27 Skin

The discussion of the skin will be divided into three subsections: melanocytic lesions, non-melanocytic lesions, and inflammatory (systemic) disorders. Skin biopsies are usually performed because the clinician sees a lesion, such as a mass, a rash, or a macule. However, skin biopsies are also sometimes used to diagnose systemic conditions. Usually the history is enough to direct you to one of the major three categories. Inflammatory skin conditions are not usually diagnosed by the general surgical pathologist, but a working knowledge of their classification can be very helpful. Melanocytic lesions are also more and more the exclusive domain of dermatopathologists, but any surgical pathologist should at least be able to tackle the most benign and most malignant ends of the spectrum.

The grossing of skin biopsy specimens varies a bit by the shape, size, and purpose of the excision, but for diagnostic specimens of tumors, the margins must be entirely examined in perpendicular cuts. See your grossing manual, and consult with your attending, for the best way to cut in a specimen.

Melanocytic Lesions

Melanocytes are specialized cells in the epidermis and elsewhere that are derived from neural crest cells. They have a neuralish, dendritic morphology and stain with S100, like peripheral nerve cells. They also produce melanin pigment, which is exported from the cell and taken up by surrounding epidermal cells. Normal melanocytes do not have much visible pigment; in fact, the cytoplasm is clear, as the pigment leaves the cell (Figure 27.1). Densely pigmented cells along the basal layer of the epidermis are usually basal keratinocytes, not melanocytes. It is this pigment distribution that creates shades of skin color.

Abnormal melanocytes can accumulate pigment, and this can be a useful clue in identifying dysplastic melanocytes (discussed below) or identifying an unknown metastasis as melanoma. However, there are plenty of melanomas with no melanin to be found, so do not rely on that. Also beware the melanophage, spindly macrophages in the dermis full of chunky globs of melanin—they are eating it, not making it (Figure 27.2).

Become familiar with the melanocyte; spend a few seconds looking for them when you encounter normal skin. Melanoma is a treacherous area precisely because there are no strict diagnostic rules about when something is malignant and when it is not, and much of the diagnosis (in subtle cases) relies on recognizing atypical melanocytes that are up to no good. The only way to learn this skill is to see lots of normal melanocytes.

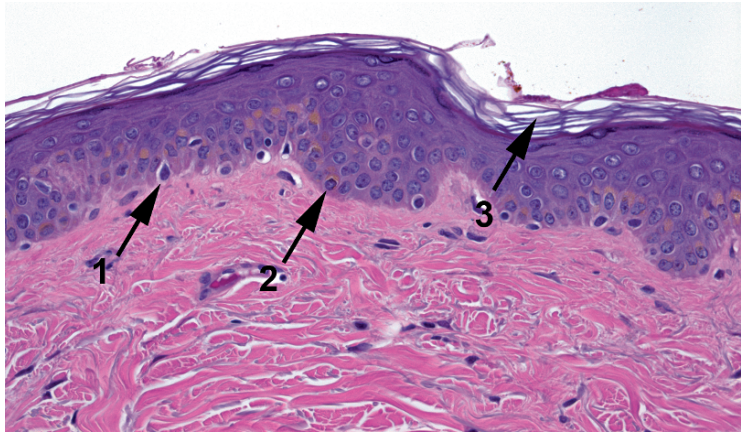

Figure 27.1. Normal melanocyte and skin. A normal melanocyte (1) stands out within a clear halo of cytoplasm. The pigmented component of the skin is actually the basal keratinocytes (2), which absorb the melanin. Typical basket weave or orthokeratin is present (3).

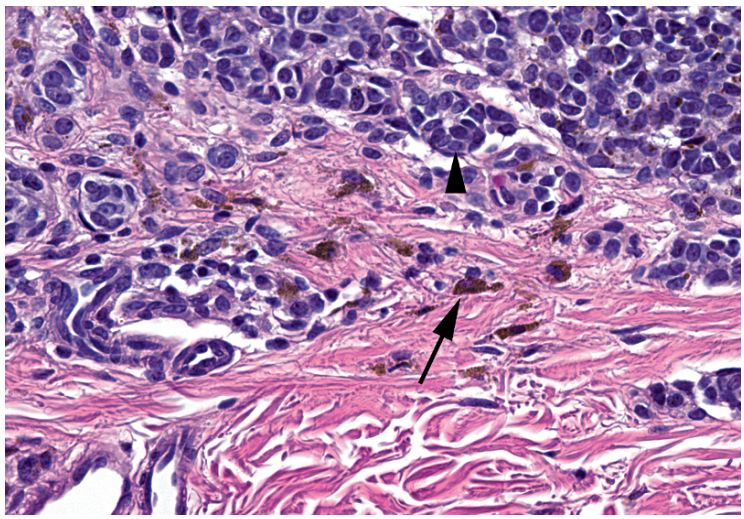

Figure 27.2. Melanophages in an intradermal nevus. The nevus cells (arrowhead) have focal small specks of pigment, but the macrophages digesting the excess melanin (arrow) stand out.

Terminology

As a pathologist, you now know that a "mole" is a type of gestational trophoblastic disease, and you are sophisticated enough to refer to a bump on the skin as a nevus. However, the word *nevus* really does mean just a *bump on the skin*, and there are things called *nevus* that have nothing to do with melanocytes. In this chapter, we will just be discussing the melanocytic nevi.

A melanocytic nevus is a proliferation of benign melanocytes. It begins along the basal layer of the epidermis, where melanocytes live, and the very earliest manifestation of this is an increased number of melanocytes along the dermoepidermal junction (DEJ) in a single layer. This produces a dark patch on the skin, and the lesion is called a *lentigo simplex* (Figure 27.3). The word *lentigo* or *lentiginous* refers to "along the DEJ" and is used in several different contexts.

The next step in the life cycle of a nevus is the proliferation of melanocytes into little nests, or *theques*, along the DEJ. These are technically intraepidermal, although it is sometimes hard to appreciate that. This lesion is called a *junctional nevus*, and it appears as little clusters of bland melanocytes hanging from the DEJ (Figure 27.4).

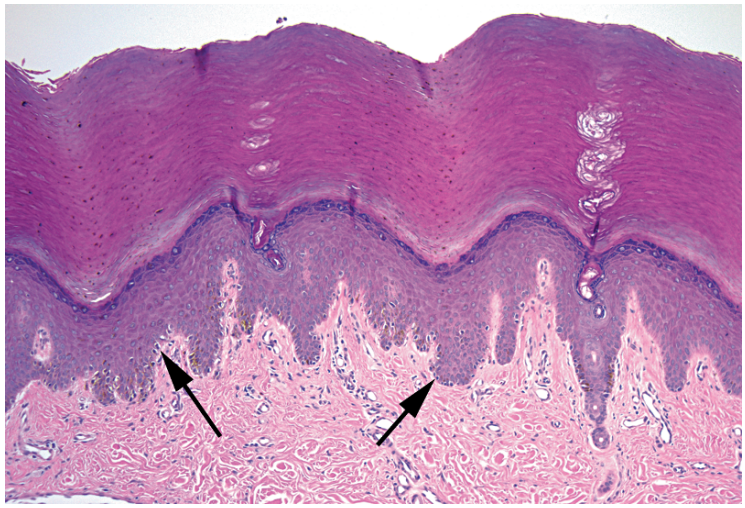

FIGURE 27.3. Lentigo simplex in acral skin. The dense keratin seen here is typical of acral skin (hands and feet). There is a linear proliferation of single benign melanocytes along the dermoepidermal junction (arrows).

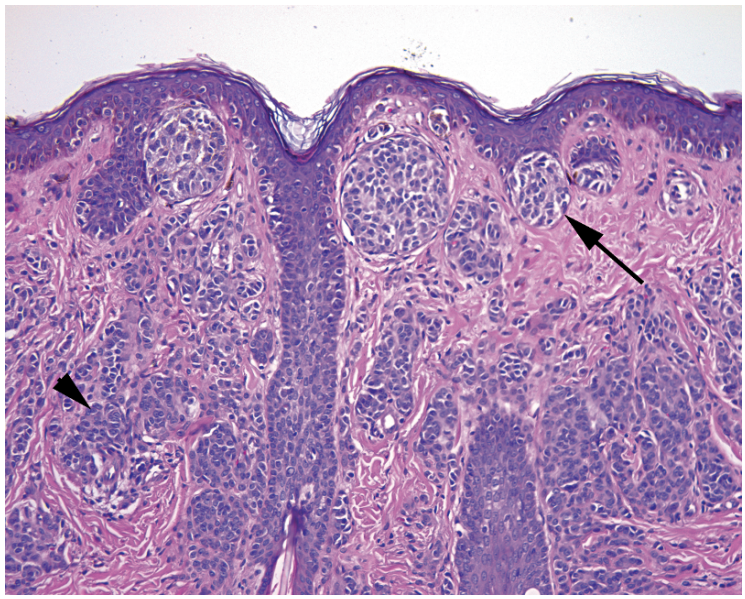

FIGURE 27.4. Compound nevus. This nevus shows nests of nevocellular (melanocytic) cells attached to the dermoepidermal junction (arrow). A nevus with only dermoepidermal junction nests would be a junctional nevus. In this example, as there are also nevus cells dropping down into the dermis (arrowhead); this is a compound nevus. In a compound nevus, the cells at the deepest point should appear slightly smaller and more bland than those at the dermoepidermal junction ("maturation").

