we are evaluating the ability of dermoscopy to predict the histopathologic diagnosis rather than the patient's true disease status.

REFERENCES

Argenziano, G., Fabbrocini, G., Carli, P., et al., 1998, Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. *Arch Dermatol*, 134, 1563–70.

Argenziano, G., Soyer, H., Chimenti, S., et al., 2003, Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet, *J Am Acad Dermatol*, 48, 679–93.

Bafounta, M.L., Beauchet, A., Aegerter, P. & Saiag, P., 2001, Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. *Arch Dermatol*, 137, 1343–50.

Benelli, C., Roscetti, E., Pozzo, V.D., et al., 1999, The dermoscopic versus the clinical diagnosis of melanoma. *Eur J Dermatol*, 9, 470–6.

Binder, M., Puespoeck-Schwarz, M., Steiner, A., et al., 1997, Epiluminescence microscopy of small pigmented skin lesions: short-term formal training improves the diagnostic performance of dermatologists. *J Am Acad Dermatol*, 36(2 Pt 1), 197–202.

Binder, M., Schwarz, M., Winkler, A., et al., 1995, Epiluminescence microscopy. A useful tool for the diagnosis of pigmented skin lesions for formally trained dermatologists. *Arch Dermatol*, 131, 286–91.

Carli, P., De, G., Naldi, L. & Dosi, G., 1998, Reliability and inter-observer agreement of dermoscopic diagnosis of melanoma and melanocytic naevi. Dermoscopy Panel. *Eur J Cancer Prev*, 7, 397–402.

Carli, P., de Giorgi, V., Chiarugi, A., et al., 2004a, Addition of dermoscopy to conventional naked-eye examination in melanoma screening: a randomized study. *J Am Acad Dermatol*, 50, 683–9.

Carli, P., De Giorgi, V., Crocetti, E., et al., 2004b, Improvement of malignant/benign ratio in excised melanocytic lesions in the "dermoscopy era": a retrospective study 1997–2001. *Br J Dermatol*, 150, 687–92.

Cristofolini, M., Zumiani, G., Bauer, P., et al., 1994, Dermatoscopy: usefulness in the differential diagnosis of cutaneous pigmentary lesions. *Melanoma Res*, 4, 391–4.

Dummer, W., Doehnel, K. & Remy, W., 1993, Videomicroscopy in differential diagnosis of skin tumors and secondary prevention of malignant melanoma. *Hautarzt*, 44, 772–6.

Kittler, H., Pehamberger, H., Wolff, K. & Binder, M., 2002, Diagnostic accuracy of dermoscopy. *Lancet Oncol,* 3, 159–65.

Krähn, G., Gottlöber, P., Sander, C. & Peter, R.U., 1998, Dermatoscopy and high frequency sonography: two useful non-invasive methods to increase preoperative diagnostic accuracy in pigmented skin lesions. *Pigment Cell Res*, 11, 151–4.

Lorentzen, H., Weismann, K., Petersen, C.S., et al., 1999, Clinical and dermatoscopic diagnosis of malignant melanoma. Assessed by expert and non-expert groups. *Acta Derm Venereol*, 79, 301–4.

Mayer, J., 1997, Systematic review of the diagnostic accuracy of dermatoscopy in detecting malignant melanoma. *Med J Aust*, 167, 206–10.

Menzies, S.W., Ingvar, C. & McCarthy, W.H., 1996a, A sensitivity and specificity analysis of the surface microscopy features of invasive melanoma. *Melanoma Res*, 6, 55–62.

Menzies, S.W., Ingvar, C., Crotty, K.A. & McCarthy, W.H., 1996b, Frequency and morphologic characteristics of invasive melanomas lacking specific surface microscopic features. *Arch Dermatol*, 132, 1178–82.

Nachbar, F., Stolz, W., Merkle, T., et al., 1994, The ABCD rule of dermatoscopy. High prospective value in the diagnosis of doubtful melanocytic skin lesions. *J Am Acad Dermatol*, 30, 551–9.

Pehamberger, H., Steiner, A. & Wolff, K., 1987, In vivo epiluminescence microscopy of pigmented skin lesions. I. Pattern analysis of pigmented skin lesions. *J Am Acad Dermatol*, 17, 571–83.

Soyer, H.P., Smolle, J., Leitinger, G., et al., 1995, Diagnostic reliability of dermoscopic criteria for detecting malignant melanoma. *Dermatology*, 190, 25–30.

Stanganelli, I., Serafini, M. & Bucch, L., 2000, A cancer-registry-assisted evaluation of the accuracy of digital epiluminescence microscopy associated with clinical examination of pigmented skin lesions. *Dermatology*, 200, 11–16.

Stanganelli, I., Serafini, M., Cainelli, T., et al., 1998, Accuracy of epiluminescence microscopy among practical dermatologists: a study from the Emilia-Romagna region of Italy. *Tumori*, 84, 701–5.

Stolz, W., Riemann, A., Cognetta, A., et al., 1994, ABCD rule of dermatoscopy: a new practical method for early recognition of malignant melanoma. *Eur J Dermatol*, 4, 521–7.

Vestergaard, M., Macaskill, P., Holt, P. & Menzies, S.W., 2008, Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. *Br J Dermatol*, 159, 669–76

Westerhoff, K., McCarthy, W.H. & Menzies, S.W., 2000, Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. *Br J Dermatol*, 143, 1016–20.

14 Followup of melanocytic skin lesions with digital dermoscopy

Harald Kittler and Scott W. Menzies

The majority of melanocytic skin lesions can be diagnosed by experienced dermatologists with the unaided eye. For melanocytic skin lesions, which cannot be diagnosed with the unaided eye, the diagnosis can often be made by dermoscopy with certainty. But even with the use of dermoscopy, the diagnostic accuracy for melanocytic skin lesions is not 100%. This technique cannot replace histopathologic examination. When a melanocytic skin lesion is doubtful for melanoma, either by clinical examination or by dermoscopic examination, the lesion is usually excised to rule out the disease. This strategy is adequate for most clinical situations. However, when individuals have multiple, sometimes hundreds, of doubtful melanocytic lesions, it becomes impractical to excise them all. Furthermore, in the common scenario of nevus with a completely banal dermoscopic appearance presenting with a patient history of change, excision is not usually necessary. However, in such scenarios it would be reassuring to both the patient and the physician to know the actual biological dynamics of the lesion(s) in question.

It is generally agreed that patients with multiple nevi need regular skin examinations. However, the optimal surveillance strategy is still under debate. It has been recommended that these patients regularly examine their own skin to track changes in their moles, but a recent study (Dawid et al., 2002) showed that the ability of patients to identify mole changes is limited. Photographic closeups of lesions may be used for documentation to assist the patient or physician in the surveillance of moles. The advent of digital imaging equipment has made it easy to store, retrieve, and compare dermoscopic images of melanocytic lesions over time (Fig. 14.1). Dermoscopic images of melanocytic skin lesions provide a detailed view of subsurface structures that cannot be identified by conventional photographic closeups. Changes within these subsurface structures can be monitored with dermoscopy but not with conventional photography. Digital dermoscopy holds great promise for the improved monitoring of melanocytic lesions because it can improve diagnostic sensitivity for early melanoma by identifying changes in lesions over time that indicate impending or incipient malignancy, and it can reduce the number of biopsies of benign lesions that are biologically indolent (i.e., senescent, not changing).

DIGITAL DERMOSCOPIC FOLLOWUP FOR THE DETECTION OF EARLY MELANOMA

Short-Term Followup

In the study by Menzies et al., digital dermoscopy was used for short-term followup of melanocytic skin lesions (Menzies et al., 2001). This study was not restricted to patients with multiple nevi. It included melanocytic lesions, which did not display features of melanoma but were otherwise considered doubtful, for example, because of a recent history of change. These lesions may in a conventional clinical practice (without the possibility of digital monitoring) be excised or require clinical review by other methods. A total of 318 melanocytic skin lesions were followed over a median of three months. Any change except for overall solar-induced pigment changes or increase/decrease in number of milia-like cysts was considered to be a significant change (Table 14.1). Of these monitored lesions, 81% remained unchanged. Sixty-one lesions showed morphologic changes. All changing lesions were excised. Of the 61 changing lesions, seven (11% of changed and 2% of total lesions) were found to be early melanoma (five in situ and two invasive with a Breslow thickness of 0.25 and 0.28 mm, respectively). According to the authors, none of these melanomas developed any classic clinical or dermoscopic features of melanoma, and therefore could be identified only by morphologic change recognizable on comparative analysis. The authors concluded that short-term monitoring is a useful adjunct in the assessment of melanocytic lesions, since it enables early detection of featureless melanomas while decreasing the need for excision of clinically suspicious benign lesions.

Since the above initial observations, larger series on short-term followup have confirmed the identification of dermoscopic featureless melanoma using short-term (6 weeks to 4.5 months) followup (Altamura et al., 2008; Kittler et al., 2000b; Kittler et al., 2000a; Kittler & Binder, 2001; Kittler & Binder, 2002). Importantly, no specific type of morphologic change can distinguish melanoma from nevi when lesions are monitored over this short duration, with any change during this period requiring excision (Figs. 14.1, 14.2) (Kittler et al., 2006). Importantly, 99.2% of lesions remaining unchanged at 2.5–4.5 months were confirmed benign on further followup (Altamura et al., 2008). Although 94% of melanoma (non–lentigo maligna type) were observed to change during the short-term interval (2.5–4.5 months), only 75% of lentigo maligna change at this time interval. For this reason, a second monitored interval between 6 and 12 months following the baseline image is recommended where lentigo maligna is in the differential diagnosis (Altamura et al., 2008).

Long-Term Followup

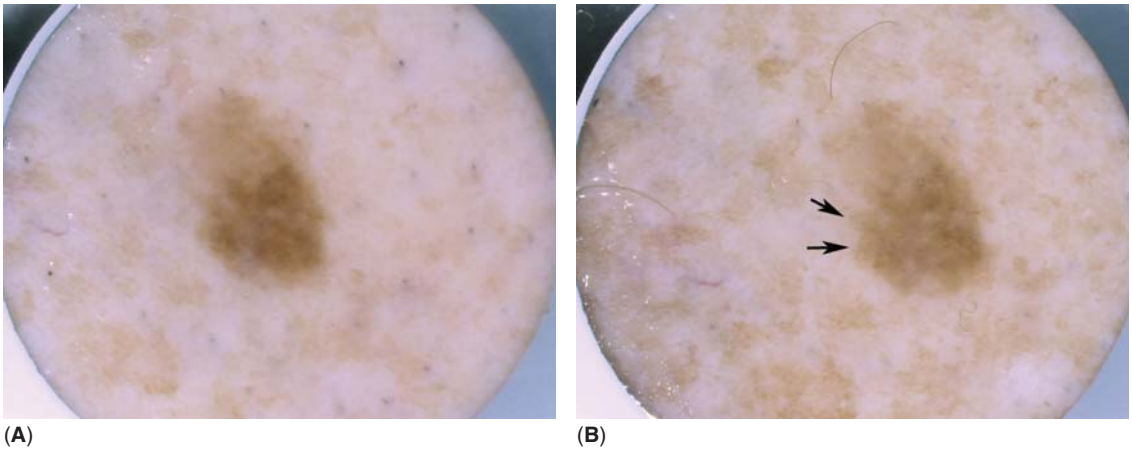
A study by Kittler et al. (2000) was tailored for patients with multiple doubtful melanocytic skin lesions. These patients have an increased risk of developing melanoma and were under life-long regular surveillance skin examinations. In a cohort study including 202 patients with multiple melanocytic nevi, 1862 melanocytic lesions were monitored with digital dermoscopy over a median followup period of one year. Interestingly, 96% of the lesions remained stable over time or showed minor, nonsubstantial changes, for example, darker or lighter overall pigmentation (Table 14.1). This finding is important because it shows that even for patients with multiple nevi, in the vast majority of lesions, substantial changes will not occur; patients can thus be reassured. Substantial changes occurred in 75 melanocytic skin lesions (4%), of which eight were histologically diagnosed as early melanomas. Substantial changes were defined as (Table 14.1):

- Asymmetric enlargement
- Change in shape
- Color changes other than overall pigment lightening or darkening
- Changes of dermosopic structures except for those considered nonsignificant and are listed below.

Nonsignificant changes included:

- Darker or lighter overall appearance
- Change in number or distribution of brown globules
- Decrease in number of black dots
- Disappearance of inflammatory reaction
- Disappearance of parts of the network and replacement with diffuse brown pigmentation. (NB: Although this change was considered nonsignificant, it should be noted that this change can also be seen in slow-growing melanomas (Argenziano et al., 2007; Argenziano et al., 2010; Terushkin et al., 2012).

All melanomas identified during followup were thinner than 0.75 mm, and the five of the eight melanomas were in situ. Six of the eight patients with melanoma were unaware that the lesion had changed over time, confirming that patients have difficulties detecting subtle changes in lesions. Two melanomas in this study did not enlarge but showed



(**A**) (**B**)

Figure 14.1 (**A**) *Short-term monitoring—baseline image.* (**B**). *Short-term monitoring–three month followup image.* The arrows indicate the focal increase in size and internal architectural change of the lesion. Any change during the short-term monitoring period (2.5–4.5 months) requires excision. Diagnosis: in situ melanoma.

Table 14.1 Classification of Changes

Change	Short-term mole monitoring (3 months)	Long-term mole monitoring (6–12 months)
Significant	Any change other than nonsignificant changes	Asymmetric enlargement Focal changes in pigmentation or structure Regression features Change in color
Non-significant	Global change in pigmentation	Darker or lighter overall appearance Change in number or distribution of brown globules Decrease in number of black dots
	Loss or appearance of milia-like cysts	Disappearance of inflammatory reaction Disappearance of small foci of pigment network within central portion of the lesion and replacement by diffuse brown pigmentation

changes only in their dermoscopic structures. Thus, these tumors probably would have been missed or detected much later in the clinical course if followed only by conventional clinical photography. Other studies on long-term followup showed similar results, although there was some variation in the ratio of excised melanomas and monitored lesions (Robinson & Nickoloff, 2004; Schiffner et al., 2003; Bauer et al., 2005; Fuller et al., 2007; Haenssle et al., 2006; (Banky et al., 2005). The changes observed by digital monitoring are more pronounced when the followup intervals are longer. This is true for melanocytic nevi but also for melanomas. In contrast to short-term followup, in long-term followup changes observed in melanomas are different from those observed in nevi. Melanomas more frequently grow asymmetrically (change in size and shape), whereas nevi more frequently grow symmetrically (change in size but not in shape). Structural changes (appearance of new structures) and color changes (appearance of new colors) are more frequently observed in melanomas than in nevi. The interpretation of followup images, therefore, strongly depends on the length of the observation period, no matter if the initial intention was short-term or long-term followup.

