

The skin is generally considered to consist of three major layers: epidermis, underlying dermis, and subcutaneous fat. Depending on anatomic site, there are four to five layers of the epidermis. The layer closest to the basement membrane is the stratum basalis (or basal layer), which consists of a single layer of cuboidal cells that have a slightly basophilic cytoplasm and high nucleus to cytoplasm ratio. The stratum spinosum (or spinous layer) is above the stratum basalis and is so-called because of the prominent intercellular connections and pointed ends of the cells. The stratum granulosum (or granular layer) consists of flattened cells that contain coarse, basophilic granules. The stratum corneum (keratinous layer) is most superficial and consists of anucleate cells arranged in a basketweave pattern. On acral skin an additional layer called stratum lucidum is also present. The dermis consists of papillary dermis, consisting of a fine network of collagen and elastic fibers located immediately beneath the epidermis, and reticular dermis, which consists of thicker dense collagen bundles and extends to the subcutaneous fat. The thickness of the epidermis and dermis varies depending on the region of the body. Finally, the subcutis is composed of lobules of adipocytes separated by fibrous septae. Within the septae are blood vessels, lymphatics, and nerves.

The skin contains within it numerous adnexal structures such as hair follicles, sebaceous glands, eccrine and apocrine glands, as well as neurovascular elements. The number and appearance of adnexal structures vary at different body sites and can be a clue to a specific location on the body. For example, on facial skin there are numerous small

vellus hair follicles rooted superficially in the dermis. Large sebaceous lobules are associated with those hair follicles. Apocrine glands, for example, are mostly present on certain body sites such as the axilla and on the genitalia. In addition, the amount of actinic damage signified by the presence of elastotic (fragmentation of the elastic fibers that appears as irregular basophilic clumps) material can also provide clues to location of site.

Folliculo-Sebaceous Unit

The folliculo-sebaceous unit consists of a hair follicle and its associated sebaceous unit. In vertically oriented sections, the mature hair follicle in anagen phase consists of three parts: lower segment, which extends from the base of the follicle to the attachment of the muscle of hair erection or arrector pili muscle, middle segment (or isthmus), which extends from the attachment of arrector pili muscle to the entrance of the sebaceous duct, and upper segment (or infundibulum), which extends from the entrance of the sebaceous duct to the ostium of the hair follicle. The area where the arrector pili muscle attaches is also known as follicular “bulge.” Emanating from the sides of the hair follicle, at the junction of infundibulum and isthmus, are symmetrical cords of epithelial cells that extend laterally for a short distance, and then descend parallel with the follicle. This is referred to as the mantle of the follicle. It gives rise to the sebaceous glands and ducts. The lowest part of a follicle is named the bulb because it resembles

Fig. 2.1 Longitudinally transected hair follicles with associated sebaceous glands