From there, the melanocytes may begin to proliferate down into the dermis. They do so as small nests, sheets, or single cells, and they grow in a lobular pattern. Cytologically they are bland, round, clear cells, and they tend to "mature" (become smaller and more bland) the deeper into the dermis they progress. They become so numerous that they make a little nodule in the skin, forming the classic "mole" a la Cindy Crawford. Most adults have 10–20 of them. A nevus with a dermal component plus a junctional component is called a *compound nevus*. Eventually, with age, the junctional component regresses and you are left with just an *intradermal nevus* (Figure 27.5). These can be pedunculated, hyperkeratotic, hair bearing, and so forth. Note that melanoma arising in a benign intradermal nevus is vanishingly rare.

All of these phases of the nevus share some histologic features of benignity:

- Symmetry
- Size < 3 mm in diameter
- Lateral borders consisting of nests, not individual trailing melanocytes
- Lack of atypia in the melanocytes (nuclei are no larger than a keratinocyte nucleus and have small dense nucleoli, if any; multiple nuclei are okay)
- Maturation into the dermis
- Chunky brown-black pigment

Other Benign Nevi

The common *blue nevus* consists of a diffuse scattering of pigmented, dendritic (stellate), single melanocytes in the dermis (Figure 27.6). They are mixed in with melanophages.

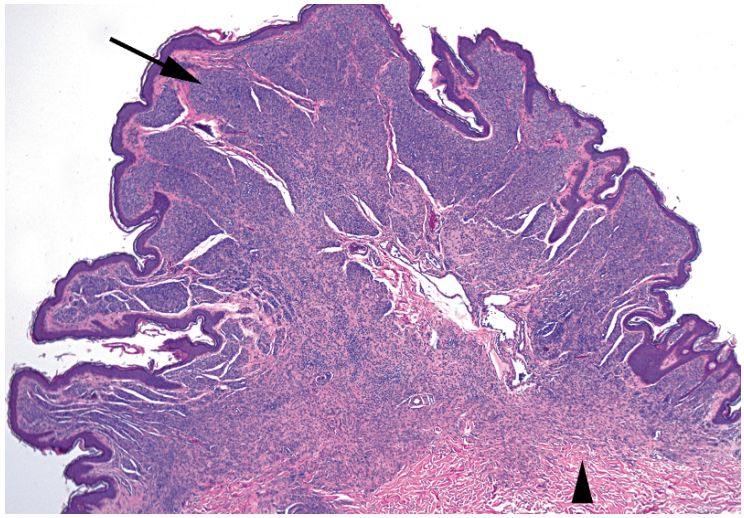

Figure 27.5. Intradermal nevus. This exophytic nevus has only dermal nests of nevus cells (arrow). The lesion is roughly symmetric, and the cells are smaller and more mature at the base (arrowhead).

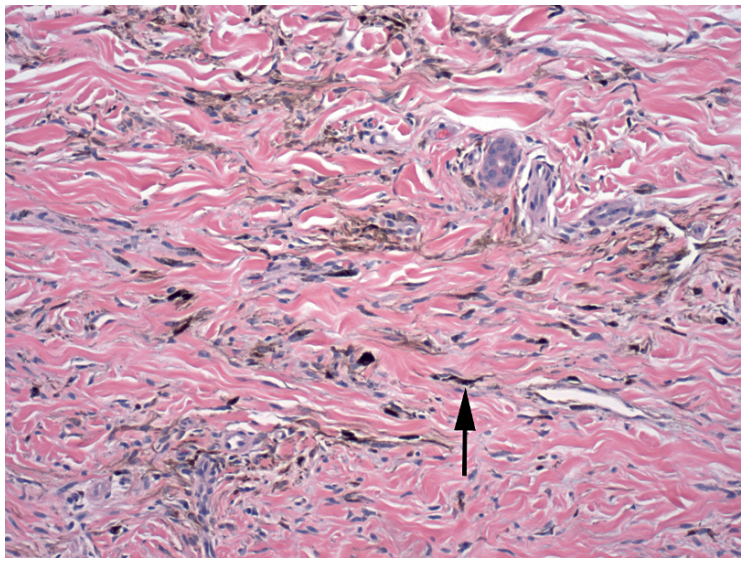

Figure 27.6. Blue nevus. Small, indistinct, pigmented cells are scattered throughout the dermal collagen (arrow). The cells are elongated and fusiform or stellate and do not make rounded nests like typical nevus cells. Some of the larger cells with chunky pigment are likely melanophages.

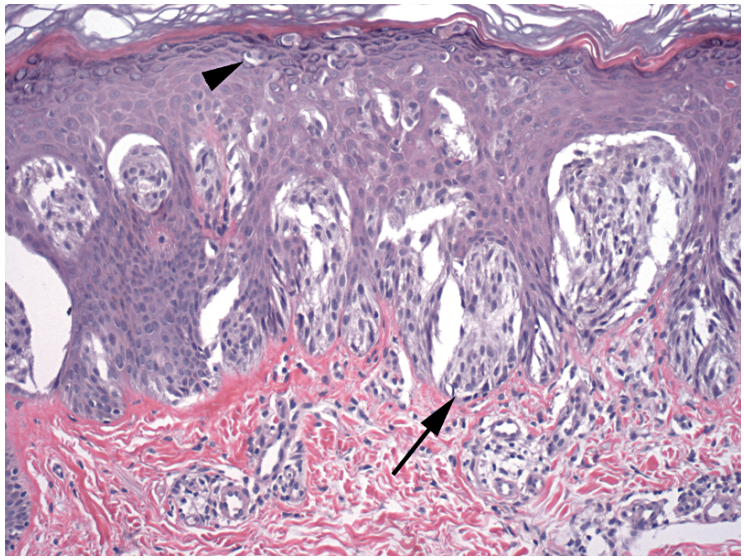

Figure 27.7. Spitz nevus. This nevus in a child shows nests of large, spindly melanocytes at the dermoepidermal junction (arrow) and rare melanocytes spreading up through the epidermis (arrowhead). In an adult, this pattern would be very worrisome.

The *Spitz nevus* is usually found on the head and neck of children and adolescents. At low power it is circumscribed and symmetric, and large nests of melanocytes are found between skinny elongated rete (Figure 27.7). Eosinophilic Kamino bodies may be seen at the DEJ. The reason this lesion is so troublesome is that the melanocytes may be large, spindled, pleomorphic, or atypical, and they may even show rare mitoses, which suggests melanoma.

Acral and genital nevi—nevi of the hands and feet, genital regions, and breasts—are allowed some atypical features. These nevi have prominent lentiginous growth, with occasional ascending cells mimicking pagetoid spread. However, they should not have cytologic atypia.

Most nevi are acquired during childhood to early adulthood, but some are congenital. To have *congenital features* means that the dermal melanocytes tend to track down the adnexal structures.

Dysplastic nevi

There are some nevi that begin to show some features more commonly associated with melanoma. These nevi are clinically distinct looking, and although they are not considered actual precursors to melanoma, patients with multiple dysplastic nevi are at significantly higher risk of developing melanoma. However, "dysplastic nevus" is a clinical diagnosis, and as pathologists we merely describe the features we see. There are two components to dysplasia in this context: architectural disorder and atypia. These lesions are signed out as, for example, *Compound nevus with architectural disorder and severe cytologic atypia*. (However, in some texts you will find this entity listed as "lentiginous melanocytic nevus.")

There are four features of *architectural disorder*: Architectural disorder is not graded but simply present or absent.