THE NATURAL HISTORY OF MELANOCYTIC NEVI REVEALED BY DIGITAL DERMOSCOPY

In contrast to melanomas enlarging melanocytic nevi typically show symmetrical enlargement without structural changes. The dermoscopic sign of a peripheral rim of brown globules is highly characteristic for symmetrically enlarging melanocytic nevi in youth but can also be found in eruptive nevi in immunocompromised patients, for example, after renal transplantation (Fig. 14.3). As long as these lesions manifest a single row of peripheral brown globules, develop in younger individuals (Fig. 14.4), and do not display any melanoma-specific structures (e.g., atypical network, negative network, atypical streaks, shiny white lines, atypical dots and globules, irregular blotch, blue-white veil, regression structures, atypical vessels, and peripheral brown structureless areas), then there is no need for the excision of these lesions. These nevi represent benign nevi that are growing in a radial (horizontal) plane (Fig. 14.3). Once these nevi enter senescence, the peripheral globules are no longer visible and the nevus will usually manifest a reticular or homogenous pattern (Fig. 14.5). Further scrutiny of these enlarging nevi reveals that most contain relatively small, homogenous brown peripheral globules that have the same color as the rest of the nevus. Furthermore, the rest of the nevus will usually have a reticular or homogenous pattern (Figs. 14.3, 14.5). Histopathology and confocal microscopy have shown that the peripheral globules correspond to junctional nevomelanocytic nests at the tips of rete ridges in Clark-type nevi. In contrast to the nevus with a single row of peripheral globules, nevi with multiple rows of peripheral globules as seen in Figure 14.6 (also known as tiered globules) are classified as lesions having a starburst pattern (see chap. 7e, on Spitz nevus). The starburst pattern, whether created by tiered globules or by streaks, is usually associated with Spitz/Reed nevus. However, both the peripheral globular pattern and the starburst pattern are signs of active radial growth occurring in these nevi. Thus, it can be anticipated that nevi manifesting the aforementioned patterns will enlarge,

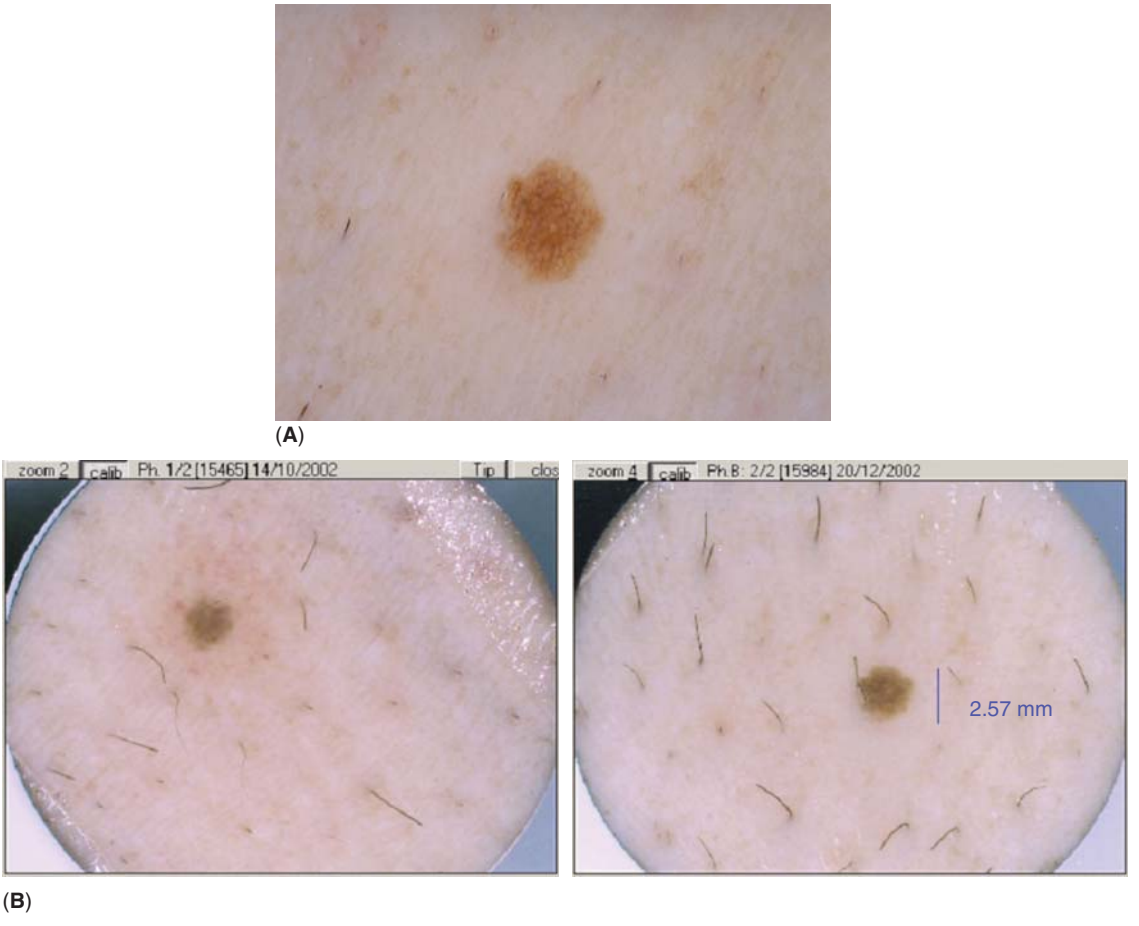


Figure 14.2 (**A**) *Baseline image.* The advantage of short-term monitoring is that lesions that would normally be observed such as this dermoscopically banal lesion can be monitored in the appropriate clinical setting. This 2.5 mm diameter lesion on the anterior tibia was noted to be new and changing by this 38-year-old woman. Under dermoscopic examination it is seen as a symmetrical lesion with graduated network at the periphery. However, because of the history of change the lesion was monitored. (**B**). *Short-term monitoring—baseline image and 2.5-month followup image.* Here the lesion has clearly enlarged over the short-term followup. Diagnosis: in situ melanoma. Nearly two-thirds of melanomas detected by short-term monitoring lack specific dermoscopy features of melanoma.

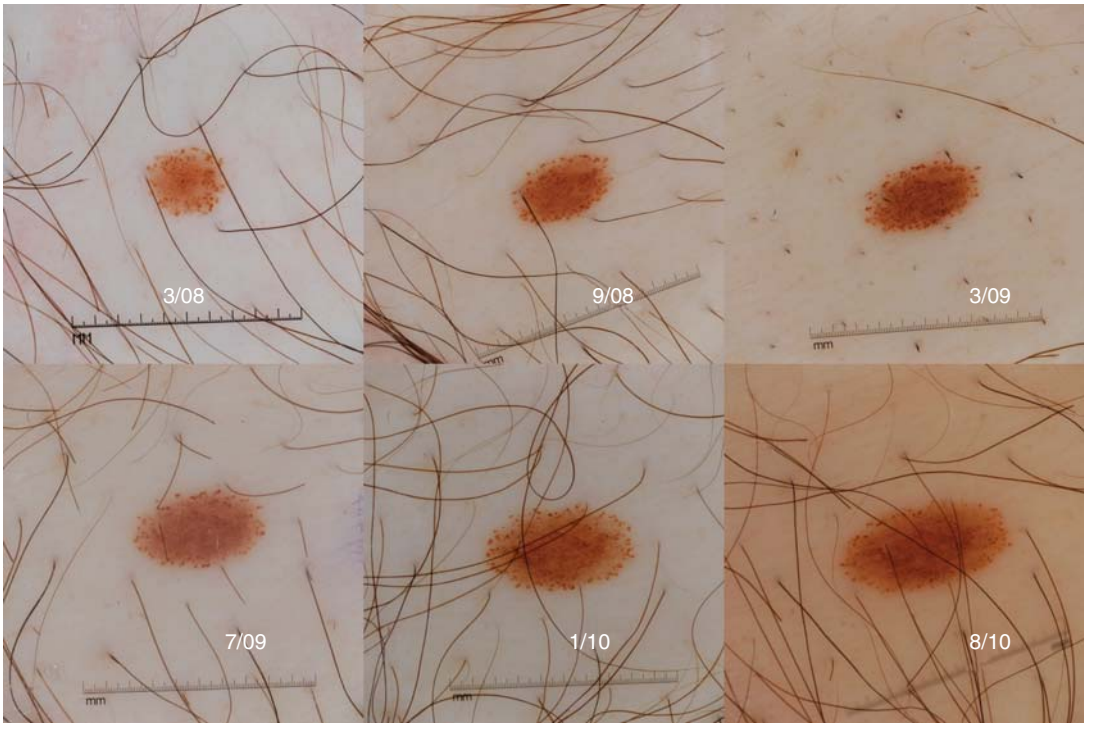


Figure 14.3 This lesion manifested with a peripheral rim of globules. This pattern is predictive of a growing nevus as can be seen in the images provided.

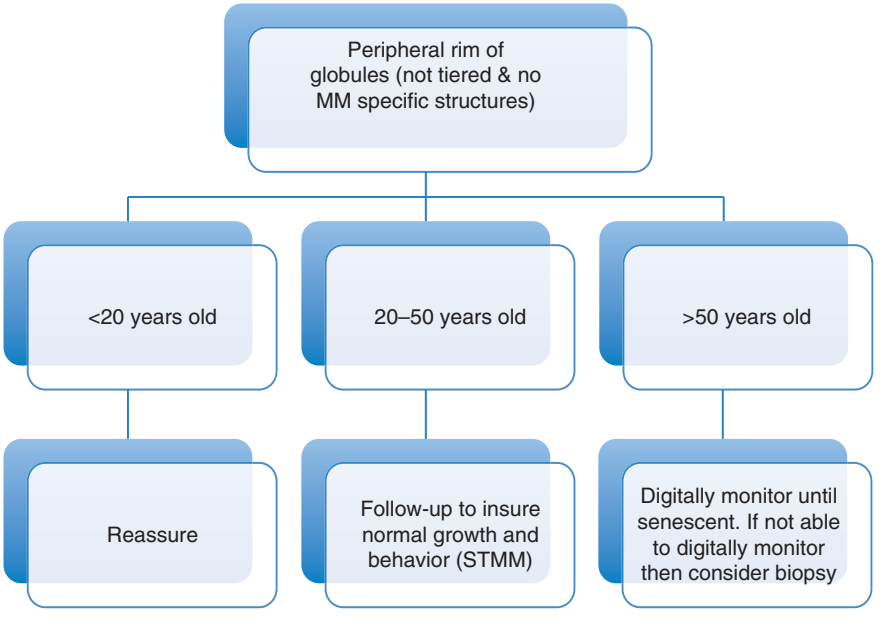


Figure 14.4 In a recent study (Zalaudek et al., 2011), the management approach for nevi with a peripheral rim of globules was outlined. The authors noted that this pattern was common in youth, then its prevalence started to decline rapidly after the third decade of life and was not observed at all after the sixth decade of life. Based on these observations this management algorithm was proposed.

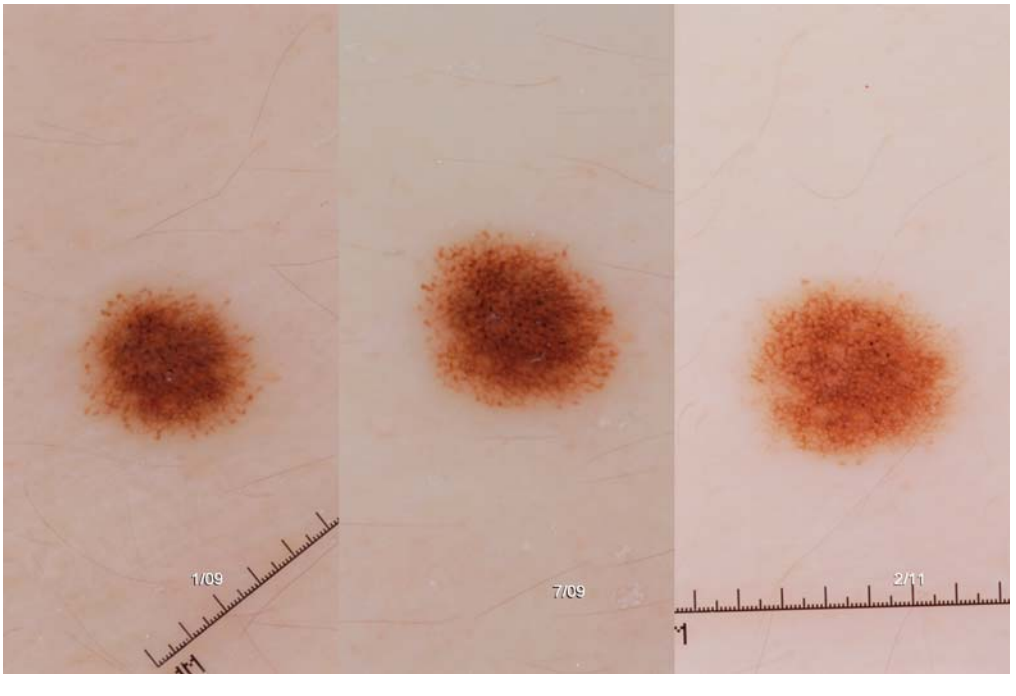


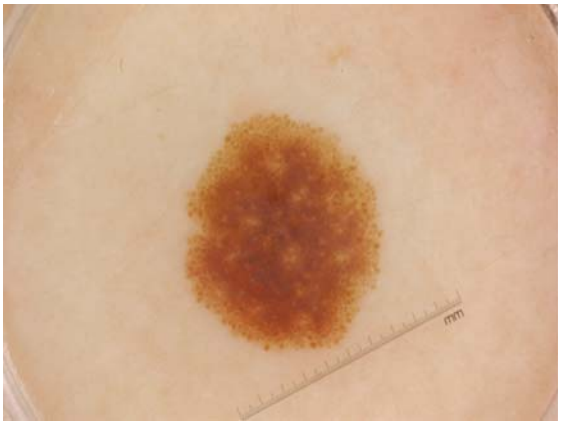
Figure 14.5 This lesion had a peripheral rim of small brown globules. The lesion grew in a symmetric fashion. Once it stopped growing, the peripheral rim of globules were no longer present and the lesion only revealed network (reticular pattern).

usually in a symmetric fashion, and once the radial growth phase is over and the nevus has entered senescence the peripheral globules, streaks, or tiered globules will no longer be visible (Fig. 14.5).

Although most growing nevi enlarge in a symmetric fashion, some show asymmetrical enlargement (Fig. 14.7). We generally recommend to biopsy these lesions to rule out melanoma. Loss of pigmentation may occur in a melanocytic nevus resulting in partial to complete disappearance (Fig. 14.8). Although this process can occur in youth, it is more common to see it in adults and elderly individuals. It represents the last step in the natural evolution history of a melanocytic nevus and is termed involution. This process should not be called regression because regression is an active process with inflammation occurring in lesions with a halo reaction or with dermoscopic regression structures.

Finally, with digital monitoring we can on occasion observe a melanoma arising in a congenital nevus. An example of a melanoma in situ arising in a congenital nevus is shown in Figure 14.9.

▲ **Figure 14.6a** Clinical image of a Spitz nevus.



◀ **Figure 14.6b** This lesion has a starburst pattern consisting of peripheral rim of tiered globules. Tiered globules consist of one peripheral rim of globules staked on top of another.

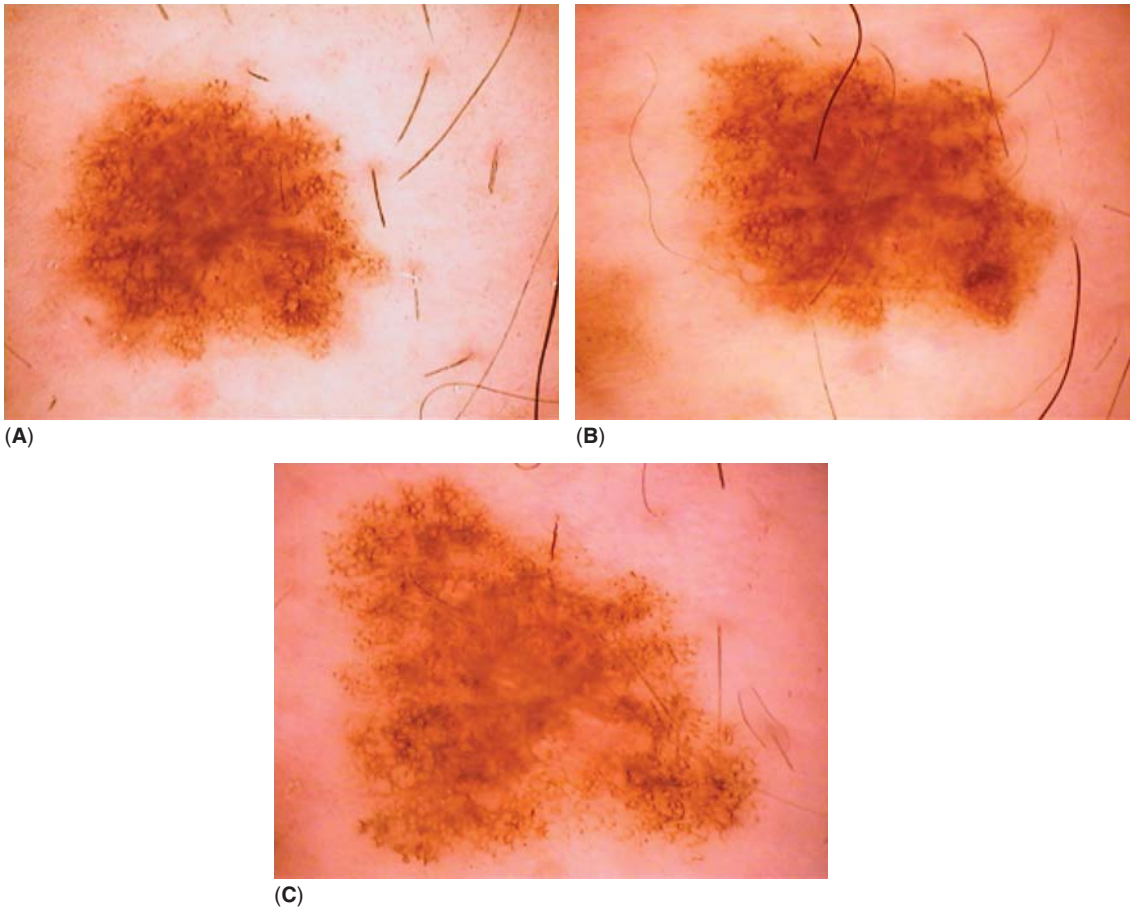


Figure 14.7 (**A–C**) Asymmetrically enlarging melanocytic nevus. These lesions are usually excised to rule out melanoma. (**A**) Baseline image; (**B**) one-year followup; (**C**) two-year followup.