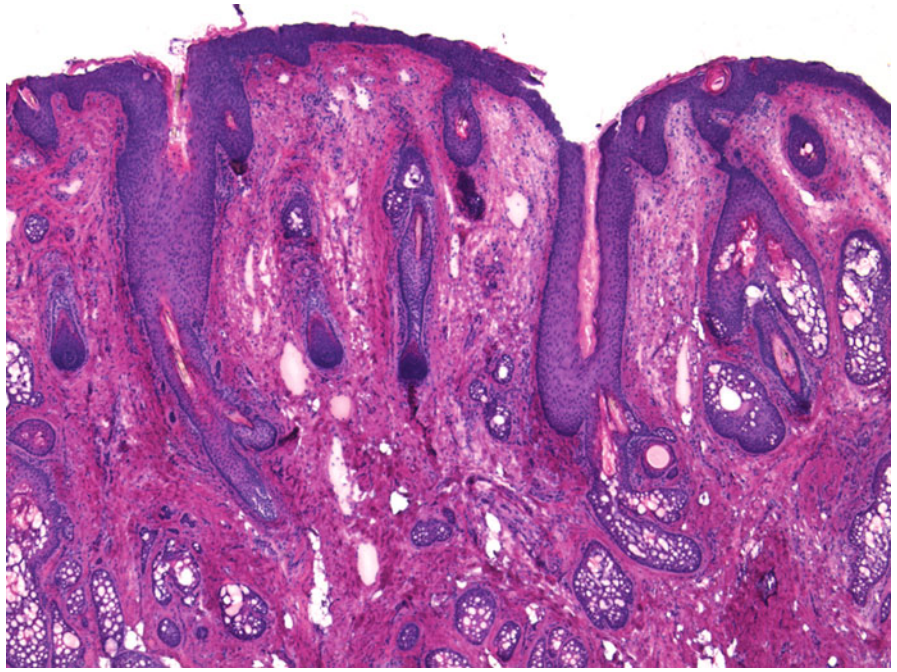
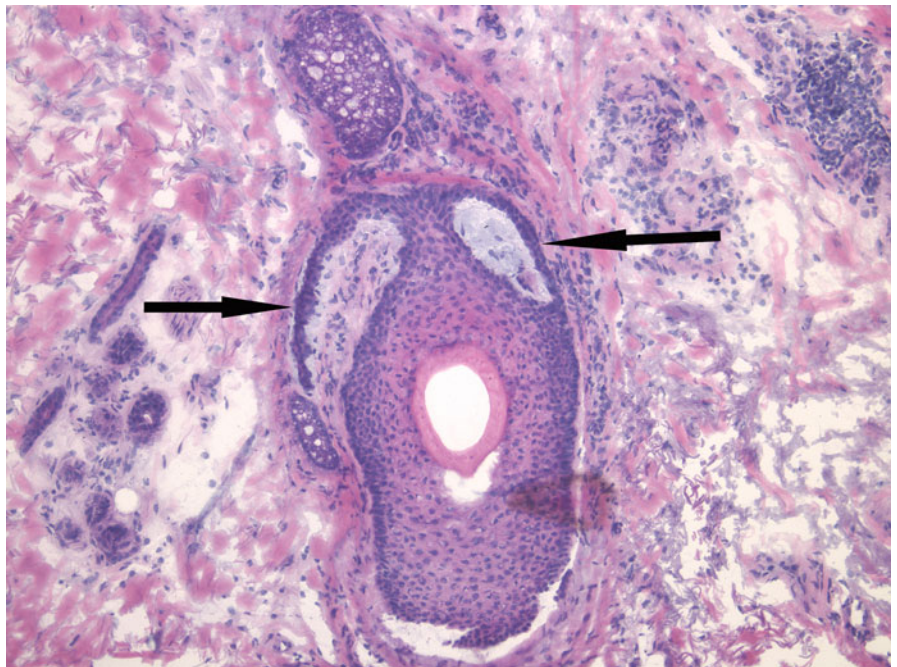


Fig. 2.2 Although seen as two cords of epithelial cells on longitudinal sections, the mantle (*arrows*) is actually an umbrella-like three-dimensional structure that encircles the hair follicles



the bulb of a tulip or an onion, and contains the matrix and germinative cells from which the hair shaft itself grows. The bulb also contains melanocytes, which are responsible for the color of the hair. The hair bulb surrounds a somewhat conical, highly vascularized area of connective tissue called

the papilla, which is responsible for blood supply to this area of high metabolic activity. The follicular papilla is separated from the epithelial cells by a basement membrane, which is continuous with the external glassy membrane surrounding the follicle.