- Lentiginous spread of atypical melanocytes (along the DEJ in a creeping line)
- Shouldering (the lentiginous component is wider than the dermal component)
- Bridging of rete (nests attached to adjacent rete ridges fuse; Figure 27.8)
- Fibroplasia (a feathering of the dermal collagen that looks like pink cotton candy)

The features of *cytologic atypia* include the following:

- Hyperchromatic nuclei, increased nuclear to cytoplasmic ratio
- Large red nucleoli
- Accumulation of dusty grey-brown melanin (see Figure 27.8)
- Atypical mitoses

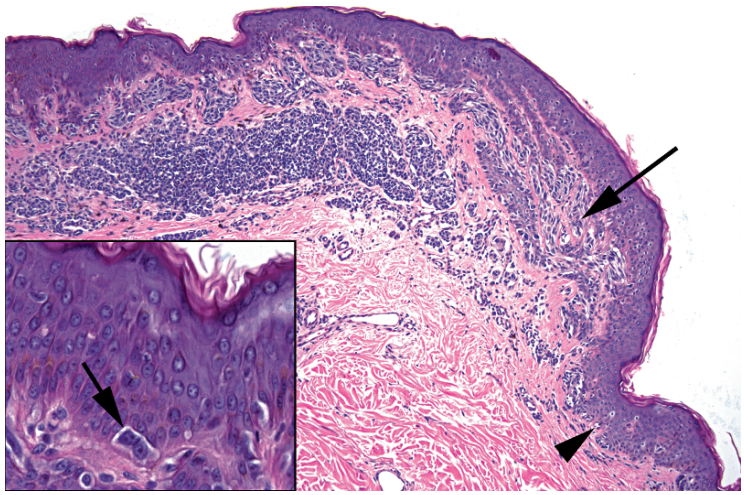

Figure 27.8. Dysplastic nevus. At low power, elongated nests of spindly melanocytes are seen bridging across adjacent rete (arrow), and single melanocytes trail off to the lateral edge of the lesion (arrowhead). These are features of architectural disorder. **Inset**: Atypical melanocytes with large nuclei and nucleoli are seen at the dermoepidermal junction.

Atypia is graded as mild, focally severe, or severe.

In general, these nevi tend to be suspicious enough that you must take a few moments to prove to yourself that they are *not* melanoma (see next section).

Melanoma

The best way to think about melanoma is as the presence of malignant melanocytes. Because melanocytes can proliferate in many ways and still be benign, it takes considerable experience to decide if a melanocyte is malignant or not. However, setting that aside for a moment, the types of melanoma include the following:

- *Lentigo maligna*: malignant melanocytes proliferating only along the DEJ.
- *Melanoma in situ*: malignant melanocytes along the DEJ, *and* percolating up through the epidermis in a pagetoid fashion (something benign melanocytes just do not do)
- *Malignant melanoma*: malignant melanocytes along the DEJ, pageting through the epidermis *and* invading the dermis
  - *Superficial spreading melanoma*: melanoma in a "horizontal growth phase," meaning it is spreading laterally along the DEJ but also involves the dermis (clinically, this is a macular lesion [flat])
  - *Nodular melanoma*: melanoma with a "vertical growth phase," meaning that it is primarily growing down into the dermis (almost like an intradermal nevus, but with malignant cells) and that it produces a raised lesion

Most melanomas have both a horizontal and a vertical component, which is the classic irregularly shaped dark macule with a central raised or ulcerated papule.

Features of Malignancy

Unfortunately there is no single feature than can rule melanoma in or out. As with many types of neoplasia, there are certain features that suggest malignancy, and the presence of enough of them can convince you of the diagnosis. Many of these criteria are subjective and require experience, which is why dermatopathology is such a booming subspecialty these days.

On low power, look for the following:

- Asymmetry
- Poorly circumscribed, pleomorphic, discohesive nests of melanocytes

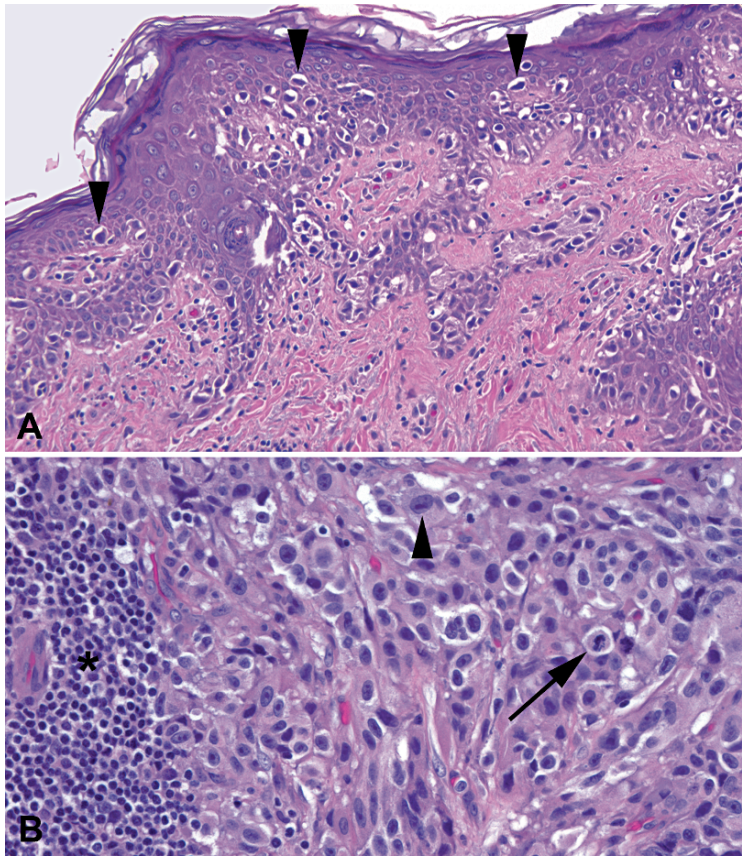

FIGURE 27.9. Melanoma. **(A)** Large, dark, irregular melanocytes can be seen infiltrating upward through the epidermis (arrowheads) in pagetoid fashion. If there were no dermal component, this would qualify as melanoma in situ. **(B)** Malignant melanocytes deep in the dermis. Large atypical nuclei with large nucleoli (arrowhead) plus the presence of mitoses (arrow) is diagnostic of invasive melanoma. Adjacent lymphocytes (asterisk left side of the field) are common.

- Shouldering (lateral spread) of atypical melanocytes
- Pagetoid spread through the epidermis (Figure 27.9)
- Associated lymphocytes, especially band-like

On high power, look for the following:

- Atypia, as described earlier
- Lack of deep maturation (for dermal component)
- Mitoses or atypia in the dermis (see Figure 27.9)
- Melanocytic necrosis

Sign Out Criteria

All diagnoses of invasive (into the dermis) melanoma must include certain prognostic features. The first is the depth of invasion. This is called Breslow's thickness and is the depth (to the hundredth of a millimeter) of invasion from the top of the epidermal granular layer to the deepest malignant cell. It is functionally equivalent to stage; the deeper the invasion, the poorer the prognosis. Clark's level is a related concept but is based on the histologic layers or levels of the dermis, not the absolute depth.

The second important prognostic feature is the presence or absence of ulceration. The third is the margin status, both deep and lateral.

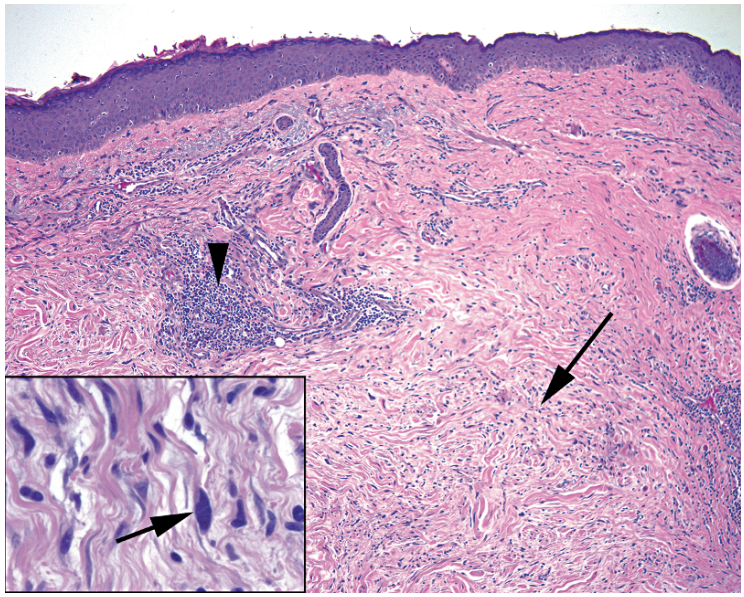

Figure 27.10. Desmoplastic melanoma. At low power, there appears to be a hypocellular scar in the dermis (arrow). The clue to melanoma lies in the collection of lymphocytes (arrowhead). **Inset**: On higher power, there are enlarged and hyperchromatic cells (arrow) in the "scar." These would be positive for S100, unlike fibroblasts.

Special Types of Melanoma

In *desmoplastic* and spindle cell melanoma, melanocytes can become very spindly and sarcomatoid. With an unidentified spindle cell lesion in the dermis, you must always rule out melanoma. The scariest and most subtle form is the desmoplastic melanoma, which is not only spindly but often sparsely cellular in a background of dense collagen; in other words, it looks just like a scar. A useful tip-off to a lurking desmoplastic melanoma is, aside from a slightly "busy" dermis, the presence of bands or clumps of lymphocytes (Figure 27.10).