The Risks and the Benefits of Followup

In a study by our group, digital dermoscopic monitoring of melanocytic skin lesions was compared against standard decision-making without the possibility of followup (Kittler & Binder, 2001). The study was designed to simulate a dermatologist's decision-making process in the following situations:

- without the possibility of followup
- with the possibility of followup, and
- after presentation of followup images.

Interestingly, with the possibility of followup using digital dermoscopic monitoring, dermatologists required a higher level of suspicion at the patient's first visit before excising a lesion. In other words, with the knowledge that followup imaging is an option, their sensitivity for melanoma detection decreased at the time of first consultation, which increased the chances of missing a melanoma at the patient's first visit. Not surprisingly, after the presentation of followup images, sensitivity was regained. The availability of followup images substantially improved the detection rate for melanoma while at the same time reducing the excision rate of benign lesions. This study also showed that the utility of sequential imaging critically depends on patient compliance with followup. If the patient does not come back to followup, the loss of sensitivity may prove problematic.

Currently, no prospective study exists that compares the efficacy of wholesale removal of atypical lesions against close followup using digital dermoscopy. Uncritical use of digital dermoscopy therefore cannot be recommended. The indication for followup of melanocytic lesions with digital dermoscopy should be considered carefully, and the potential benefits have to be weighed

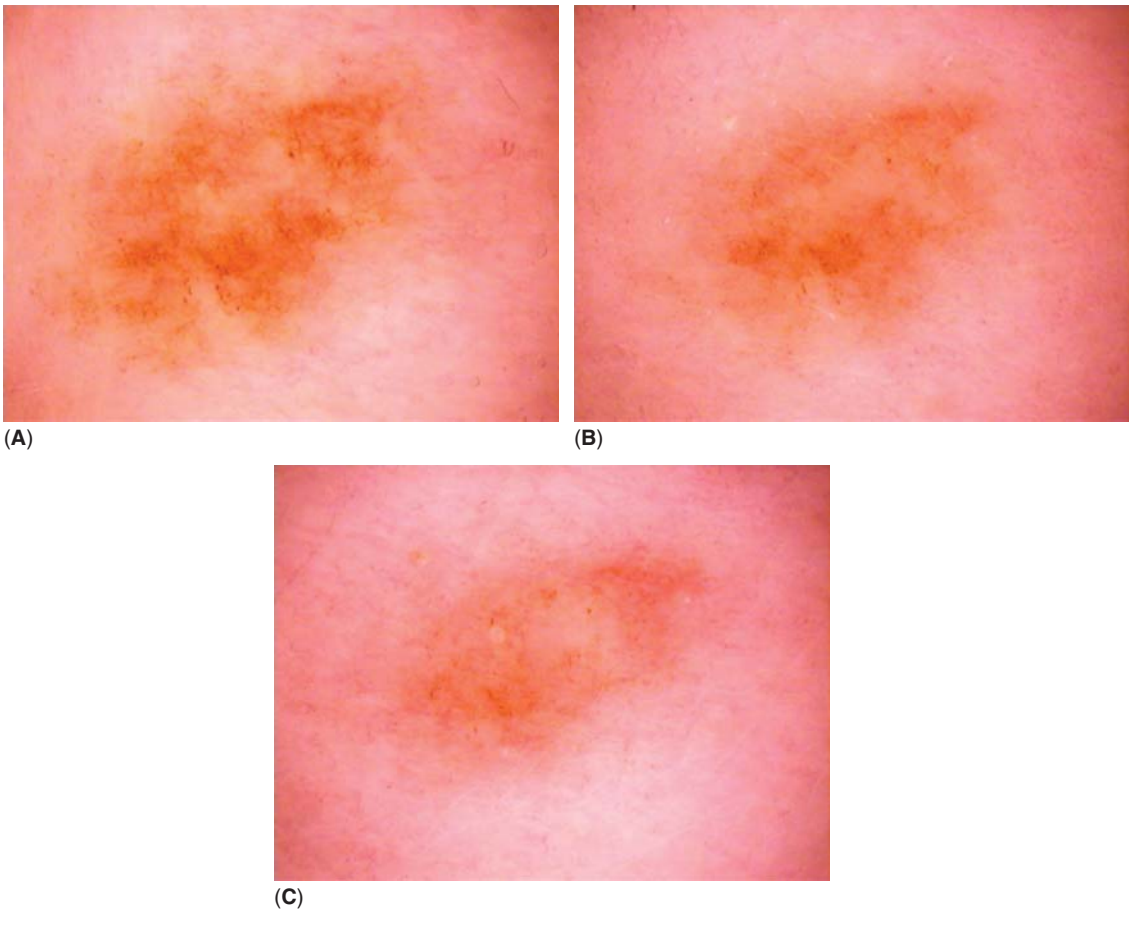


Figure 14.8 (**A–C**): Loss of pigmentation in a melanocytic nevus (involution). (**A**) Baseline image; (**B**) after six months; (**C**) after one year.

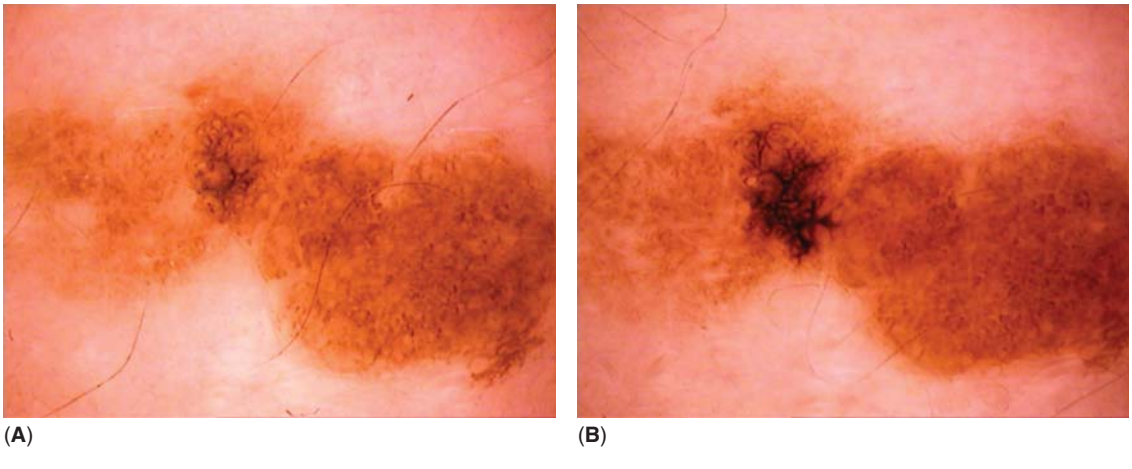


Figure 14.9 (**A, B**) Melanoma in situ arising in a congenital nevus. (**A**) Baseline image; (**B**) after four months.

against the potential risks, including the risk of missing a melanoma at the patient's first visit and the risk of noncompliance of the patient. However, in the common scenario of mildly suspicious nevi, which would normally be observed or excised depending on patient preference, the use of short-term digital monitoring will allow the detection of incipient melanoma in a subset of these lesions, while reducing excisions of benign nevi. In selected patients with numerous doubtful melanocytic lesions, excision of all doubtful lesions might not be feasible. Instead, a close followup with clinical images and digital dermoscopy may be offered, depending on the patient's preferences and the physician's judgment of the patient's compliance.

SUMMARY

1. Digital dermoscopic followup is restricted to flat or slightly raised melanocytic lesions that are only mildly atypical.
2. Any morphologic change seen at three months from baseline (short-term monitoring) requires excision.

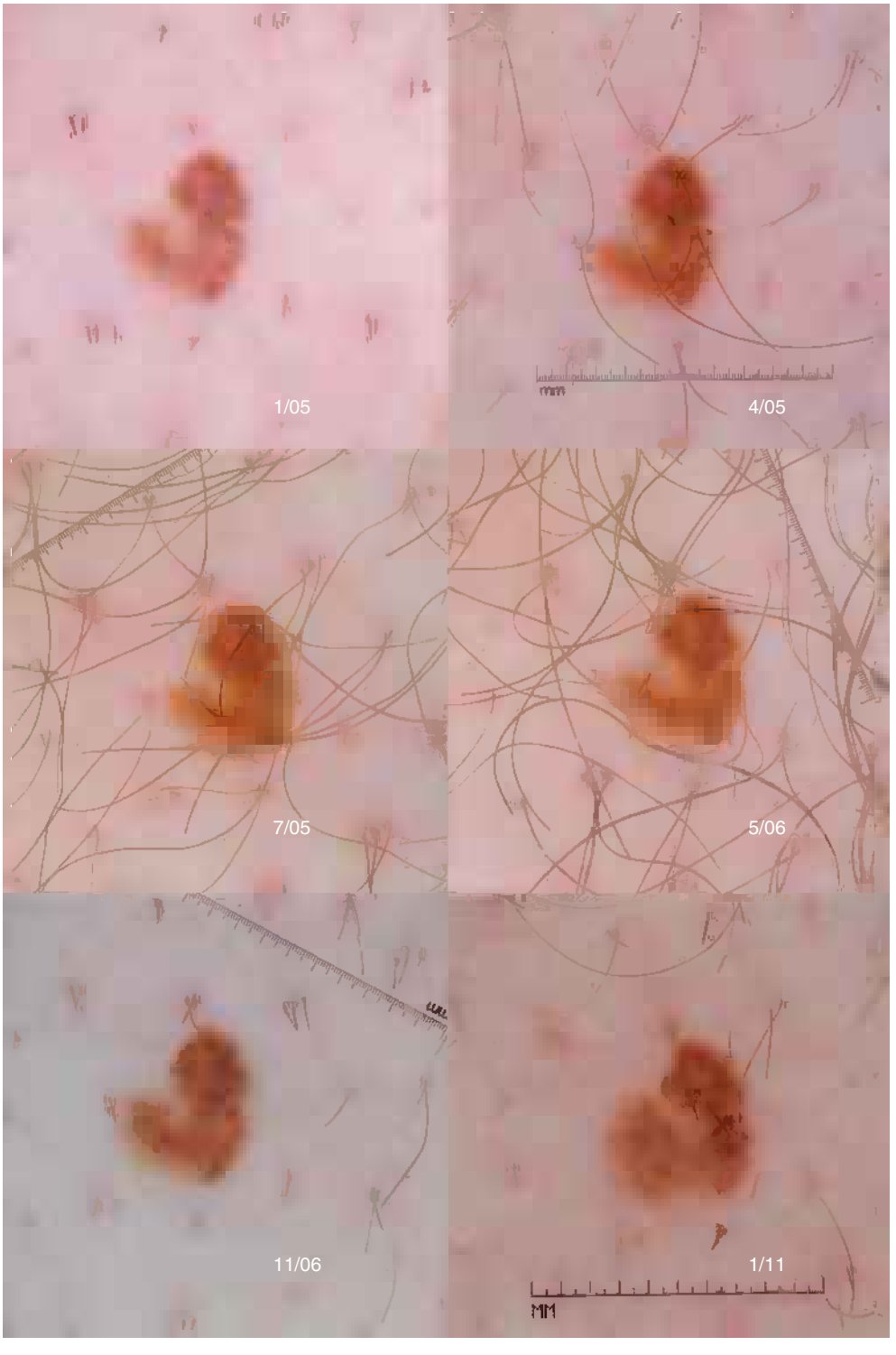


Figure 14.10 Long-term monitoring: this is a lesion that was digitally monitored over six years. This is a slow-growing melanoma manifesting change in shape, size, and color. This lesion was biopsied and was a 0.15 mm thick melanoma.

3. The changes in lentigo maligna melanoma can develop very gradually and thus a longer followup interval is necessary to detect some of these melanomas. We are of the opinion that a 6- to 12-month followup interval will suffice at detecting lentigo maligna.
4. In general, changes are more pronounced during long-term followup.
5. When followup is six months or longer, any lesion with asymmetrical increase in size, appearance of new structures or appearance of new colors requires excision to rule out melanoma (Figs. 14.10, 14.11).

REFERENCES

Altamura, D., Avramidis, M. & Menzies, S.W., 2008, Assessment of the optimal interval for and sensitivity of short-term sequential digital dermoscopy monitoring for the diagnosis of melanoma. *Arch Dermatol*, 144, 502–6.

Altamura, D., Zalaudek, I., Sera, F., et al., 2007, Dermoscopic changes in acral melanocytic nevi during digital follow-up. *Arch Dermatol*, 143, 1372–6.

Argenziano, G., Kittler, H., Ferrara, G., et al., 2010, Slow-growing melanoma: a dermoscopy follow-up study. *Br J Dermatol*, 162, 267–73.

Argenziano, G., Zalaudek, I. & Ferrara, G., 2007, Fast-growing and slow-growing melanomas. *Arch Dermatol*, 143, 802–3; author reply 803–4.

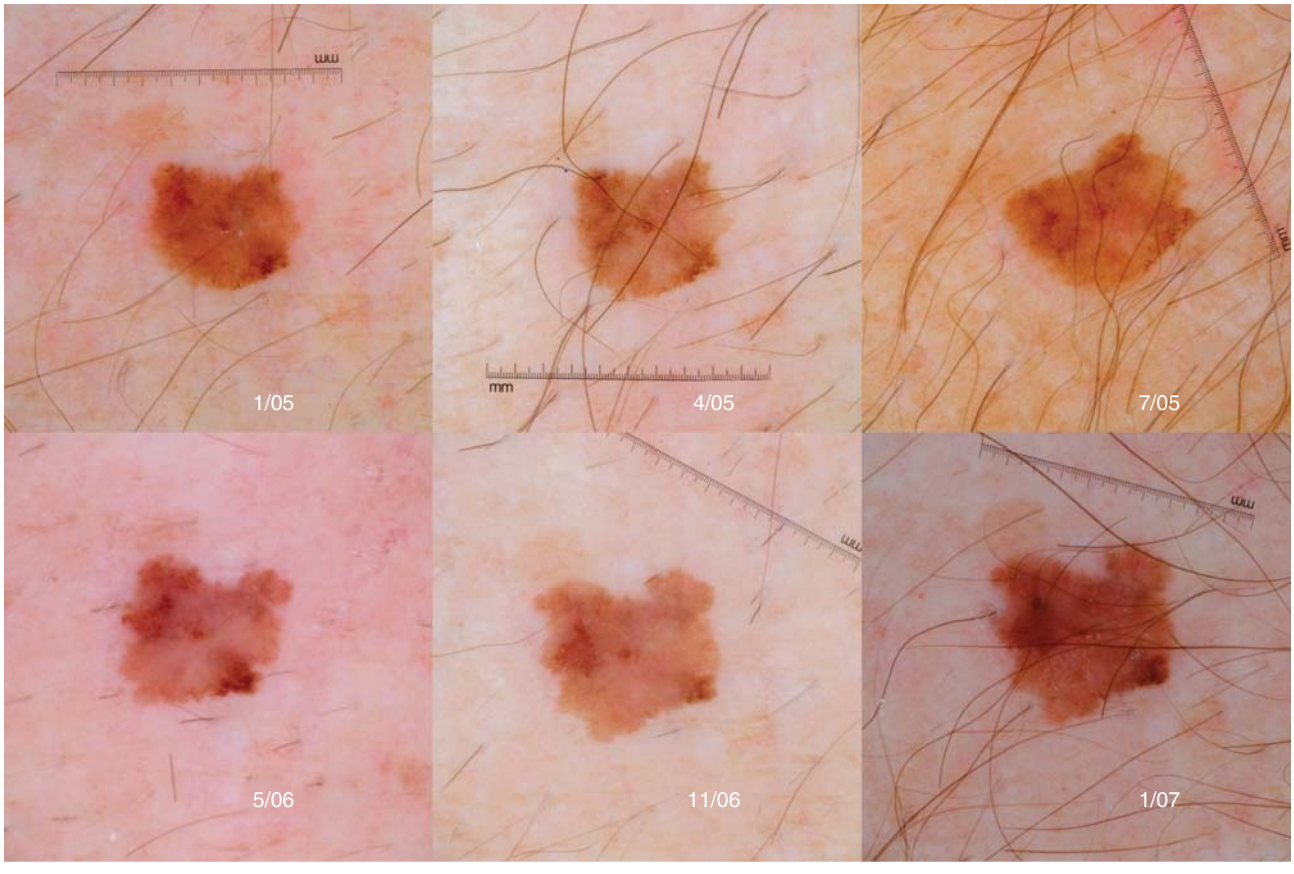


Figure 14.11 Long-term monitoring: This slow-growing melanoma was digitally monitored for two years. Concern for melanoma was obvious at the first three months monitoring interval but the patient refused to have the lesion biopsied. Notice that there are marked changes in size, shape, and color. The lesion has also developed changes in dermoscopic structures. This lesion was eventually biopsied and was a 0.2 mm melanoma. This lesion and the one in figure 14.10 highlight that a delay in diagnosis does not necessarily equate with a worse prognosis.

Banky, J.P., Kelly, J.W., English, D.R., Yeatman, J.M. & Dowling, J.P., 2005, Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. *Arch Dermatol*, 141, 998–1006.

Bauer, J., Blum, A., Strohhäcker, U. & Garbe, C., 2005, Surveillance of patients at high risk for cutaneous malignant melanoma using digital dermoscopy. *Br J Dermatol*, 152, 87–92.

Dawid, M., Pehamberger, H., Wolff, K., Binder, M. & Kittler, H., 2002, Evaluation of the ability of patients to identify enlarging melanocytic nevi. *Arch Dermatol*, 138, 984–5.

Fuller, S.R., Bowen, G.M., Tanner, B., Florell, S.R. & Grossman, D., 2007, Digital dermoscopic monitoring of atypical nevi in patients at risk for melanoma. *Dermatol Surg*, 33, 1198–206; discussion 1205–6.

Haenssle, H.A., Krueger, U., Vente, C., et al., 2006, Results from an observational trial: digital epiluminescence microscopy follow-up of atypical nevi increases the sensitivity and the chance of success of conventional dermoscopy in detecting melanoma. *J Invest Dermatol*, 126, 980–5.

Kittler, H. & Binder, M., 2001, Risks and benefits of sequential imaging of melanocytic skin lesions in patients with multiple atypical nevi. *Arch Dermatol*, 137, 1590–5.

Kittler, H. & Binder, M., 2002, Follow-up of melanocytic skin lesions with digital dermoscopy: risks and benefits. *Archives of Dermatology*, 138, 1379.

Kittler, H., Guitera, P., Riedl, E., et al., 2006, Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. *Arch Dermatol*, 142, 1113–19.

Kittler, H., Pehamberger, H., Wolff, K. & Binder, M., 2000a, Follow-up of melanocytic skin lesions with digital epiluminescence microscopy: patterns of modifications observed in early melanoma, atypical nevi, and common nevi. *J Am Acad Dermatol*, 43, 467–76.

Kittler, H., Seltenheim, M., Dawid, M., et al., 2000b, Frequency and characteristics of enlarging common melanocytic nevi. *Arch Dermatol*, 136, 316–20.

Menzies, S.W., Gutenev, A., Avramidis, M., Batrac, A. & McCarthy, W.H., 2001, Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. *Arch Dermatol*, 137, 1583–9.

Robinson, J. & Nickoloff, B., 2004, Digital epiluminescence microscopy monitoring of high-risk patients. *Arch Dermatol*, 140, 49–56.

Schiffner, R., Schiffner-Rohe, J., Landthaler, M. & Stolz, W., 2003, Long-term dermoscopic follow-up of melanocytic naevi: clinical outcome and patient compliance. *Br J Dermatol*, 149, 79–86.

Terushkin, V., Dusza, S.W., Scope, A., et al., 2012, Changes observed in slow-growing melanomas during long-term dermoscopic monitoring. *Br J Dermatol*, 166, 1213–20.

Zalaudek, I., Karin, S., Marghoob, A., et al., 2011, Frequency of dermoscopic nevus subtypes by age and body site: a Cross-sectional Study. *Arch Dermatol*, 147, 663–70.

15 Teledermoscopy and computer-assisted diagnosis

Dougal F. Coates and H. Peter Soyer

TELEMEDICINE AND TELEDERMATOLOGY

Telemedicine is the transfer of medical information through the use of telecommunication technologies with the goal of optimizing diagnosis, treatment, and teaching, and is a well-recognized and established facet of modern medicine.

Although the term was first coined in 1970 (Wurm et al., 2008), doctors have long taken advantage of new and novel forms of communication; Wilhelm Einthoven, inventor of the electrocardiogram (ECG), created the telecardiogram to monitor ECGs from a distance. In the 1950s, closed-circuit TV allowed doctors to conduct interviews with psychiatric patients from a remote location. As 21st century society becomes increasingly interconnected through technical advances, dermatology, perhaps the most visual of medical specialties, is uniquely positioned to take advantage of this field of medicine.

Teledermatology is a subcategory of telemedicine that has only recently evolved. Perednia and Brown (1995), responding to a lack of regional dermatologists, first used teledermatology in rural Oregon in 1995. Zelicksin and Homan (1997) studied the diagnostic capabilities of teledermatology on 29 nursing home patients in Minneapolis, and found a concordance of 88% between face-to-face and teledermatology. Subsequent to this early experience, teledermatology has become far more widespread, and provides an invaluable resource for a wide range of doctors and their patients, most notably in restricted areas with a paucity of dermatologists.

TELEDERMOSCOPY

Dermoscopy (dermoscopy, epiluminescence microscopy, and surface microscopy) is a noninvasive, in vivo technique, which allows the clinician to examine morphologic features not evident with naked-eye examination. It is proved to be a more accurate tool in the diagnosis of melanoma than naked-eye examination (Vestergaard et al., 2008).

Teledermoscopy represents a rapidly developing field of teledermatology, allowing a remote teleconsultant to give an opinion through "store and forward" or less commonly "real-time systems." Teledermatology has limitations that are not restrictive to teledermoscopy, such as a preference for 3D over 2D images, the importance of patient history and total body assessment, and the aid of palpation in face-to-face consultation (Warshaw et al., 2011). Ultimately, a large number of patients would also prefer to see a dermatologist in person rather than have a teledermatology consultation (Williams et al., 2001). Teledermoscopy has the potential for greater patient acceptance in this regard, as rather than replacing the traditional consultation and doctor–patient interaction, it simply provides an avenue for diagnostic assistance for beginner dermoscopists or in difficult cases.

As a product of the quality of captured images, ease of transmitting teledermoscopic photos, and the recent emergence of this field, a number of active discussion forums have materialized in which inquisitive doctors and interested experts come together to discuss diagnoses and dermoscopic concepts. Examples of more active forums include the following:

- http://www.dermoscopy-ids.org/discussion
- http://www.dermoscopyatlas.blogspot.com
- http://dermoscopic.blogspot.com

EQUIPMENT

Digital dermoscopic images are obtained through the use of a digital consumer camera with a special lens or adaptor, and it is a simple matter to send these images through secure email or other techniques to experts in a remote location. Essentially any practitioner with a computer, internet, and email access, and compliant dermoscope/digital camera has the facility to participate in teledermoscopy. Some systems allow the additional feature of computer-assisted diagnosis (Fig. 15.1; Table 15.1). More recent devices are equipped with built-in color calibration, an important component of interpretation and diagnosis.

An email is typically sent in response by the teleconsultant within 24 h, offering their provisional diagnosis, any differential diagnoses, and a preferred course of action. Thus the interaction is not burdened by different time zones or the time restraints of a busy practice.

EXPERIENCE

In 1998, Provost and colleagues concluded that an accurate diagnosis was possible by compressing digital dermoscopic images and transmitting them over telephone lines (Provost et al., 1998).

Piccolo et al. (2000) later found a diagnostic concordance of 91% when comparing teleconsultation *versus* face-to-face diagnosis of pigmented skin tumors. Interestingly, the concordance did not depend on whether the diagnosis was correct. In other words, when the face-to-face diagnosis was missed, the telediagnosis was also missed. In another study of 43 pigmented skin lesions (Piccolo et al., 1999), the diagnostic accuracy of teledermoscopy varied from 77% to 95% (mean, 85%) and was congruent with the intrinsic level of diagnostic difficulty of the lesion and the experience of the teleconsultant.

OBSTACLES AND CONCERNS

Crucial to the progression of all facets of telemedicine is an acceptance of the increasing "mechanization" that it represents. This concern is counterbalanced by the convenience of a rapid service, especially in remote areas, a lower cost of consultation, and in the case of teledermoscopy, equivalent diagnostic capabilities.

In a nurse-led study on teledermatology by Williams et al. (2001), 93% of surveyed patients were happy with the teleconsultation, and 86% found it more convenient than attending an outpatient clinic.

Although there has been no comparable research on teledermoscopy, one may expect equivalent if not superior patient approval given most requests follow a face-to-face consultation with a dermatologist. In addition, teledermoscopy typically represents an "expert opinion" on a discrete lesion rather than a generalist's opinion on a more widespread problem.

It should also be noted that technologic advancements and a "computerization" of interpersonal relationships is not restricted to medicine and is inherent in 21st century society. Although generational gaps exist within this cultural re-orientation, its ongoing development and acceptance paves the way for the smoother transition of all forms of telemedicine, including teledermoscopy.

Good diagnosticians in dermatology inherently appreciate subtle morphologic patterns and variations, and one would expect a lack of uniformity in the recording, storing, or transmission of teledermoscopic images to have a negative impact on concordance with face-to-face diagnosis. However, Piccolo demonstrated in two studies (Piccolo et al., 1999; Piccolo et al., 2000) that diagnostic accuracy was independent of image quality. Massone et al. examined the potential of melanoma screening using two-megapixel phone-cameras (Massone et al., 2007), and found that despite the images being captured by directly applying a cellular phone on a pocket dermoscope, only 2/18 had suboptimal image quality with the potential to influence telediagnosis.

Despite these early findings, the ultimate goal is clearly standardization of image documentation and transmission. Until such a point is reached, however,

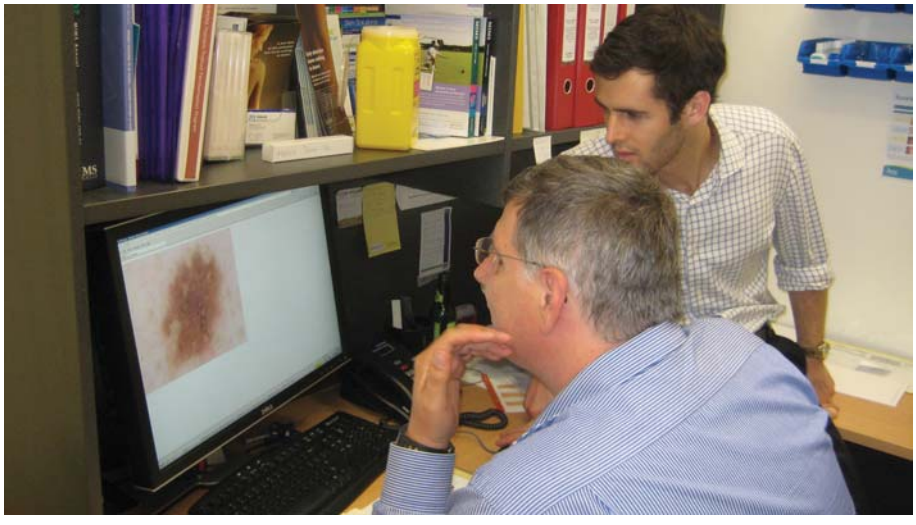


Figure 15.1 The authors discuss an equivocal melanocytic lesion sent for teleconsultation.

Table 15.1 Dermoscopic Devices with the Added Features of Digital Image Capture and Analytic Algorithms

Device Name[a]	Function	Company	Website
DB-Dermo Mips	ANN and "similarity" classifier	Biomips srl	www.skinlesions.net
DermoGenius Ultra	ABCD-characteristics and Digital Standardized Dermatologic Point Score	BIOCAM GmbH	www.biocam.de
Fotofinder Dermoscope	Comparison with a reference bank	TeachScreen Software	www.fotofinder.de
Melafind	Multispectural image analysis and comparison with a reference bank	Electro-Optical Sciences	http://www.melasciences.com/
MicroDerm	DANAOS–ANN classifier	VisioMED	www.visiomedag.com
Molemax III	ABCD and 7-point score	Derma Medical Systems	www.dermamedicalsystems.com

Clinical and dermoscopic digital image capture for all instruments.
[a]Device names are registered trademarks.
Abbreviation: ANN, artificial neural network.

the current standing parallels that in dermatopathology, whereby the teleconsultant has the right to reject a consult based on its poor quality, but once that image has been accepted and an opinion given, the teleconsultant assumes complete responsibility. The latest generation of devices have built-in color calibration, which may go a long way to solving this problem.

As an evolving field, the legislature surrounding teledermoscopy is nebulous and without precedent. It is not yet established whether malpractice insurance for a dermatologist includes work as a teledermoscopist. In addition, if professional licensure is required it remains unclear if that covers all countries or just the teleconsultant's country of practice. Further confusion surrounds whether legal responsibility in the case of misdiagnosis or management lies with the referring doctor or the teleconsultant, and if the teleconsultant is found to be negligent are they charged in their own country or that of the patient.

All these questions assume, however, that foreign governments would even permit overseas consultants to receive and respond to teledermoscopic images, as inherent in any countries' medical legislature is an attempt to protect citizens from underqualified and incompetent doctors. Perhaps facilitating a worldwide acceptance is the understanding that teledermoscopy is currently only undertaken by world-recognized experts in the field, in addition to the well-established precedent in medicine and dermatology, whereby world experts commonly give opinions requested from overseas consultants on challenging cases.

In the author's opinion, licensure is only likely to be required in the country the teleconsultant practices, but the teleconsultant will hold the primary duty of care regarding the diagnosis and management of the referred lesion. All legal issues become increasingly relevant in teledermoscopy, as consultations are stored and easily tracked.

To date, most teledermoscopy projects have been pilot studies or between friends, and resultantly lacked financial reimbursement. An important question remains the degree, if any, a government would subsidize such a service, particularly if the teleconsultant were not a citizen of that country, as well as whether the teleconsultant would receive a fixed rate per image or a percentage of the consultation fee.

Finally, concern exists for protecting patient data and images, given that these are transmitted during a teleconsultation and international standards, such as encryption protocols are yet to be defined.

With the aforementioned issues taken into account there are now a few professional nurse-led teledermoscopy services provided worldwide. Patients can go to one of these teledermoscopy centers, get all their nevi imaged, have the images analyzed by a dermoscopy expert, and have the expert render an opinion on each lesion. In addition, patients can re-visit the center at a future date and have their lesions re-imaged. The teledermoscopist now has the added advantage of being able to evaluate the sequential dermoscopy images of the patient's nevi. The report issued by the expert tele-dermoscopist can be sent to the patient or referring physician. Currently these centers are: MoleMap in New Zealand and Australia (http://www.molemap. co.nz/ and http://www.molemap.net.au/), MoleSafe in the United States of America (http://www.molesafe. com/) and MoleClinic in the United Kingdom (http://www.themoleclinic. co.uk).

Furthermore, it is the opinion of the editors that it is only a matter of time before Apps and inexpensive iPhone dermoscopy attachments will

become available that will permit patients to take dermoscopy images of their own lesions and submit them for analysis to a tele-dermoscopy center. The diffusion and acceptance of this technology is likely to happen at a rapid pace over the next few years.

FUTURE DIRECTION

The diagnostic accuracy of dermatopathology has been shown to be improved by focusing the pathologist's attention toward clinically suspicious areas of the lesion (Soyer, 2000). An exciting area thus exists whereby a clinician could send a specimen accompanied by a teledermoscopic image, perhaps with an attached comment indicating a particular focus of concern. A dermatopathologist with training in dermoscopy could then compile a dermoscopic–pathologic report with correlates, and include the original dermoscopic image on paper adjacent to the report. In the author's opinion this represents an exciting opportunity for teaching and reflection in concert with improved diagnosis.

CONCLUSION

The progressive subspecialization of medicine and concentration of experts in fewer medical centers, juxtaposed to an increasingly litigious society and enhanced public awareness of skin cancer and melanoma, has meant that general practitioners are dealing with increased numbers and adopting a more cautious approach in the diagnosis of pigmented skin lesions. Resultantly, they may be more likely to seek a second opinion for diagnosis and management by utilizing a teledermoscopy service.

Teledermoscopy, based on two-dimensional images and being introduced in an ever expanding and accepting technologic society, represents an ideal referral pathway to meet this need.

Perhaps the greatest barrier to establishing a worldwide teledermoscopic network lies in the complicated legal issues. Patient acceptance of teledermoscopy is also yet to be established, and issues, such as data protection and financial reimbursement are evolving. Nonetheless, teledermoscopy is simple, convenient, and has proven diagnostic capabilities, with the potential for both optimizing patient outcome and also teaching/upskilling of referring clinicians, and is likely to occupy a reliable place in armamentarium of future clinical practice.

Computer-Assisted Diagnosis

Dermoscopic evaluation, despite the "repetitive" morphologic structures of lesions and refinement of diagnostic criteria, is at times subtle and a highly subjective field. The complexity of patterns and their interpretation becomes particularly challenging for beginners and the untrained (Piccolo et al., 2002). With the consequences of misdiagnosing melanocytic lesions so severe, a strong interest in objective analysis and subsequent enhanced diagnostic accuracy has seen the emergence of digital image analysis systems, or computer-assisted diagnosis.