Another type of melanoma is *acral lentiginous*. *Acral* refers to the distal extremities. Like the benign acral nevus, this lesion is characterized by prominent lentiginous growth. It can be very difficult to distinguish from an acral nevus.

Metastases can look like anything at all; they can be spindly, epithelioid, rhabdoid, small cell, and so forth. However, common features of metastases include alveolar (nested) architecture, large pink-to-violet cells with big nuclei and red nucleoli, and occasional melanin pigment. As a rule of thumb, if you don't know what it is, consider melanoma.

Re-excision of Melanomas

When a melanoma is diagnosed on excisional biopsy, it is nearly always given a wide re-excision. You will see these huge ellipses on surgical pathology. Pathologists differ in how much of the re-excision to submit, but at the least the entire biopsy scar, to the lateral margins, should be submitted. Carefully scan not just the epidermis but also the dermis deep to the biopsy site.

Special Stains

S100 is the workhorse stain for melanoma, as it stains all types. HMB-45 and Melan-A are also melanoma markers, but notably do not stain spindled or desmoplastic melanomas. Also remember that there is a whole family of tumors that are HMB-45 positive but not melanoma (angiomyolipoma and the perivascular epithelioid cell tumors).

Sentinel nodes for melanoma, if negative by H&E, are stained using HMB-45 and Melan-A. There are inherent S100-positive cells in lymph nodes, so it is not a good screening stain for this purpose.

There are, unfortunately, no stains that can differentiate a benign nevus from a malignant melanoma. However, in general, HMB-45 should only stain the most superficial cells in a nevus, as the deeper maturing component loses the antigen. Similarly, Ki-67, a proliferation marker, should only be positive at the surface of a nevus, not deep.

Nonmelanocytic Lesions

This section will address the lesions, both neoplastic and hyperplastic, that are not made of melanocytes. These include squamous lesions, cysts, adnexal tumors, and miscellaneous common soft tissue tumors of the dermis.

Sun Damage

The first major category of tumors is the spectrum of disease seen in sun-exposed skin, typically the face, neck, and arms of adults. A general marker of sun exposure is *solar elastosis*, which is an accumulation of grey wispy damaged elastin in the dermis (Figure 27.11). Ironically, it represents a loss of elasticity (wrinkles). One of the benign changes seen in the context of sun exposure is the *solar lentigo* (lentigo senilis, age spot), which appears as a finger-like proliferation of hyperpigmented rete growing down from the epidermis (Figure 27.12). Keratinocytes, not melanocytes, are the pigmented cells.

The solar lentigo may then develop into a dysplastic lesion called an *actinic keratosis*. Actinic keratoses have a wide variety of appearances, from very thin with subtle atypia to very hypertrophic with full-thickness atypia. However, the defining features of an actinic keratosis should include the following:

- Squamous atypia of varying thickness, often noticeable only in comparison to the surrounding uninvolved epidermis (Figure 27.13)
- Alteration of the keratinization to become pink and parakeratotic
- Sparing of the keratin above the hair follicles, classically resulting in alternating columns of parakeratosis and orthokeratosis
- Underlying solar elastosis

Actinic keratosis is regarded, conceptually, as a form of carcinoma in situ, but its natural history is unpredictable. Actinic keratoses can (rarely) invade before they reach full-thickness

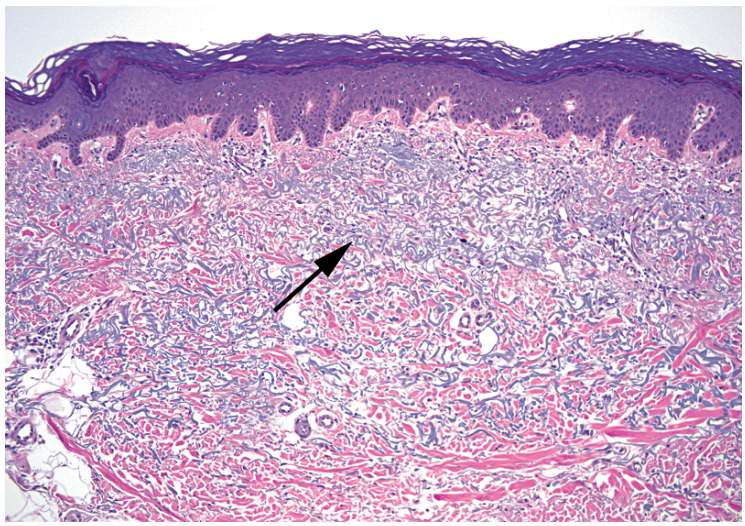

Figure 27.11. Solar elastosis. This is the typical microscopic appearance of sun-damaged skin. The collagen is replaced by wispy gray-blue strands of elastin (arrow).

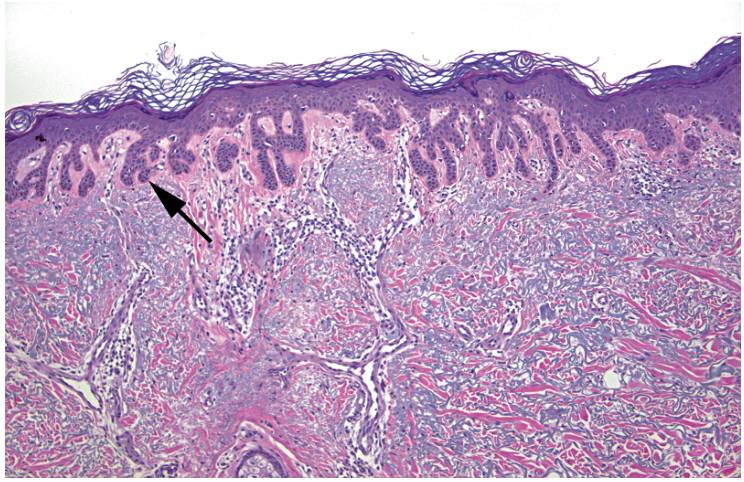

Figure 27.12. Solar lentigo. Prominent rete are growing down from the epidermis (arrow), with increased basal pigmentation (not clearly visible at this power). Notice the underlying solar elastosis. Compare this lesion to the lentigo simplex (see Figure 27.3), which, in contrast, shows a proliferation of melanocytes.

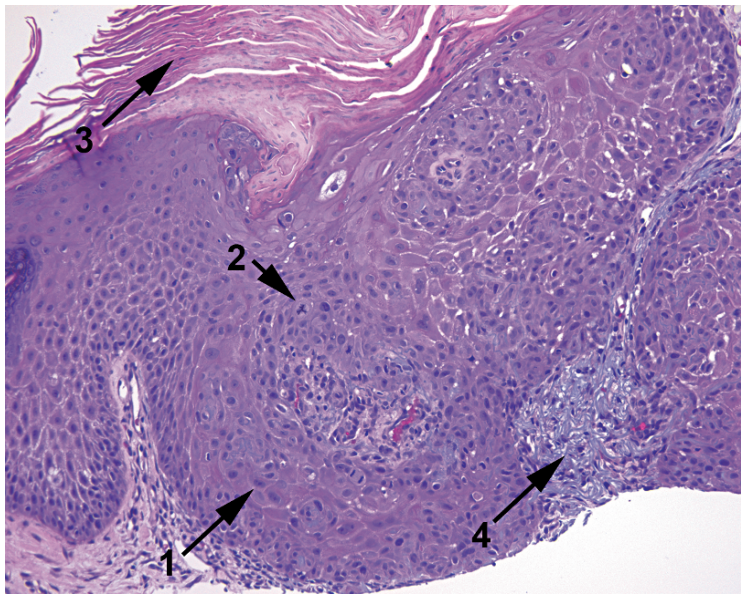

Figure 27.13. Actinic keratosis. This example shows an area of disorganized and enlarged nuclei (1) with prominent and atypical mitoses (2), consistent with dysplasia. There is overlying hyperkeratosis and parakeratosis (3) and underlying solar elastosis (4). This is a slightly tangential cut through the skin, making the lesion appear very thick.

atypia, unlike squamous lesions of the cervix. However, when the atypia does reach full thickness (assuming no invasion), these lesions may be called *bowenoid actinic keratosis* or just *squamous cell carcinoma in situ* to emphasize the severity of the lesion.

Carcinoma in situ is a simple concept in other organs, but in the skin it is a source of great debate. Most dermatopathology chapters are littered with the phrase "*we* use the term…"—meaning each camp has their own philosophy and style. Part of the problem is that the path from dysplasia to invasive carcinoma looks more like a metro subway map than a straight line. However, the basic idea is that carcinoma in situ has not yet crossed the basement membrane

and that there is some degree of epidermal dysplasia. Entities that fall under the category of carcinoma in situ include the following:

- Actinic keratosis (as discussed earlier) and bowenoid actinic keratosis
- Bowen's disease—often used as a synonym for carcinoma in situ but actually describes a particular clinical presentation that occurs on non–sun-damaged skin and does not spare the hair follicles, unlike the actinic keratosis family
- Bowenoid papulosis—a human papillomavirus–related lesion of genital sites

Invasive squamous cell carcinoma is most likely to arise from the sun-damaged, actinic keratosis–type pathway and hence is usually seen in the background of solar elastosis and actinic keratosis–like changes. Features that suggest invasion include penetration of nests deep into the dermis, accompanied by an aberrant deep keratinization (pinkness). Finding single cells invading the dermis is fairly conclusive (Figure 27.14). The appearance of squamous cell carcinoma is similar to that found in other sites (see Chapters 16 and 22).

Basal cell carcinoma is another of the common sun-related tumors. It is the most common cutaneous malignancy and, despite its reputation as a sort of ho-hum and uninteresting tumor, has a very wide range of appearances. There is also some overlap between basal cell carcinoma and benign adnexal tumors; the latter are probably often missed. Features of basal cell carcinoma include the following:

- Lobules of small, blue, basal-type keratinocytes with peripheral palisading (picket-fence) arrays of oblong nuclei (Figure 27.15)
- Formation of clefts (cracks) between the tumor nests and the stroma
- Sometimes (not always) desmoplasia, focal keratinization, or mucin production

At low power the basal cell carcinoma nests can look similar to adnexal structures, making margins challenging. However, basal cell carcinoma tumor cells should have darker chromatin, more apoptosis and mitoses, and paler cytoplasm than the hair follicles.

Special types of basal cell carcinoma include *nodular* (the usual type), *superficial multicentric*, and *sclerosing*. The superficial multicentric form tends to hang off the epidermis like stalactites, without forming a mass, and can have skip areas (harder to excise). The sclerosing form shows a prominent desmoplastic response. There are up to 20 more subtypes; a large dermatopathology atlas will show the many faces of basal cell carcinoma.

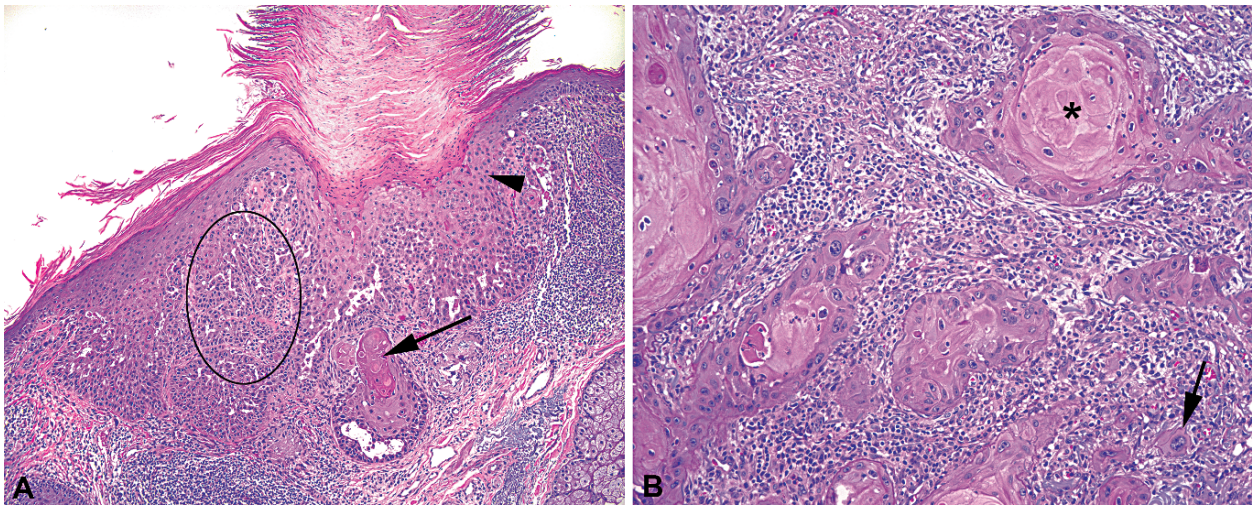

FIGURE 27.14. Squamous cell carcinoma. **(A)** Superficially invasive squamous cell carcinoma, showing the paradoxic deep keratinization (arrow), indicating an invasive nest. Actinic keratosis–type changes are seen in the overlying epidermis (arrowhead), including hyperkeratosis. In one area, the pattern of thin cords of cells infiltrating the stroma (oval) is too complex to be explained by a funny plane of section and is another pattern of invasion. **(B)** Higher power view of invasive squamous cell carcinoma, showing keratin pearls (asterisk) and infiltrating single cells (arrow).

Other Hyperkeratotic but Nonneoplastic Lesions

Seborrheic keratoses are very common, benign lesions that have many, many forms, but the usual picture is a hyperkeratotic, orthokeratotic lesion with a markedly thickened epidermis. It often forms a raised plaque on the skin; on the slide, the epidermis looks as though it was accidentally cut *en face*, with convoluted, confluent cords of epidermis. Horn cysts, which are entrapped whorls of orthokeratin, are common (Figure 27.16). (These are quite different from the squamous pearls of carcinoma, which are pink and parakeratotic.) Pigment and inflammation may be seen; atypia is not. These are not necessarily associated with sun damage.

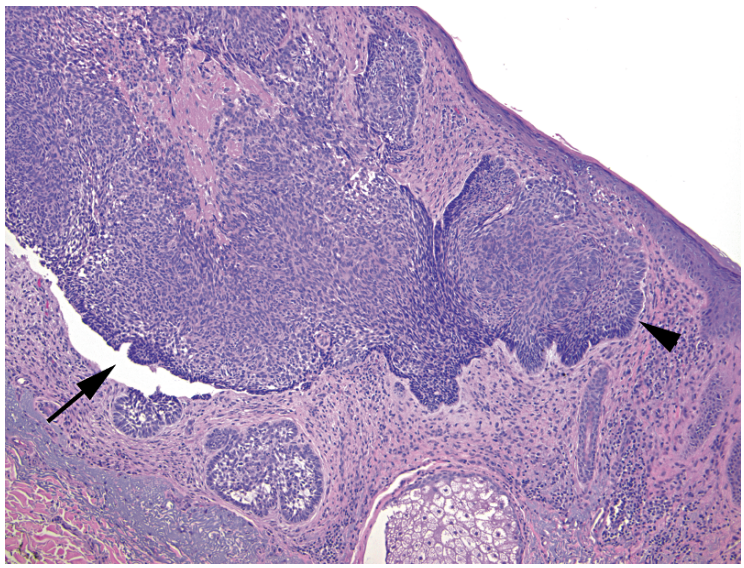

Figure 27.15. Basal cell carcinoma. Blue nests of cells appear to drop down from the epidermis. There is prominent palisading of the basal cells at the periphery of the nests (arrowhead) and clefting of the tumor cells away from the stroma (arrow).

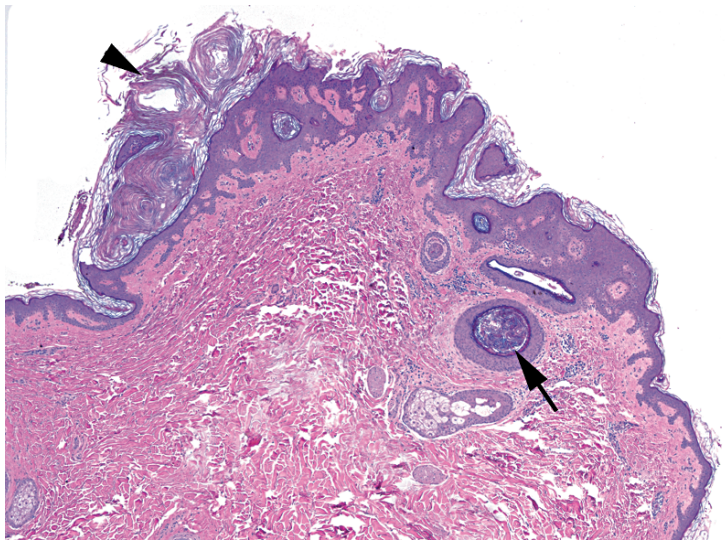

Figure 27.16. Seborrheic keratosis. This exophytic lesion shows hyperkeratosis (arrowhead) but not parakeratosis (no visible nuclei in the keratin). The epidermis takes on a complicated pattern of intertwining rete, and in some areas foci of keratin are trapped within the lesion, forming horn cysts (arrow). Compare these blue, acellular, lamellated balls of keratin with the pink keratin pearls of squamous cell carcinoma (see Figure 27.14).