Numerous digital analysis systems have been developed by different groups over the last two decades (Blum, 2008). These systems extract lesions from background skin and make an analysis based on colors, hue, texture, symmetry, border regularity, diameter, perimeter, length, and area. Unfortunately, comparing the results achieved by each system is difficult given

- A lack of standardized calibration and different recording systems
- Insufficient lesion numbers to permit proper statistical analysis
- Different data sets, that is, variations in melanocytic: nonmelanocytic lesions, benign: malignant tumors, or difficult/histopathologically equivocal lesions (Spitz nevi, severely dysplastic nevi, and so on)
- Varying median Breslow's tumor thickness of melanomas
- Nondisclosure of diagnostic algorithms
- No cross-analysis of image sets by different approaches

Nevertheless, the results of these studies suggest that computer-assisted diagnosis is at least equivalent to the clinical and dermoscopic accuracy (sensitivity and specificity) obtained by a trained expert in dermoscopy (Blum, 2008).

An interesting concept is that of different automated systems to match the clinical application of each device. If a system is to be used in a general setting by a nonexpert user (shopping center/pharmacy/general practitioner), it should operate at very high sensitivity so that malignant lesions are not missed. The same system may prove to be redundant to an experienced dermoscopist, who may prefer a system with a higher specificity or one that is able to distinguish atypical benign lesions from malignant tumors.

Some of the dermoscopic devices with added features of digital image capture and analytic algorithms are shown in Table 15.1.

PROS AND CONS

It is unlikely that a digital image analysis system will ever completely replace an expert in dermoscopy; however, several advantages exist including

- Objective extraction of a lesion from surrounding skin
- Diagnosis uninfluenced by different levels of attention
- Diagnostic accuracy comparable to human experts (Blum, 2008; Rosado, 2003).
- Diagnosis available without intervention of an expert
- Utilization of data by clinicians to enhance visually recognizable criteria
- Reassurance for anxious patients and untrained doctors

Offsetting some of these advantages include drawbacks, such as

- The application of any diagnostic system relies on some degree of discretion in terms of potential for malignancy
- Time and cost involved in documenting and analyzing numerous lesions
- Atypical lesions (Spitz nevi, seborrheic keratoses, atypical nevi) easily diagnosed by a good dermatologist, can be missed by analyzing systems
- Additional criteria (subtle clinical history, ugly duckling sign, and others) not accounted for in computer analysis.

CONCLUSION

Computer-assisted diagnosis is an exciting new area of development in dermoscopy. The specifications, standardization, and accuracy of systems are yet to be properly established, as is the role of these devices in variable clinical settings. Although they are likely to make a significant contribution to clinicians, both expert and beginner, it is doubtful whether they would ever assume a role above that of a "double-check" system (diagnostic aid). However, we remain open-minded and welcome the invention of a completely automated diagnostic system (diagnostic test) to help differentiate skin cancer from benign lesions with a high degree of accuracy.

REFERENCES

Blum, A., Zalaudek, I. & Argenziano, G., 2008, Digital image analysis for diagnosis of skin tumours. *Semin Cutan Med Surg*, 27, 11–15.

Massone, C., Hofmann-Wellenhof, R., Ahlgrimm-Siess, V., et al., 2007, Melanoma screening with cellular phones. *PloS One*, 5, e483.

Perednia, D.A. & Brown, N.A., 1995, Teledermatology: one application of telemedicine. *Bull Med Libr Assoc*, 83, 42–7.

Piccolo, D., Ferrari, A., Peris, K., et al., 2002, Dermoscopic diagnosis by a trained clinician vs. a clinician with minimal dermoscopy training vs. computer-aided diagnosis of 341 pigmented skin lesions: a comparative study. *Br J Dermatol*, 147, 481–6.

Piccolo, D., Smolle, J., Argenziano, G., et al., 2000, Teledermoscopy – results of a multicentre study on 43 pigmented skin lesions. *J Telemed Telecare*, 6, 132–7.

Piccolo, D., Smolle, J., Wolf, I.H., et al., 1999, Face-to-face diagnosis vs telediagnosis or pigmented skin tumours: a teledermoscopic study. *Arch Dermatol*, 135, 1467–71.

Provost, N., Kopf, A.W., Rabinovitz, H.S., et al., 1998, Comparison of conventional photographs and telephonically transmitted compressed digitised images of melanomas and dysplastic naevi. *Dermatology*, 196, 299–304.

Rosado, B., Menzies, S., Harbauer, A., et al., 2003, Accuracy of computer diagnosis of melanoma: a quantitative meta-analysis. *Arch Dermatol*, 129, 361–7.

Soyer, H.P., Kenet, R.O., Wolf, I.H., et al., 2000, Clinicopathological correlation of pigmented skin lesions using dermoscopy. *Eur J Dermatol*, 10, 22–8.

Vestergaard, M.E., Macaskill, P., Holt, P.E., Menzies, S.W., 2008, Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. *Br J Dermatol*, 159, 669–76.

Warshaw E.M., Hillman, Y.J., Greer, N.L., et al., 2011, Teledermatology for diagnosis and management of skin conditions: a systematic review. *J Am Acad Dermatol*, 64, 759–72.

Williams, T., May, C., Kelly, S., et al., 2001, Patient satisfaction with store-and-forward technology. *J Telemed Telecare*, 7, 45–6.

Wurm, E., Hofmann-Wellenhof, R., Wurm, R., et al., 2008, Telemedicine and teledermatology: Past, present, and future. *JDDG*, 6, 106–1.

Zelicksin, BD. & Homan L., 1997, Teledermatology in the nursing home. *Arch Dermatol*, 133, 171–4.

16 Beyond dermoscopy

Natalia Jaimes-López and Allan C. Halpern

The need for more sensitive and reliable diagnostic methods for skin cancer has resulted in the proliferation of noninvasive in vivo imaging techniques. Some of the newer and more sophisticated methods, such as high-frequency ultrasonography, optical coherence tomography, spectrophotometry, and confocal scanning laser microscopy (CSLM) offer interesting prospects as research tools and aids for the early detection of melanoma. In this chapter, we review the basic concepts and developments on these imaging techniques, with special emphasis on confocal microscopy.

ULTRASONOGRAPHY

Ultrasound scanning has entered the domain of clinical dermatology in recent years. It was first shown in 1979 to be useful in determining skin thickness. Ultrasonography is based on the generation of ultrasonic waves by an ultrasonic transducer that transforms an electrical current into mechanical vibration. Vibrations are then transmitted and propagated in the form of an ultrasonic wave. Ultrasonic waves are partially reflected at an interface separating two media of different acoustic impedance (Jasaitiene et al., 2011). It is a safe and relatively cheap technology that is well tolerated by patients.

Ultrasound images can be presented in three different modes: one-dimensional A-scan mode, which measures the skin thickness; two-dimensional B-scan mode, which captures a cross-sectional view of the skin and is useful in clinical dermatology and dermatological research (Fig. 16.1); and three-dimensional C-scan mode, which is helpful for the reconstruction of tumors (Jasaitiene et al., 2011).

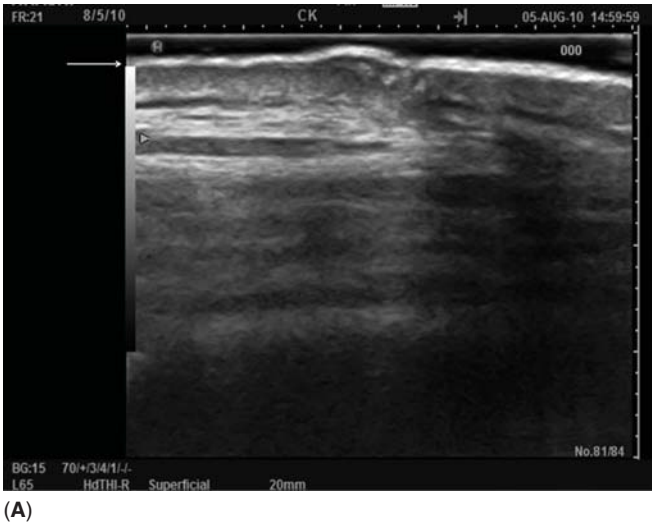
Higher frequencies provide better resolution but have reduced ability to penetrate deeper into the tissue. Scanners utilizing a frequency of 7.5 MHz probe up to a depth of 7 cm, 2–3 cm for 10 MHz scanners, and 7 mm for 20 MHz scanners (Wang et al., 2004). Currently, ultrasound frequencies of 7.5–15 MHz are used to examine lymph nodes and soft tissue tumors (Jasaitiene et al., 2011), to direct fine-needle biopsy and detect subclinical recurrences in the followup of melanoma patients. (Dill-Muller & Maschke, 2007) It is a helpful method in discriminating between lymph node and soft tissue metastases from other subcutaneous masses. Moreover, additional important information on the vascularization patterns in lymph nodes can be obtained with color-Doppler ultrasonography to help distinguish between benign and malignant lymphadenopathy (Dill-Muller & Maschke, 2007).

The frequency of transducers used in the evaluation of skin structures operate in the 20–100 MHz range (Jasaitiene et al., 2011). The most commonly used frequency for skin imaging is between 20 and 25 MHz. Scanners at this frequency allow visualization of the epidermis, dermis, and subcutaneous fat (Schmid-Wendtner & Burgdorf, 2005).

High-frequency ultrasonography is indicated in the study of skin layers, including epidermis, dermis, and hypodermis. In addition, it has been used for the assessment of pigmented and nonpigmented tumors, for preoperative and postoperative evaluation of skin tumors and for monitoring treatment responses (Badea et al., 2010). A group of investigators recently reported on the ability to predict with high reliability the thickness of invasive melanoma using 75 MHz ultrasonography (Guitera et al., 2008). However, given that most skin tumors appear as hypoechoic areas in comparison with the surrounding hyperechoic dermis, ultrasonography alone is not helpful in differentiating benign from malignant pigmented skin lesions (Fig. 16.1) (Dill-Muller & Maschke, 2007).

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) imaging is based on the principle of low-coherence interferometry. Infrared light (900–1500 nm) is delivered to the imaging site through a single-mode optical fiber. The signals that are generated from the interference of the reflected light and a reference beam are recorded from different tissue depths as the incident light scans across the tissue (Olmedo et al., 2006). Thus, measurement of the interference pattern allows to determine the position of tissue components, such as cell membranes, collagen, and melanin, which provide the



(**A**)

(**B**)

Figure 16.1 (**A**) A 14–16 MHz ultrasound image of a seborrheic keratosis (center of the image in the region of the epidermis). Hyperechoic horizontal line representing the interface between the gel pad and stratum corneum (*arrow*). The basement membrane is represented by a hyperechoic line, which is parallel and inferior to the aforementioned interface. The region between both hyperechoic horizontal lines represents the epidermis. The hypoechoic area under the dermis represents subcutaneous fat. (**B**) A 14–16 MHz ultrasound image of a pilar cyst appearing as a relatively hypoechoic lesion. The small areas of hyperechogenicity in the center of the lesions represent calcification. The hyperechoic region deep inferior to the lesion, which is parallel to the epidermis represents the trabecular bone of the skull.

contrast in the images (Tadrous, 2000). OCT is similar to ultrasound in that it can provide two-dimensional images of the epidermis and dermis (Fig. 16.2). Cross-sectional images of the skin can be obtained with a high spatial resolution of 15 μm (Welzel et al., 1997). The most recent machines can penetrate a depth of 2–4 mm. First introduced to noninvasively examine lesions in the human eye, OCT offers promise in the noninvasive diagnosis of skin cancer. OCT, however, did not allow examination of single cells or subcellular structures. Olmedo et al. (2006) investigated OCT for the characterization of basal cell carcinoma (BCC). Forsea et al. investigated the utility of OCT for the diagnosis of nonmelanocytic lesions, including BCC, Kaposi sarcoma, actinic keratoses, squamous cell carcinomas, and seborrheic keratoses, and concluded that OCT is a valuable technique for in vivo diagnosis of early neoplastic cutaneous lesions with equivocal clinical and/or dermoscopic aspect (Forsea et al., 2010).

Considered to be more suitable than high-frequency ultrasound for the study of the epidermis and dermoepidermal junction, OCT also allows a simple and quick measurement of epidermal thickness and a quantitative assessment of skin appendages. OCT equipment is still very costly compared with other techniques, and therefore only available in very few centers. The major limitation of OCT is the impossibility to obtain information on the cellular level, the limited penetration depth and the field size (Fig. 16.2) (Forsea et al., 2010).

SPECTROPHOTOMETRY

Spectrophotometric analysis of the skin involves the measurement of radiation reflected from the skin after being illuminated with light in the visible and infrared spectrum (400 nm) (Aspres et al., 2003). Spectrophotometric intracutaneous analysis (SIA) is a technique for imaging pigmented skin lesions that employs a device named the SIAscope. The SIAscope analyses the reflected light and generates high-resolution images (SIAscans) that provide information regarding the concentration and distribution of collagen, blood, and melanin within the epidermis and papillary dermis (Fig. 16.3) (Moncrieff et al., 2002).

Moncrieff et al. (2002) performed the first clinical trial with SIAscopy and reported a sensitivity of 83% and a specificity of 80% for melanoma. SIAscopy features that were found to be highly reproducible and reliable were presence of dermal melanin, collagen holes (signifying papillary dermal invasion), and erythematous blush with blood displacement (representing local vasodilatation and fibrosis during early dermal invasion and displacement of blood from the papillary dermis later). When used by clinical nurse specialists as a screening tool for pigmented lesions, the SIAscope had a sensitivity of 94.4% and a false-negative rate of 3.7% for melanoma (Fig. 16.3).

The SIAscope has also been applied to the study of nonmelanoma skin cancer (NMSC). In one prospective study involving a referred population, Tehrani et al. (2006) reported that the technique had a sensitivity of 98% and a specificity of 95.7%. Through the recognition of branched vessels, paleness, and vascular flare, NMSC can be diagnosed with an overall accuracy of 98.2%. The same group also reported that the sensitivity and specificity of the SIAscope were comparable with that of a hospital specialist, suggesting that the use of the SIAscope could reduce the number of unnecessary biopsies performed while maintaining a high NMSC identification rate. However, Terstappen and colleagues analyzed 22 pigmented BCCs with SIAScope and dermoscopy; with the aim of evaluating whether or not SIAScopy was useful in diagnosing pigmented BCC. From their results, the authors stated that SIAScopy does not have any advantage over dermoscopy when evaluating BCC; therefore, it cannot be used as a tool to differentiate pigmented BCC from melanoma (Terstappen et al., 2007).

CONFOCAL SCANNING LASER MICROSCOPY

CSLM is a novel imaging tool that permits the real-time examination of the skin at a resolution approaching histologic detail. Among the imaging techniques described, CSLM offers the best resolution for the in vivo analysis of cutaneous pathology.

Core Principles

Figure 16.4 shows a schematic view of a confocal microscope. Confocal microscopy involves the use of a point source of light focused tightly on a specific point in the skin. Only the light returning from the point of focus is collected and used to form an image. By moving the beam horizontally a raster of points are collected to construct horizontal microscopic sections. Repeating the process focused at different depths within the skin results in vertical stacks of horizontal images (Aspres et al., 2003). The backscattering of light, primarily the result of differences in the refractive indices of different structures and variations in the size of tissue components, imparts the bright contrast in confocal images. Cells that contain melanin and melanosomes appear bright in confocal microscopy (Rajadhyaksha et al., 1995).

The commercially available confocal microscope employs a low power (<30 mW) near-infrared 830 nm diode laser and a 30 ×, 0.9-numerical aperture water immersion objective lens that provides a lateral resolution of 1–2 μm and axial resolution of 3–5 μm. The maximum penetration depth of the confocal microscope is about 150–350 μm, allowing imaging from the surface of the skin to the papillary or upper reticular dermis (Rajadhyaksha et al., 1999).

While conventional histology yields 5 μm-thick vertical sections of the skin, confocal microscopy produces horizontally oriented optical images less than 5 μm in thickness. Confocal images hence closely match the resolution of conventional histology taken in the horizontal plane provided the presence of adequate contrast in the tissue under study (Lieb et al., 2008).