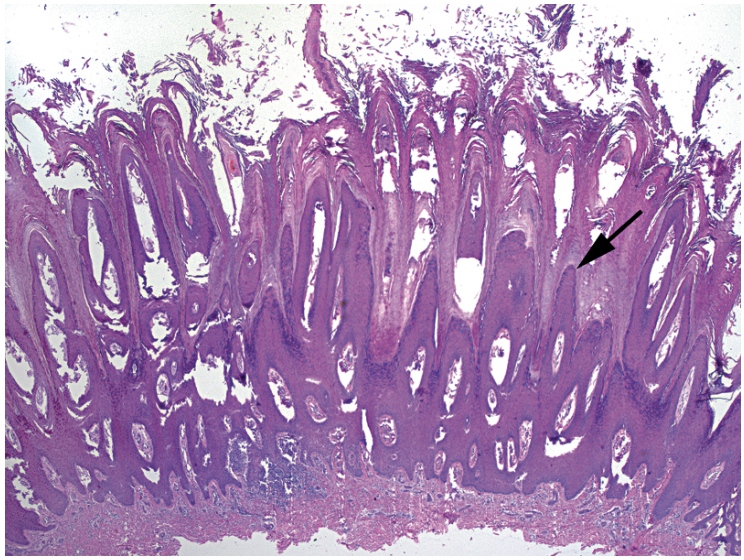

Figure 27.17. Verruca vulgaris. The epidermis in this wart is thrown up into sharply pointed spires, which are topped by hyperkeratosis and parakeratosis.

Verruca vulgaris (the common wart) is a virally induced circumscribed lesion, usually on the fingers, which shows a striking epidermal proliferation ("church spires") with overlying hyperkeratosis (Figure 27.17). The tips of the spires are often topped by parakeratosis, which can lead to a striped effect. Koilocytes (review the description of this viral change in Chapter 16) may be hard to identify. Related lesions are the planar (flat) and plantar (endophytic) warts, as well as the condylomata (genital).

If you cannot quite tell if a lesion is a seborrheic keratosis or a wart, compromise and call it a verrucous keratosis. Verrucous carcinoma, a deceptively innocuous cancer, is not usually in the differential diagnosis for skin: it is mainly seen on mucosal sites.

Adnexal Tumors

Adnexal tumors are a large, mystifying, shape-shifting group of lesions encompassing follicular, eccrine, apocrine, and sebaceous lesions. Some of the more readily identifiable tumors are listed here. Most of these are benign, although carcinomas do exist. Of the carcinomas, many are similar to those found in breast or salivary gland (similar embryologic origin), such as adenoid cystic carcinoma, mucoepidermoid carcinoma, and ductal adenocarcinomas.

The *eccrine poroma/acrospiroma/hidradenoma* group are tumors of the sweat ducts and get different names depending on where in the dermis or epidermis they arise. They are composed of cells that look similar to keratinocytes but that try to form ducts (usually tiny lumens in a sheet of cells). The cells are streamy, pale, and disorganized, not unlike usual ductal hyperplasia in the breast (Figure 27.18).

Eccrine spiroadenomas are "blue cannonballs in the dermis." Tumor balls consist of two basaloid cell lineages (often hard to separate) and have noticeable cords and droplets of hyaline basement membrane substance running through them (Figure 27.19). A related lesion is the cylindroma.

The *cylindroma* ("jigsaw puzzle") also has basaloid (blue) nests in the dermis, also with two cell populations and basement membrane matrix. However, the tumor nests are mosaic in shape.

The *syringoma* is a collection of round, dilated tubules in the dermis with characteristic comma-like or tadpole tails (Figure 27.20). *Trichoepithelioma* is a benign tumor of hair follicle differentiation that looks a lot like a basal cell carcinoma except with horn cysts, hair formation, little abortive follicles, fibrotic stroma, and a lack of clefting. *Microcystic adnexal carcinoma* (sclerosing sweat duct carcinoma), although rare, is the malignant one you do not

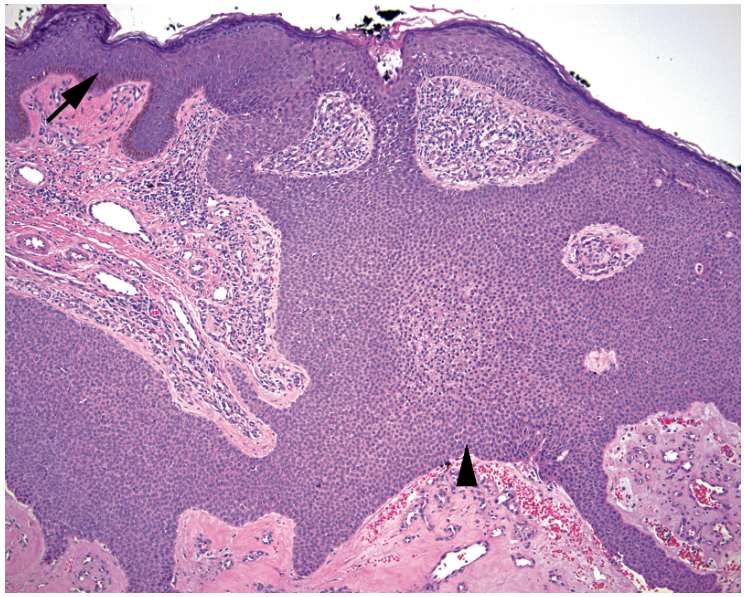

Figure 27.18. Poroma. This eccrine tumor is continuous with the epidermis, which can be seen at left (arrow). The tumor cells (arrowhead) are uniform, small, round, and pale and in some areas may form rudimentary duct spaces.

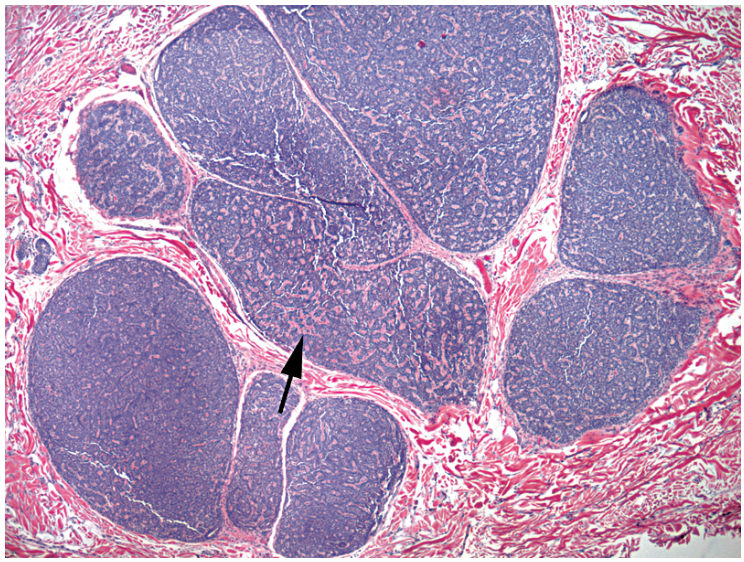

Figure 27.19. Eccrine spiroadenoma. "Cannonballs in the dermis" is the catch phrase for this tumor. Like the poroma, the cells are small and bland. Cords of hyaline pink basement membrane material are seen throughout the tumor (arrow).

want to miss. It looks similar to syringoma, with tubules and cords of bland cells, and also has horn cysts (Figure 27.21). What differentiates it from syringoma is the deep infiltration of the dermis, so dermatopathologists like to see the base of an adnexal lesion.

Cysts

The most common cysts you will see are the epidermoid cyst (sometimes called epidermal inclusion cyst) and the trichilemmal or pilar cyst (Figure 27.22). The *epidermoid cyst* is lined

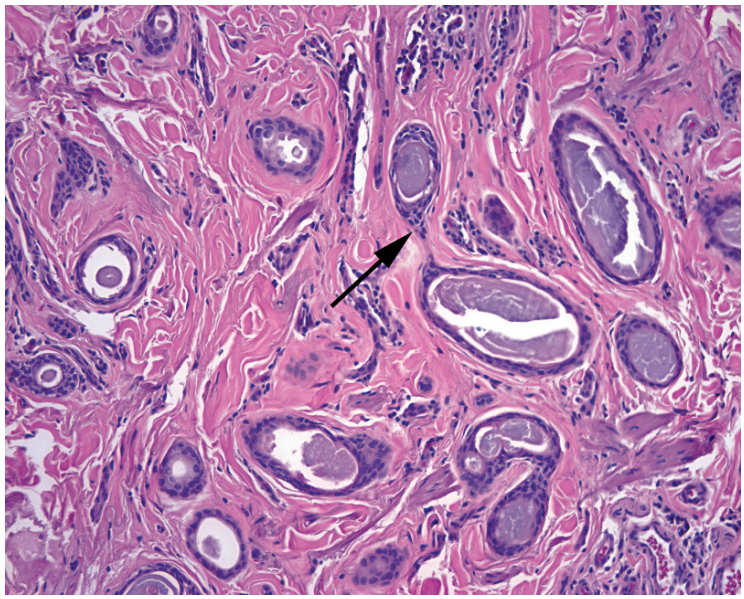

Figure 27.20. Syringoma. Small tubules with comma-like pointed tails within the dermis (arrow).