Cellular elements of melanocytic lesions are also identifiable under confocal microscopy (Fig.16.6) (Busam et al., 2001a). Melanocytes may appear as bright round to oval or dendritic cells. They can occur as solitary units or as nests at the dermoepidermal junction or dermis. Pigmented

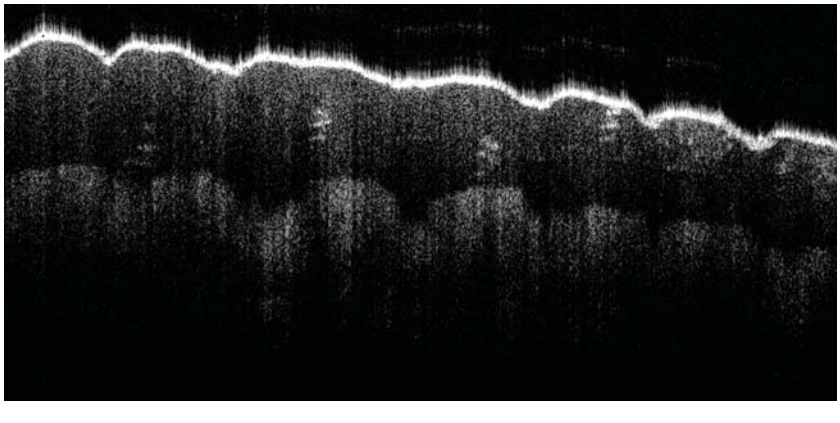


Figure 16.2 Optical coherence tomography image of normal skin of the dorsal finger.

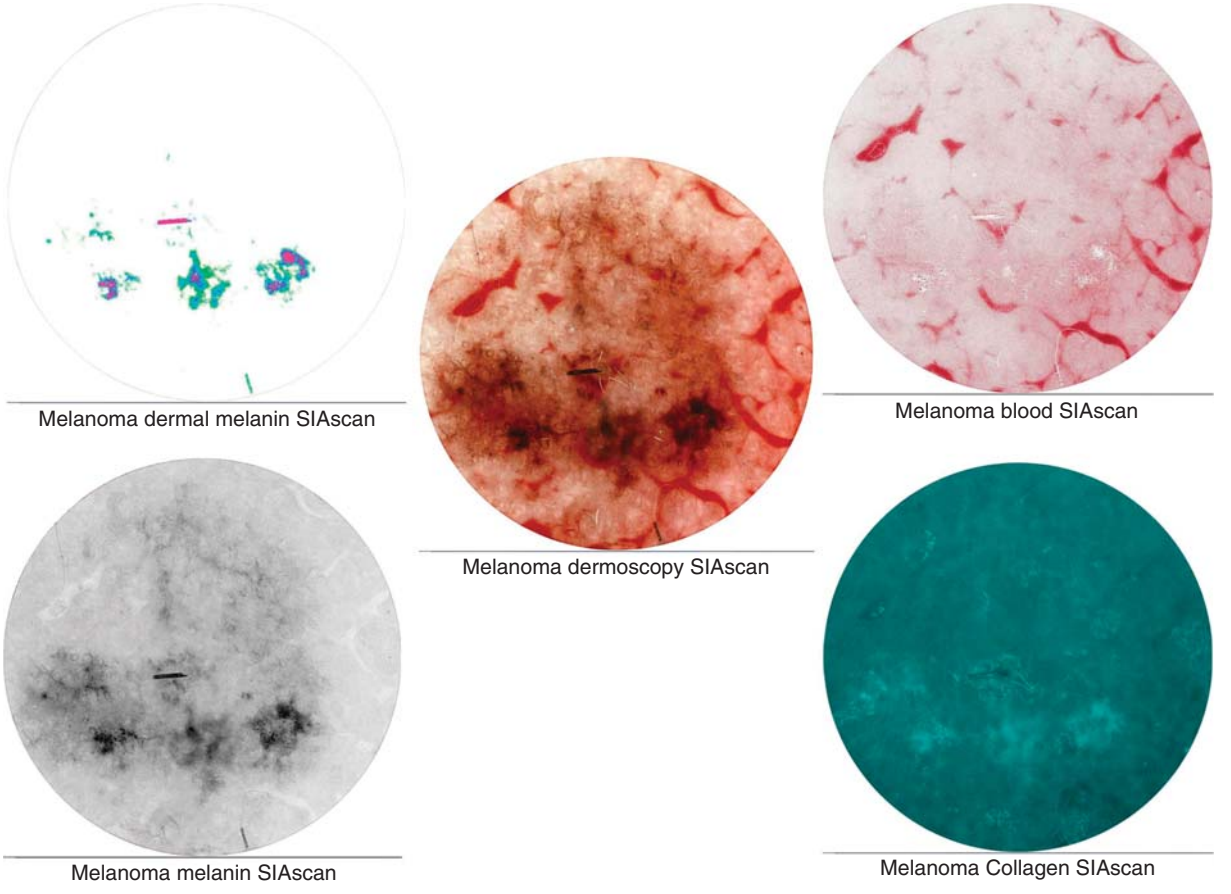


Figure 16.3 The SIAscans around the central dermoscopic image of a melanoma: blood, collagen, melanin, and dermal melanin.

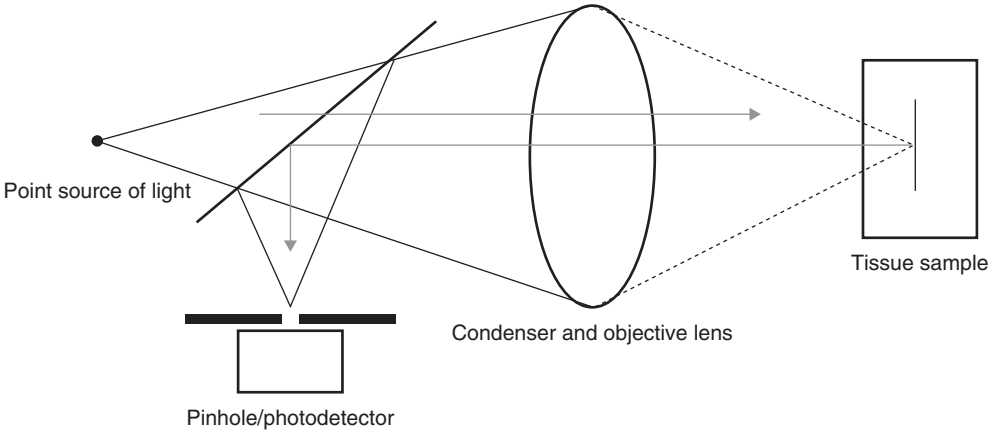


Figure 16.4 Schematic diagram of confocal scanning laser microscopy. Only light returning from the point of focus is collected and used to form an image.

keratinocytes are visible as polygonal cohesive cells with variably bright granular cytoplasms. Melanophages are usually located within the dermal papillae and appear as solitary or loosely aggregated oval or stellate cells with coarse, granular cytoplasms (Fig. 16.5).

In the field of melanocytic lesions, dermoscopic structures and global dermoscopic patterns can be precisely correlated with confocal images (Pellacani et al., 2005, Scope et al., 2007). Langley et al. examined 125 lesions of melanocytic nevi and melanomas to determine the diagnostic accuracy of confocal microscopy compared with dermoscopy. The sensitivity of confocal microscopy was higher than that of dermoscopy but the specificity was similar. The investigators further observed that combining the two methods improved the diagnostic accuracy for melanoma (Langley et al., 2007). Conversely, Guitera and colleagues evaluated 306 pigmented lesions (203 nevi and 123 melanomas) with CSLM and dermoscopy. The authors demonstrated that sensitivity was similar with both techniques (91% and 88%, respectively); but specificity for the diagnosis of melanoma was superior with CSLM when compared with dermoscopy (68% *vs* 32%, respectively). In addition, CSLM improved the diagnostic accuracy of light-colored lesions, with a specificity of 84% (Guitera et al., 2009).

The confocal features of benign nevi and melanomas have been studied, enabling a more accurate diagnosis of melanoma. Six criteria that were strongly correlated with a diagnosis of melanoma: nonedged dermal papillae, cytologic atypia at the basal cell layers, pagetoid cells, widespread

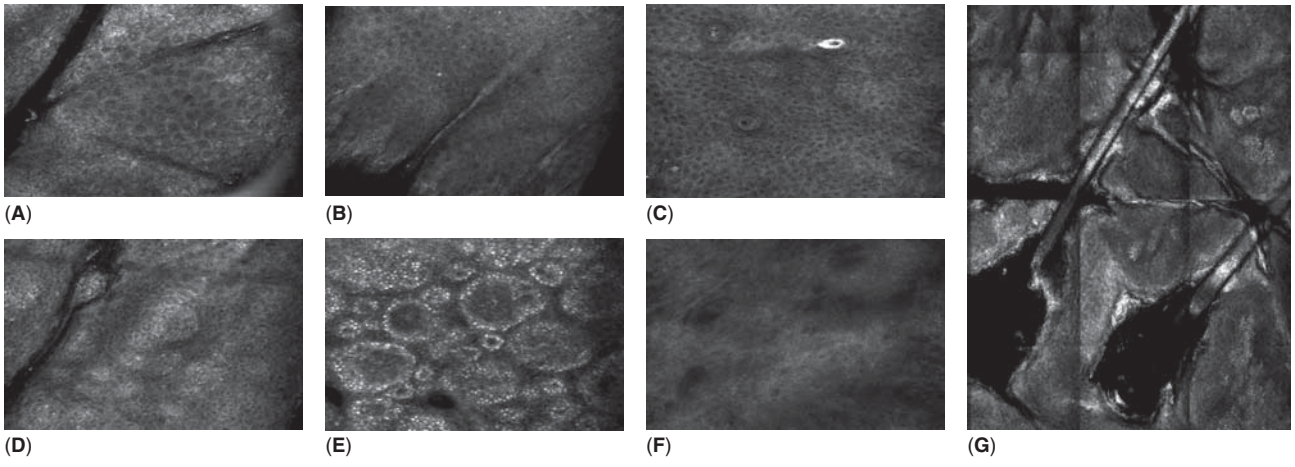


Figure 16.5 Confocal scanning laser microscopy images of normal skin. (**A**) Stratum corneum. (**B**) Stratum granulosum. (**C**) Stratum spinosum. (**D**) Stratum basale. (**E**) Dermoepidermal junction. (**F**) Dermis. (**G**) Pilosebaceous unit.

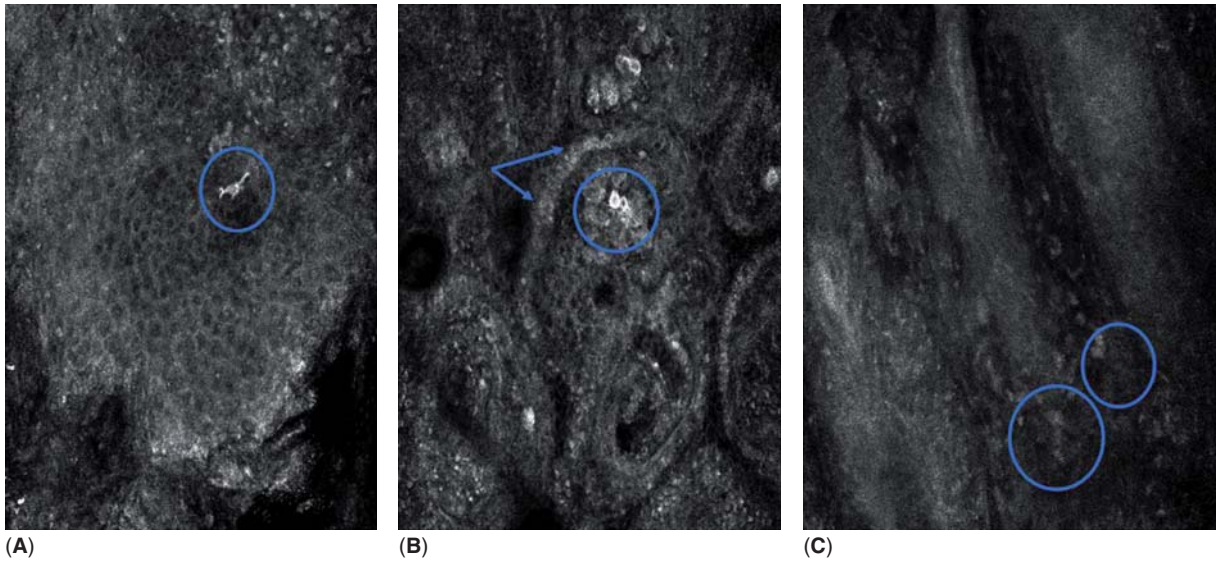


Figure 16.6 Confocal scanning laser microscopy images of cellular elements of melanocytic lesions. (**A**) Dendritic melanocytes. (**B**) Round melanocytes (*circle*) and pigmented keratinocytes (*arrows*). (**C**) Melanophages.

pagetoid infiltration, isolated nucleated cells within the dermal papilla, and cerebriform clusters (Pellacani et al., 2008). Moreover, CSLM can be used to differentiate lentigo maligna from other pigmented skin lesions on the face. As a result, Guitera and colleagues proposed a simplified score algorithm for lentigo maligna based on six features, which demonstrated a sensitivity of 93% and a specificity of 61% when the score was of 1 or more, and even a higher specificity (82%) when the threshold was of 2 or more points (Fig. 16.6) (Guitera et al., 2010).

Confocal microscopy has also been used to define surgical margins of lentigo maligna melanomas (Marghoob & Halpern, 2005), although the peripheral lentigo maligna margins are completely amelanotic (Guitera et al., 2010); BCCs, squamous cell carcinomas (Rajadhyaksha et al., 2001), and amelanotic melanomas (Busam et al., 2001b). By determining the extent of the tumor before excision, CSLM-guided presurgical mapping helps to avoid subjecting a patient to multiple-staged excisions. The technique has also been employed ex vivo during Mohs surgery to detect residual tumor cells.

The major limitation of confocal microscopy is the depth of penetration and variable contrast of tissue elements across lesions and patients. Imaging is generally limited to the level of the superficial dermis, and in hyperkeratotic lesions this imaging depth is often compromised. The current bulky version of the contact device makes the imaging of uneven surfaces difficult (Gonzalez et al., 2003). Development of a more manageable hand-held device and expansion of the technology to allow for the production of vertical and three-dimensional sections are underway.

In summary, confocal microscopy is a promising technique in the early detection of skin cancer, which has shown to improve the diagnostic accuracy for melanocytic lesions that are difficult to diagnose (Pellacani et al., 2007). Additionally, CSLM may enhance the secondary evaluation of melanocytic lesions that appear to be clinically and dermoscopically suspicious (Guitera et al., 2009; Pellacani et al., 2007). It has several research and clinical applications and may conceivably bridge the gross clinical and histopathologic evaluation of skin lesions.

ACKNOWLEDGMENTS

Biocompatibles UK Ltd for the Siascan image. Nicusor Iftimia and Mircea Mujat at Physical Sciences Inc., Boston, MA, for the optical coherence tomography image. Bahar Dasgeb, MD, for the ultrasound images.

REFERENCES

Aspres, N., Egerton, I.B., Lim, A.C. & Shumack, S.P., 2003, Imaging the skin. *Australas J Dermatol*, 44, 19–27.

Badea, R., Crisan, M., Lupsor, M. & Fodor, L., 2010, Diagnosis and characterization of cutaneous tumors using combined ultrasonographic procedures (conventional and high resolution ultrasonography). *Med Ultrason*, 12, 317–22.

Busam, K.J., Charles, C., Lee, G. & Halpern, A.C., 2001a, Morphologic features of melanocytes, pigmented keratinocytes, and melanophages by in vivo confocal scanning laser microscopy. *Mod Pathol*, 14, 862–8.

Busam, K.J., Hester, K., Charles, C., et al., 2001b, Detection of clinically amelanotic malignant melanoma and assessment of its margins by in vivo confocal scanning laser microscopy. *Arch Dermatol*, 137, 923–9.

Dill-Muller, D. & Maschke, J., 2007, Ultrasonography in dermatology. *J Dtsch Dermatol Ges*, 5, 689–707.

Forsea, A.M., Carstea, E.M., Ghervase, L., Giurcaneanu, C. & Pavelescu, G., 2010, Clinical application of optical coherence tomography for the imaging of nonmelanocytic cutaneous tumors: a pilot multi-modal study. *J Med Life*, 3, 381–9.

Gonzalez, S., Swindells, K.J., Rajadhyaksha, M. & Torres, A., 2003, Changing paradigms in dermatology: confocal microscopy in clinical and surgical dermatology. *Clin Dermatol*, 21, 359–69.

Guitera, P., LI, L.X., Crotty, K., et al., 2008, Melanoma histological Breslow thickness predicted by 75-MHz ultrasonography. *Br J Dermatol*, 159, 364–9.

Guitera, P., Pellacani, G., Crotty, K.A., et al., 2010, The impact of in vivo reflectance confocal microscopy on the diagnostic accuracy of lentigo maligna and equivocal pigmented and nonpigmented macules of the face. *J Invest Dermatol*, 130, 2080–91.

Guitera, P., Pellacani, G., Longo, C., et al., 2009, In vivo reflectance confocal microscopy enhances secondary evaluation of melanocytic lesions. *J Invest Dermatol*, 129, 131–8.