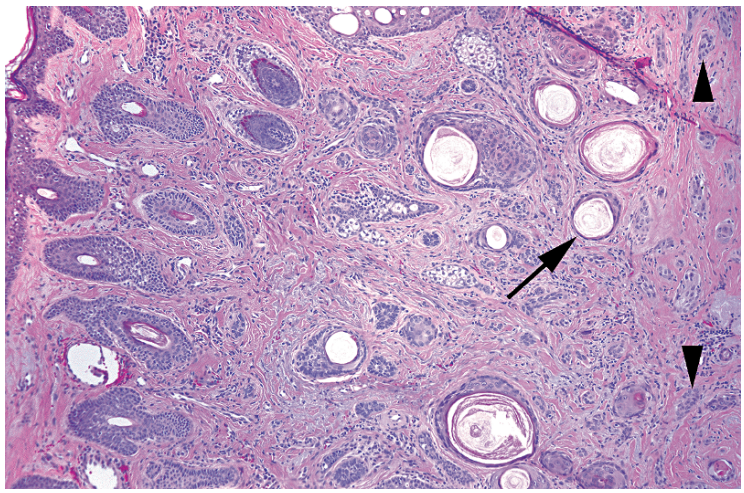

Figure 27.21. Microcystic adnexal carcinoma. A collection of small pale nests of cells can be seen in the dermis, some of them forming horn cysts (arrow). The feature that separates this from a benign lesion is the small nests that are infiltrating deeply into the base of the lesion at right (arrowheads). This small carcinoma infiltrated into the subcutaneous fat (not seen here).

by mature squamous epithelium with a granular layer and filled with layers of flaky keratin. The *pilar cyst* is lined by plump pillowy keratinocytes with *no granular layer* and is filled with dense compact keratin.

Dermal Tumors

Probably the three most common benign soft tissue tumors of the dermis are the dermatofibroma, the neurofibroma, and the hemangioma. More information about soft tissue tumors can be found in Chapter 28.

Dermatofibromas appear as an ill-defined blue haze in the dermis. On higher power, the blue haze is made up of tiny swarming nondescript cells that infiltrate the collagen and tend to packet it into thick bundles (Figure 27.23). The overlying epidermis may be hyperpigmented and hypertrophic (hence its presentation as a brown nodule). Dermatofibrosarcoma protuberans is the malignant counterpart of this lesion and is more deeply infiltrative, wrapping around the subcutaneous fat in a characteristic pattern (Figure 27.24).

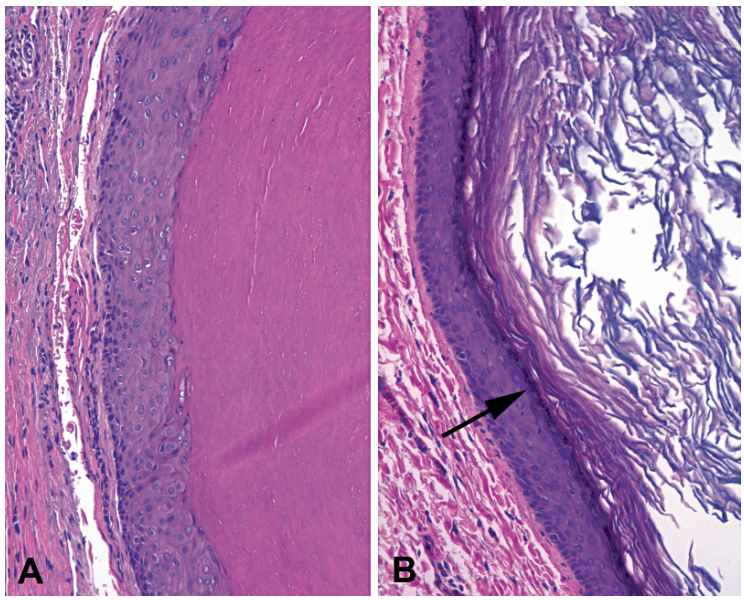

Figure 27.22. Cysts. **(A)** The trichilemmal cyst has no granular layer, with large pink puffy cells showing an abrupt transition to dense "wet" appearing keratin. **(B)** The epidermoid cyst more closely resembles epidermis, with a granular layer (arrow) and layers of "dry" flaky keratin.

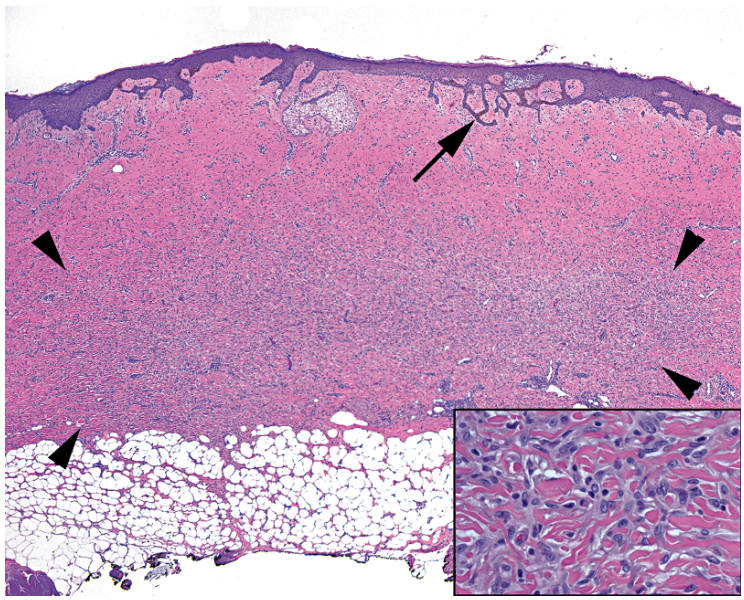

Figure 27.23. Dermatofibroma. This poorly circumscribed tumor creates a blue haze in the dermis (outlined by arrowheads), and the epidermal rete above it may become pigmented and prominent (arrow). The lesion mainly stops at the subcutaneous fat. **Inset**: The cells infiltrate between collagen bundles but have small pale round-to-oval nuclei.

Neurofibromas more often appear as a pale or grey nodule in the dermis, more defined than the dermatofibroma. It displaces the dermis rather than infiltrating it. The individual cells have wavy nuclei and wavy collagen, like overstretched elastic (Figure 27.25).

Hemangiomas are a proliferation of well-formed, dilated capillaries in the dermis (Figure 27.26). There are many variants. The malignant counterpart, angiosarcoma, is more cellular and has anastomosing channels lined by plump cells. Early Kaposi's sarcoma is so subtle it is basically invisible to the inexperienced and is not likely to simulate a hemangioma (Figure 27.27). Pyogenic granuloma, or lobular capillary hemangioma, is a common benign lesion that may be very cellular and inflamed but is identified as benign due to its rounded and circumscribed periphery.

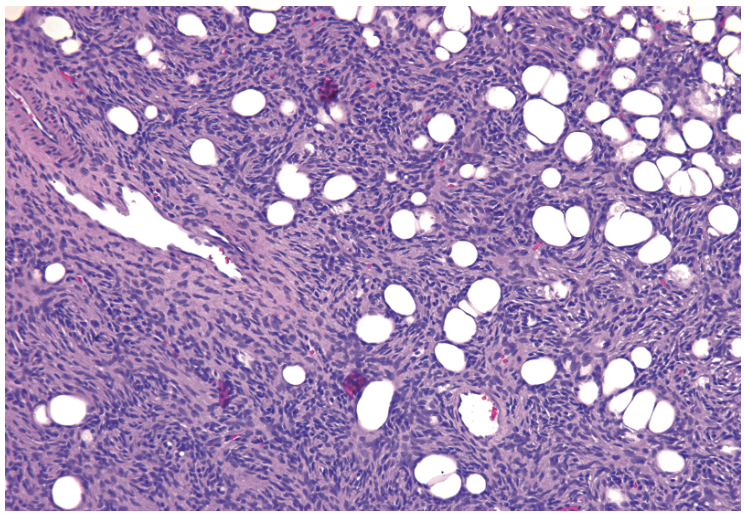

Figure 27.24. Dermatofibrosarcoma protuberans (DFSP). The DFSP is more cellular than the dermatofibroma and shows a prominent storiform pattern of spindled cells infiltrating between fat cells.