Jasaitiene, D., Valiukeviciene, S., Linkeviciute, G., et al., 2011, Principles of high-frequency ultrasonography for investigation of skin pathology. *J Eur Acad Dermatol Venereol*, 25, 375–82.

Langley, R.G.B., Walsh, N., Sutherland, A.E., et al., 2007, The diagnostic accuracy of in vivo confocal scanning laser microscopy compared to dermoscopy of benign and malignant melanocytic lesions: a prospective study. *Dermatology*, 245, 365–72.

Lieb, J.A., Gill, M., Patel, Y.G., Rajadhyaksha, M. & Gonzalez, S., 2008, Normal skin. In: S. Gonzalez, M. Gill, & A.C. Halpern, eds. *Reflectance Confocal Microscopy of Cutaneous Tumors: An Atlas with Clinical, Dermoscopic and Histological Correlations*. UK: Informa.

Marghoob, A.A. & Halpern, A.C., 2005, Confocal scanning laser reflectance microscopy: why bother? *Arch Dermatol*, 141, 212–15.

Moncrieff, M., Cotton, S., Claridge, E. & Hall, P., 2002, Spectrophotometric intracutaneous analysis: a new technique for imaging pigmented skin lesions. *Br J Dermatol*, 146, 448–57.

Olmedo, J.M., Warschaw, K.E., Schmitt, J.M. & Swanson, D.L., 2006, Optical coherence tomography for the characterization of basal cell carcinoma in vivo: a pilot study. *J Am Acad Dermatol*, 55, 408–12.

Pellacani, G., Cesinaro, A.M., Longo, C., Grana, C. & Seidenari, S., 2005, Microscopic in vivo description of cellular architecture of dermoscopic pigment network in nevi and melanomas. *Arch Dermatol*, 141, 212–15.

Pellacani, G., Guitera, P., Longo, C., et al., 2007, The impact of in vivo reflectance confocal microscopy for the diagnostic accuracy of melanoma and equivocal melanocytic lesions. *J Invest Dermatol*, 127, 2759–65.

Pellacani, G., Longo, C., Malvehy, J., et al., 2008, In vivo confocal microscopic and histopathologic correlations of dermoscopic features in 202 melanocytic lesions. *Arch Dermatol*, 144, 1597–608.

Rajadhyaksha, M., Gonzalez, S., Zavislan, J.M., Anderson, R.R. & Webb, R.H., 1999, In vivo confocal scanning laser microscopy of human skin II: advances in instrumentation and comparison with histology. *J Invest Dermatol*, 113, 293–303.

Rajadhyaksha, M., Grossman, M., Esterowitz, D., Webb, R.H. & Anderson, R.R., 1995, In vivo confocal scanning laser microscopy of human skin: melanin provides strong contrast. *J Invest Dermatol*, 104, 946–52.

Rajadhyaksha, M., Menaker, G., Flotte, T.J., Dwyer, P.J. & Gonzalez, S., 2001, Confocal examination of nonmelanoma cancers in thick skin excisions to potentially guide Mohs micrographic surgery without frozen histopathology. *J Invest Dermatol*, 117, 1137–43.

Schmid-Wendtner, M.H. & Burgdorf, W., 2005, Ultrasound scanning in dermatology. *Arch Dermatol*, 141, 217–24.

Scope, A., Benvenuto-Andrade, C., Agero, A.L.C., et al., 2007, Correlation of dermoscopic structures of melanocytic lesions to reflectance confocal microscopy. *Arch Dermatol*, 143, 176–85.

Tadrous, P.J., 2000, Methods for imaging the structure and function of living tissues and cells: 1. Optical coherence tomography. *J Pathol*, 191, 115–19.

Tehrani, H., Walls, J., Price, G., et al., 2006, A novel imaging technique as an adjunct to the in vivo diagnosis of nonmelanoma skin cancer. *Br J Dermatol*, 155, 1177–83.

Terstappen, K., Larko, O. & Wennberg, A.M., 2007, Pigmented basal cell carcinoma–comparing the diagnostic methods of SIAscopy and dermoscopy. *Acta Derm Venereol*, 87, 238–42.

Wang, S.Q., Rabinovitz, H., Kopf, A.W. & Oliviero, M., 2004, Current technologies for the in vivo diagnosis of cutaneous melanomas. *Clin Dermatol*, 22, 217–22.

Welzel, J., Lankenau, E., Birngruber, R. & Engelhardt, R., 1997, Optical coherence tomography of the human skin. *J Am Acad Dermatol*, 37, 958–63.

17 Concluding remarks

Ashfaq A. Marghoob and Natalia Jaimes-López

Dermoscopy provides details regarding the subsurface morphology of skin lesions. Analysis of this morphology leads to an improved clinical diagnostic accuracy. However, it is important to be aware that dermoscopy only provides a two-dimensional image of the lesion in question. As has been shown for melanoma, the final decision regarding the clinical diagnosis and ultimate management rests with more than just the dermoscopic morphology of the lesion seen at one moment in time (Fig. 17.1). In fact, good clinicians utilize multiple snippets of information, and by utilizing deductive reasoning process they arrive at a diagnosis and management opinion. The ultimate decision and threshold to biopsy or not to biopsy a particular lesion is dependent on a host of factors that either increase or decrease the pre-test probability of malignancy. These factors include whether or not the lesion is a:

1. new or symptomatic lesion.
2. changing lesion as determined by long- or short-term digital monitoring.
3. clinical or dermoscopic outlier lesion (ugly duckling).
4. lesion that looks similar to surrounding lesions (moles breed true). This is also known as the comparative approach (Argenziano et al., 2011).
5. lesion with a color and morphology that is congruent with the patient's skin type. Patient's skin type can influence threshold to biopsy. For example, dark melanocytic neoplasm in a fair-skinned individual or a light-colored lesion on dark-skinned individuals.
6. Spitzoid lesion (i.e., starburst pattern) in adults.
7. nevus with peripheral globular patterned in an older individual.
8. new globular nevus in an adult.

With that said, we are hopeful that this atlas will provide a stepping-stone toward becoming better clinicians. Below we provide you with a synopsis of the key points regarding diagnosis and management of skin lesions evaluated with dermoscopy (Figs. 17.2–17.7). Figures 17.2 and 17.3 are a review of the two-step dermoscopy algorithm. The benign nevus patterns are schematically presented in Figure 17.4. The 10 global melanoma-specific structures and management outline for melanocytic lesions is outlined in Figure 17.5. The global melanoma-specific structures can be seen in melanomas located anywhere on the skin. In addition, there are also location-specific melanoma-specific structures found on volar and facial skin and the algorithm for the management of a melanocytic lesion on these niche locations is presented in Figures 17.6 and 17.7.

REFERENCES

Argenziano, G., Catricalà, C., Ardigo, M., et al., 2011, Dermoscopy of patients with multiple nevi: improved management recommendations using a comparative diagnostic approach. *Arch Dermatol*, 147, 46–9.

Marghoob, A.A., Scope, A., 2009, The complexity of diagnosing melanoma. *J lnvest Dermatol*, 129, 11–13.

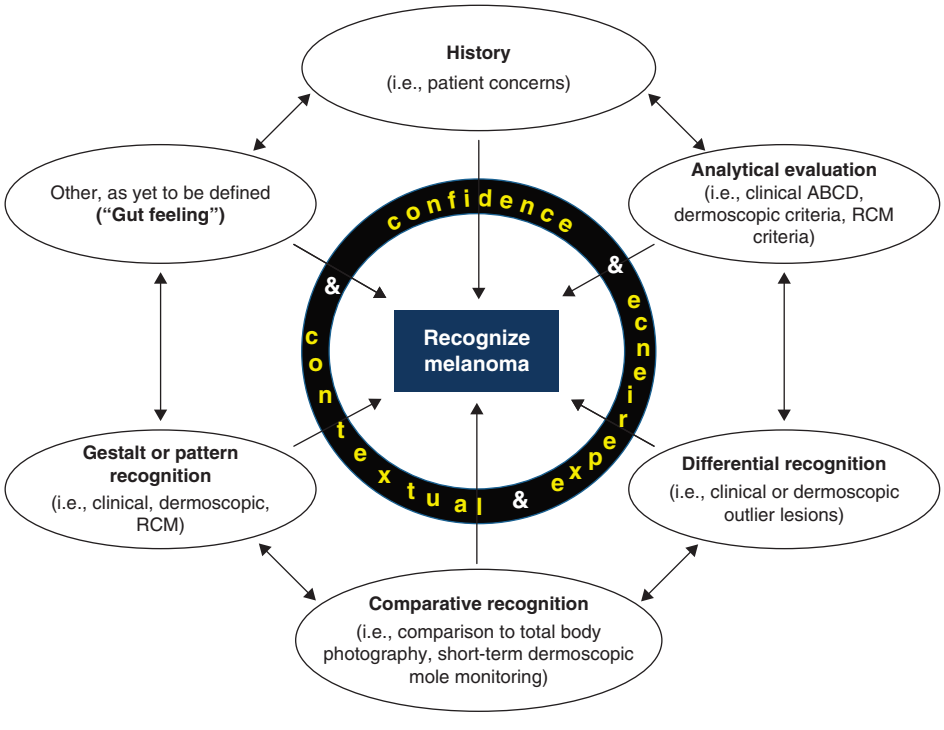


Figure 17.1 Diagnostic decision making-process (Marghoob & Scope, 2009).

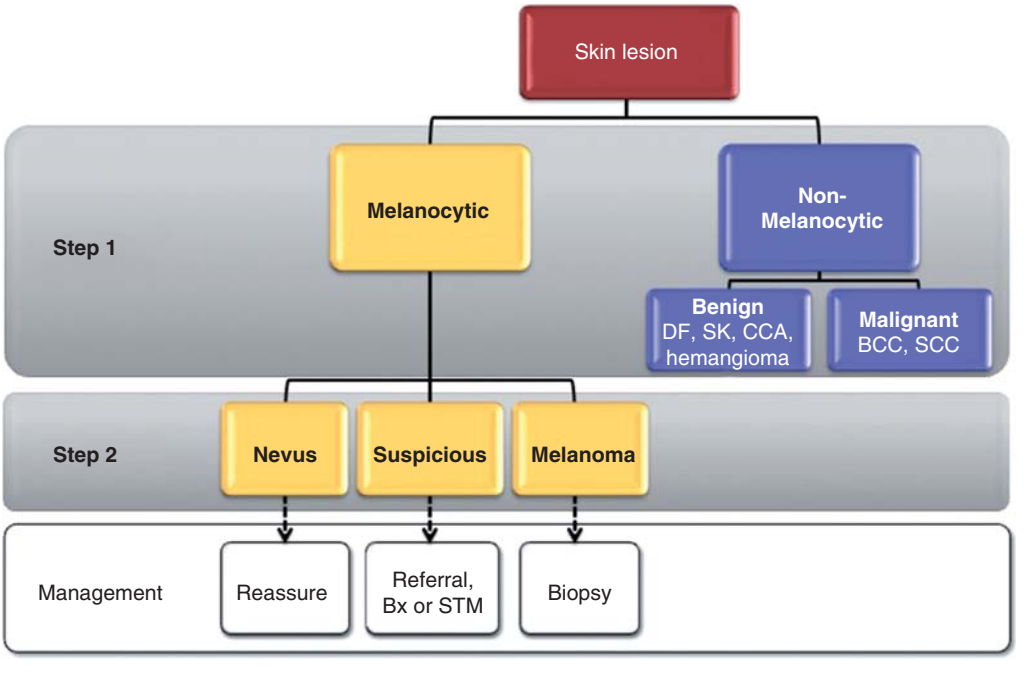


Figure 17.2 The Two Step Algorithm for dermoscopy (concept and design by Ashfaq A. Marghoob, MD and Natalia Jaimes, MD).

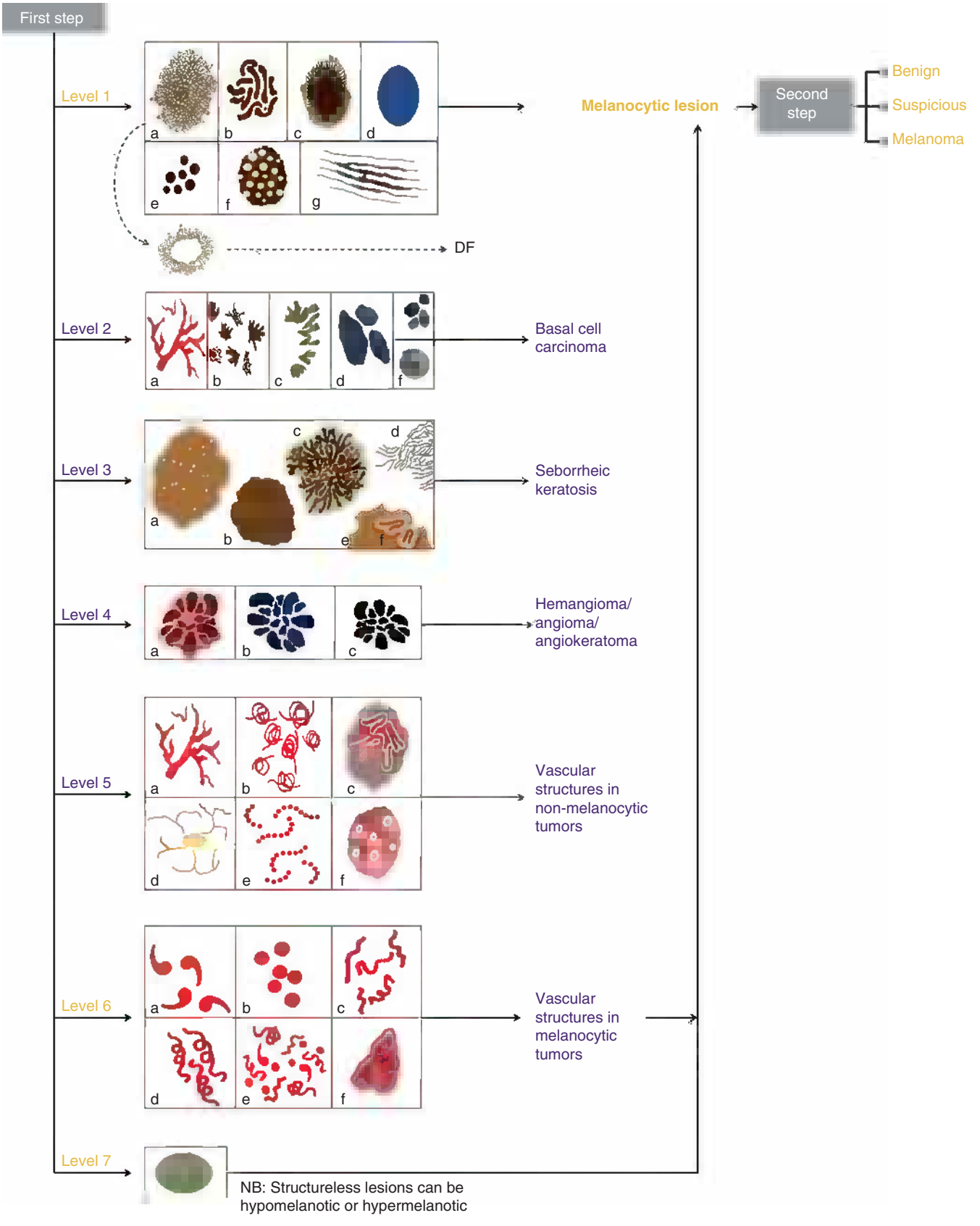


Figure 17.3 Seven-level criteria ladder for the First Step: Melanocytic versus non-melanocytic.

Step 1: Melanocytic versus non-melanocytic lesions						
Level 1: Melanocytic lesions	**Level 2: Basal cell carcinoma (BCC)**	**Level 3: Seborrheic keratosis (SK)**	**Level 4: Hemangioma/ angioma/ angiokeratoma**	**Level 5: Blood vessels in non-melanocytic tumors***	**Level 6: Blood vessels in melanocytic tumors***	**Level 7: Unclassifiable lesions**
a. Pigment network* b. Negative network c. Streaks d. Homogeneous blue pigmentation e. Aggregated globules f. Pseudonetwork (facial skin) g. Parallel pigment pattern (acral lesions) h. * Exception to pigment network: dermatofibroma (DF)	a. Arborizing vessels b. Spoken wheel-like structures/ concentric structures c. Leaf-like areas d. Large blue-gray ovoid nests e. Multiple blue-gray globules f. Ulceration g. Additional clues: shiny white structures	a. Multiple (>2) milia-like cysts b. Comedo-like opening c. Gyri and sulci (fat finger-like structures) d. Fingerprint-like structures e. Moth-eaten borders f. Hairpin vessels with white halo g. Additional features: sharp demarcation; negative wobble sign: the lesion slides	a. Red lacunae b. Blue lacunae c. Black lacunae	**Morphology** a. Arborizing vessels b. Glomerular vessels c. Hairpin vessels with white halo **Arrangement** d. Crown e. Serpiginous or string of pearls f. "Strawberry" pattern g. Focal clusters at the periphery **Distributon** • Focal • Diffuse • Central • Peripheral • Random ***Usually seen in** a. BCC b. Squamous cell carcinoma (SCC) c. SK/ keratoacanthoma d. Sebaceous hyperplasia (SH) e. Clear cell acanthoma (CCA) f. Actinic keratosis	**Morphology** a. Comma vessels b. Dotted vessels c. Serpentine vessels (linear irregular) d. Corkscrew vessels e. Polymorphous vessels f. Milky-red area **Distributon** • Focal • Diffuse • Central • Peripheral • Random ***Usually in** a. Intradermal nevi b. – f. melanoma	**None of the structures from levels 1 to 6 are noted**

Figure 17.3 (*Continued*).