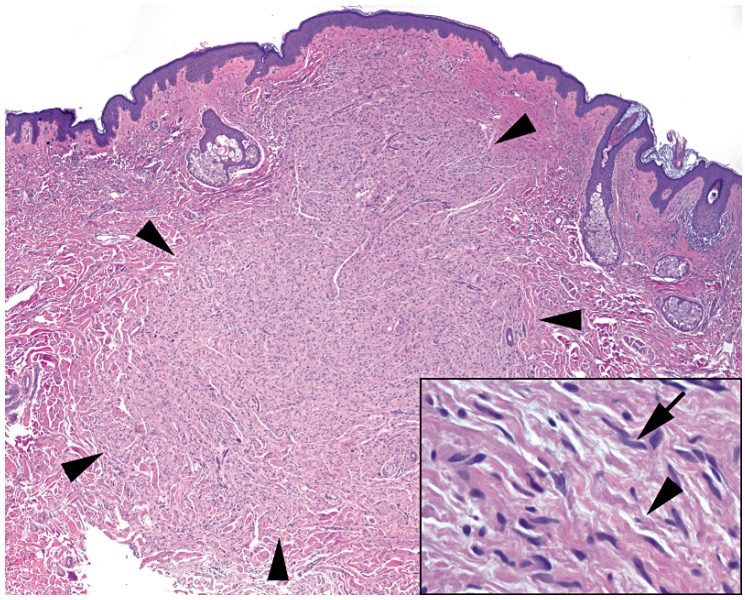

Figure 27.25. Neurofibroma. Like the dermatofibroma, this diffuse neurofibroma is a poorly defined dermal tumor (arrowheads), but, unlike the dermatofibroma, it tends to appear more pale than the surrounding dermis. **Inset**: On higher power, the tapering, undulating nuclei (arrow) are visible, as is the background of wavy collagen fibers (arrowhead).

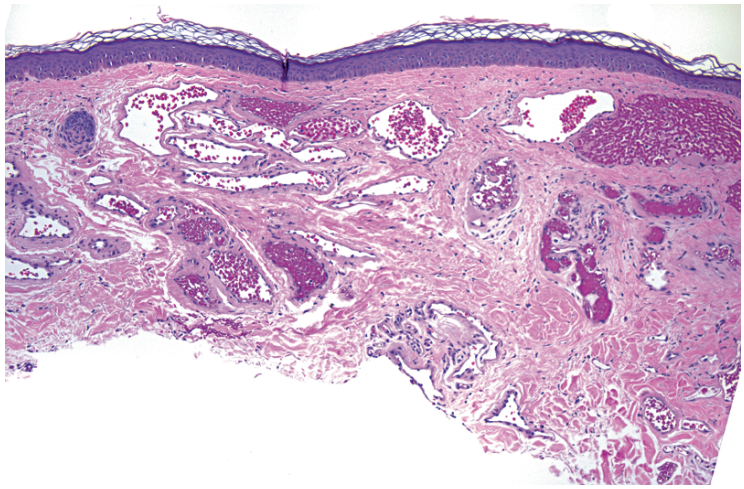

Figure 27.26. Capillary hemangioma. There is a collection of discrete, well-formed, dilated capillaries under the epidermis.

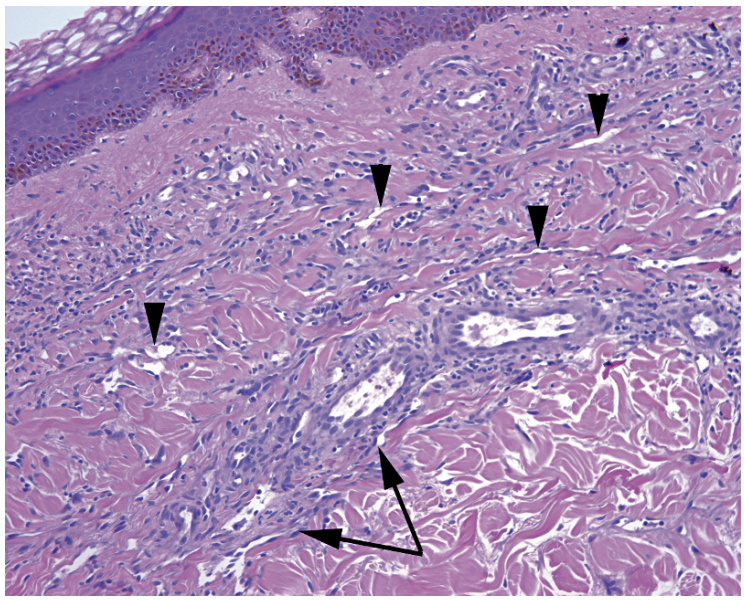

Figure 27.27. Kaposi's sarcoma. The subtle cellularity to the dermis is actually composed of slit-like vascular spaces with bland endothelium (arrowheads). The slit-like spaces are accentuated around existing capillaries (arrows), the "promontory sign."

A Brief Introduction to Nonneoplastic Skin: Patterns of Inflammation and Injury

This section is simply a primer on the terminology and classification of the inflammatory skin diseases; the details are beyond the scope of this chapter. These diagnoses are heavily influenced by the clinical presentation, so the goal here is to understand the histologic families of disease. Arriving at a specific diagnosis requires clinical information and, usually, fellowship training.

Injury to the Epidermis

1. The epidermis can become acutely damaged or inflamed. The result is edema, or *spongiosis*. This is seen as an accentuation of the spaces between keratinocytes. Severe edema can cause

intraepidermal vesicles to form (i.e., poison ivy), which have to be distinguished from true bullae (see later).

If this process continues for a while, the epidermis becomes less edematous and more hyperplastic as it responds to the chronic insult. The hyperplasia is in the form of thickening of the epidermis and elongation of the rete and is called *acanthosis*, usually accompanied by *hyperkeratosis* (a protective thickening of the keratin layer).

These changes make up the spectrum of *acute to chronic spongiotic dermatitis*, clinically eczema, and there is a large differential. Usually the pathologist signs the biopsy out descriptively, and the dermatologist combines that with the clinical features to diagnose it. *Psoriasis* fits in here, as it has histologic overlap with chronic spongiotic dermatitis, especially when partially treated.

2. Some inflammatory processes attack the basal layer of keratinocytes. This pattern is called *interface dermatitis*. Interface dermatitis has two predominant patterns that may overlap. One is an intense lymphocytic infiltrate at the DEJ, which is called *lichenoid* inflammation or dermatitis. The second is a vacuolar degeneration of the basal cells, or *vacuolar dermatitis*. Both of these patterns result in a ragged DEJ, dyskeratotic or necrotic basal cells trapped in the epidermis (colloid bodies), and a cleavage plane along the DEJ if the damage is severe enough. This can be mistaken for a bullous disease, which is a different process.

The prototypical lichenoid dermatitis is *lichen planus*. Vacuolar dermatitis has a wider differential, including *acute graft-versus-host disease, lupus*, and *erythema multiforme*.

3. A third pattern is the dissolution of the intercellular bridges that link the keratinocytes. The cells break apart and round up into individual cells, a process called *acantholysis*. This process is often antibody mediated, so immunofluorescence is important. The acantholysis can coalesce into large spaces within the epidermis, or *bullae*. Different diseases cleave the skin within different planes of the epidermis.

This group includes the inflammatory bullous diseases, such as *pemphigus, bullous pemphigoid*, and *dermatitis herpetiformis*. A noninflammatory bullous disease is *porphyria cutanea tarda*. There is also familial acantholytic disease (*Hailey-Hailey* and *Darier diseases*), transient acantholytic disease (*Grover's disease*), and focal acantholytic lesions (*warty dyskeratoma*).

Inflammation of the Dermis

The patterns of injury discussed in this section are limited to the dermis, usually with a fairly unremarkable epidermis. Many diseases begin with a nonspecific pattern of *perivascular lymphocytic inflammation* in the dermis. It is the first sign that the skin is upset. Some diseases never declare themselves beyond this stage, such as *polymorphous light eruption* and *urticaria*. If the inflammation progresses to involve neutrophils and actual damage to the vessels, the disease is called a *vasculitis*. *Leukocytoclastic vasculitis*, in which the vessels show fibrinoid necrosis and nuclear debris (karyorrhexis), has a wide clinical differential diagnosis.

Inflammatory infiltrates of the dermis are classified based on the type of infiltrate. A dense neutrophilic infiltrate is a *neutrophilic dermatosis*, such as *Sweet's syndrome*. Granulomatous inflammation may indicate infection, foreign body response, sarcoidosis, or *granuloma annulare*. *Mycosis fungoides*, or cutaneous T-cell lymphoma, can have numerous appearances, but a dense lymphocytic infiltrate should trigger a workup for mycosis fungoides.

Some diseases involve alteration of the collagen of the dermis. These include scar, keloid, *scleroderma* or *morphea*, and *lichen sclerosus. Chronic graft-versus-host disease* can look like scleroderma as well.

Inflammation of the Deep Subcutaneous Tissue (Panniculitis)

Panniculitis is divided into septal, where the inflammation is mostly in the fibrous septae between fat lobules, and lobular, where the fat itself is involved. The classic septal panniculitis is *erythema nodosum. Lupus profundus*, or deep lupus, is a lobular panniculitis.