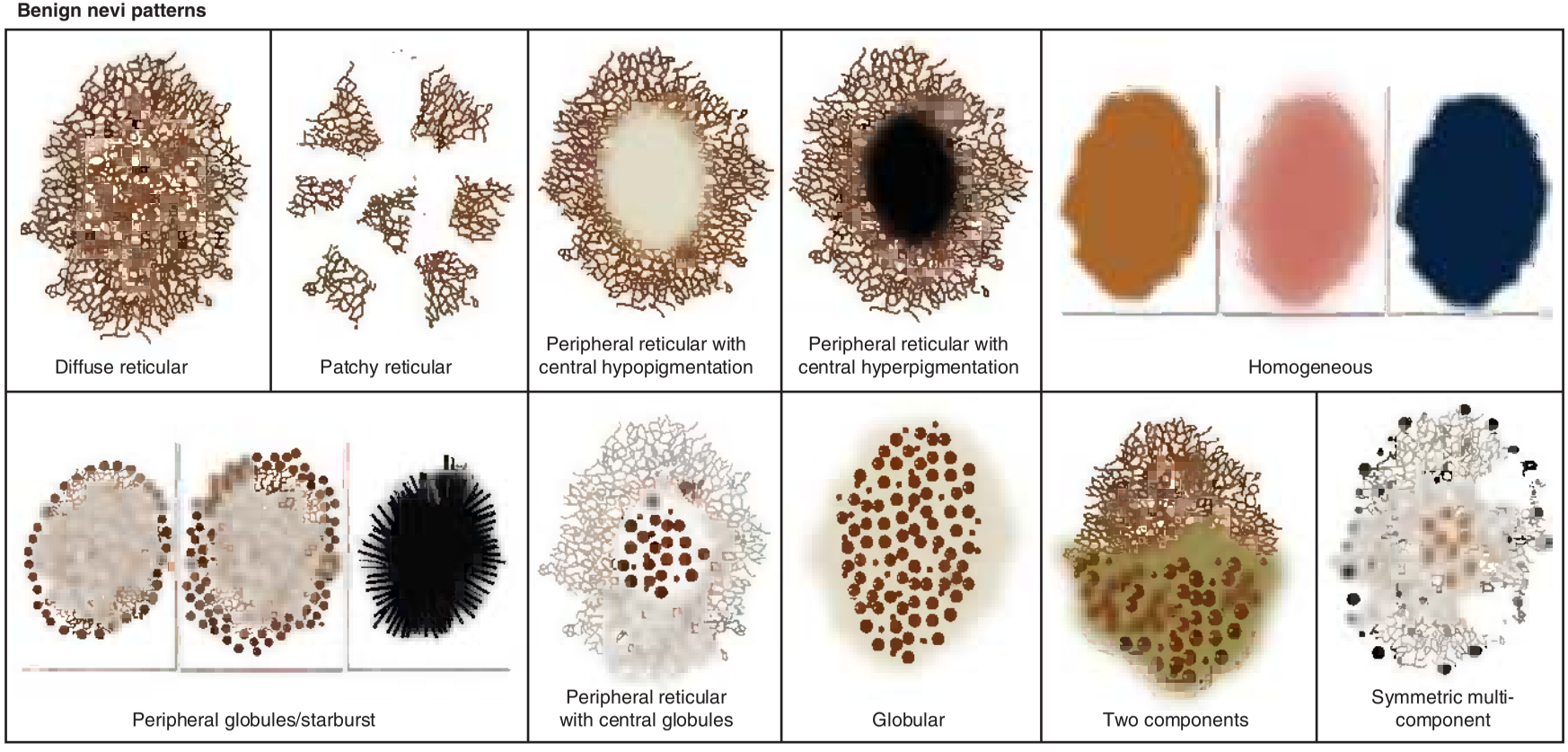


Figure 17.4 Benign nevus patterns.

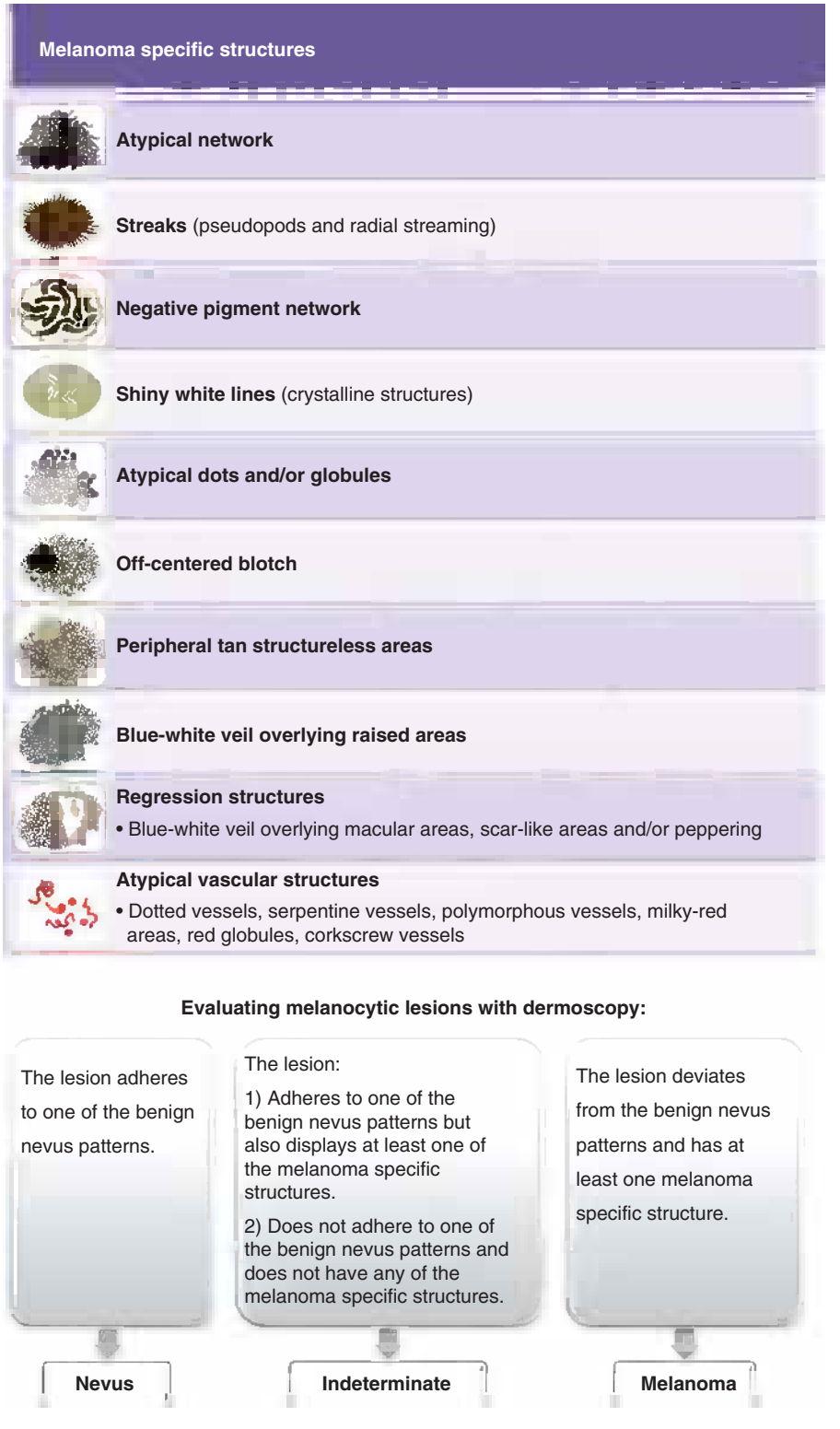


Figure 17.5 Melanoma-specific structures and final decision (benign, suspicious or melanoma) (concept and design by Natalia Jaimes, MD and Ashfaq A. Marghoob, MD).

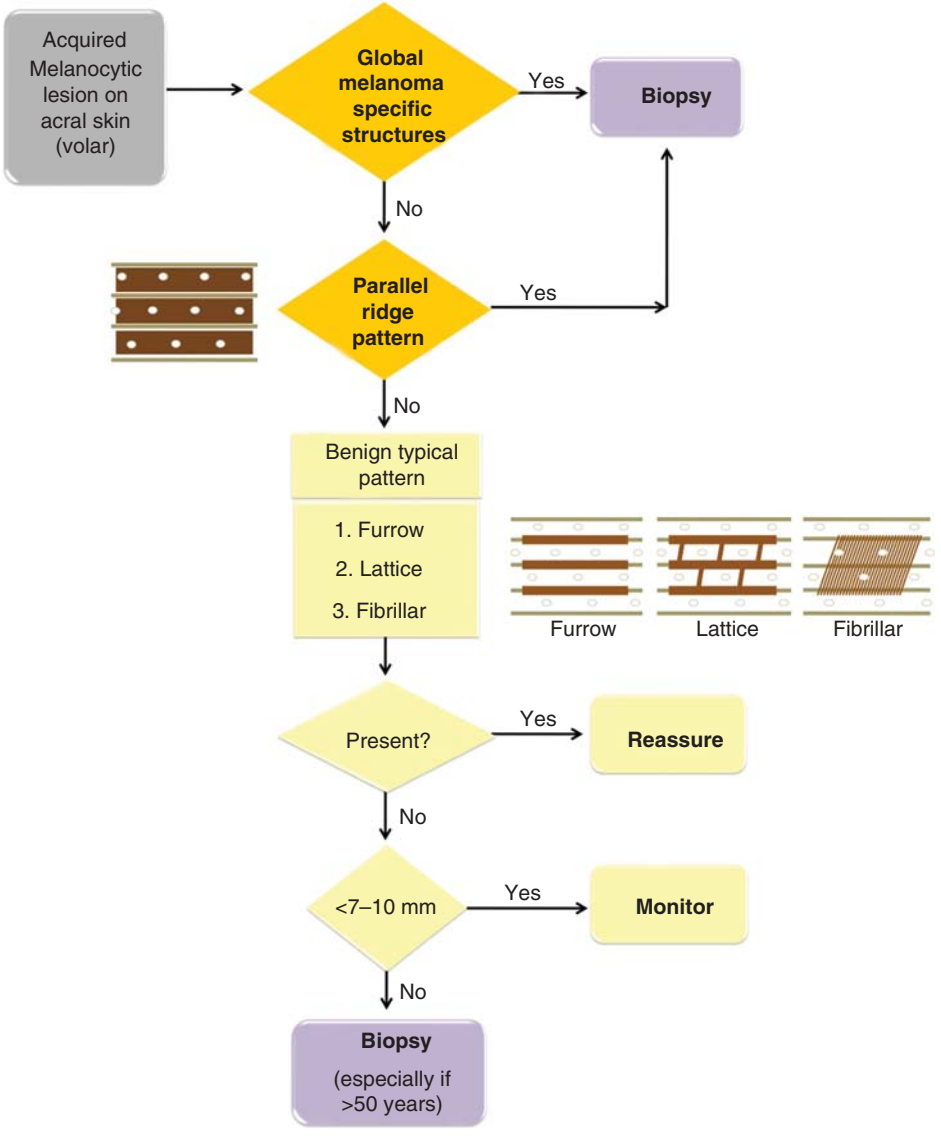


Figure 17.6 Management algorithm for lesions on volar skin (i.e. palms and soles) (concept and design by Ashfiq A. Marghoob, MD and Natalia Jaimes, MD).

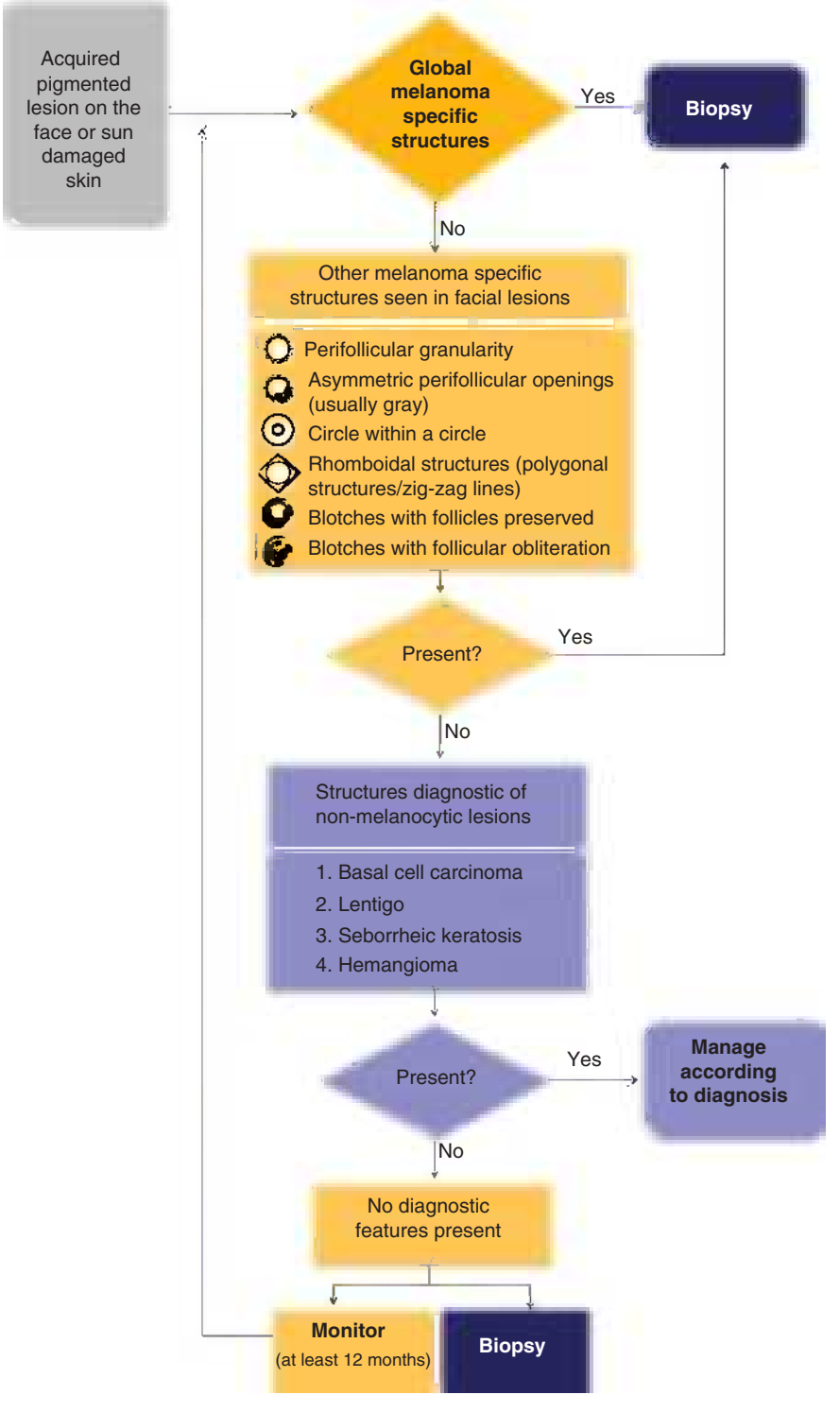


Figure 17.7 Management algorithm for lesions on facial or sun-damaged skin.

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Atlas of Dermoscopy
Second Edition

About the book

Building on a successful first edition, this revised and extended new *Atlas of Dermoscopy* demonstrates the state of the art of how to use dermoscopy to detect and diagnose lesions of the skin, with a special emphasis on malignant skin tumours. The book has extensive clinical correlation with dermoscopic images, so readers can appreciate the added benefits of dermoscopy by comparing the clinical morphology seen with the naked eye with the corresponding dermoscopic morphology; extensive illustrations from the image collections of internationally recognized experts, who have years of experience refining their techniques; and extensive schematic drawings to help readers single out the key structures and patterns to recognize in the dermoscopic images.

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