Fig. 2.3 Follicular bulb (*B*) and papilla (*P*) of a hair follicle in anagen. The hair bulb hugs the follicular papilla, which is the fibrovascular core providing nourishment. The epithelium of the hair bulb consists of matrix cells admixed with melanocytes. Bright red trichohyalin granules are seen in the upper portion. A thin rim of fibrous tissue surrounds the follicle (*arrow*)

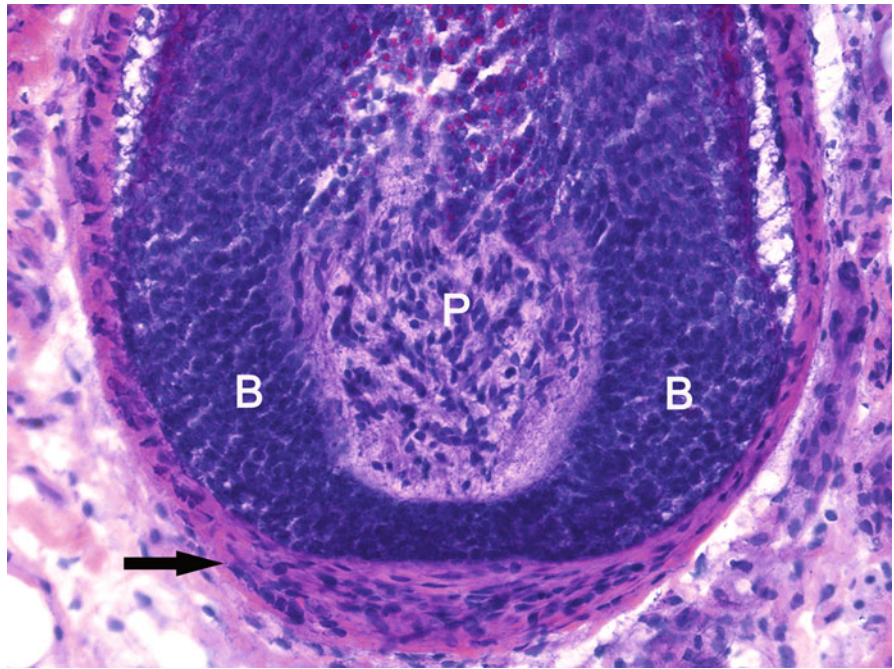
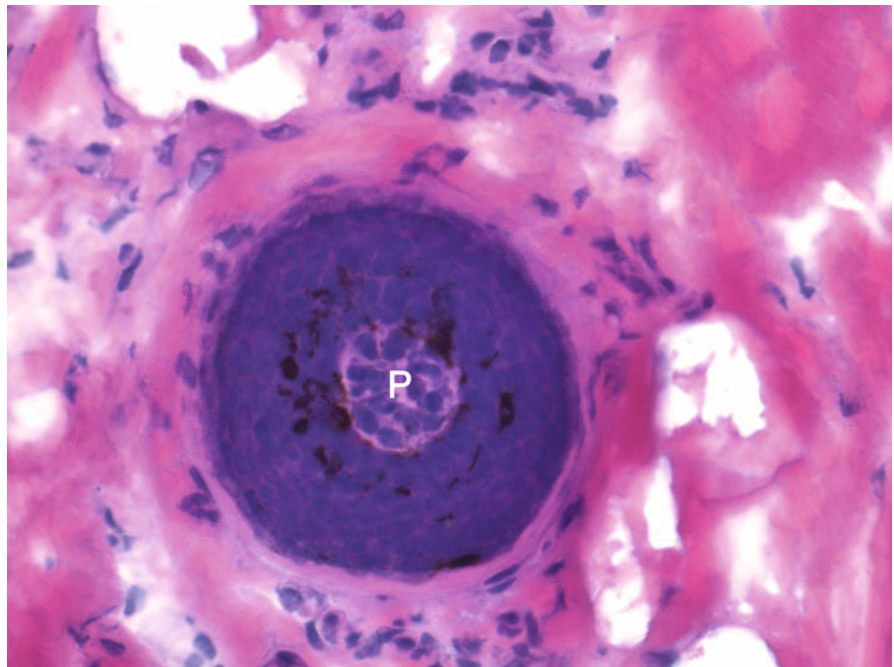


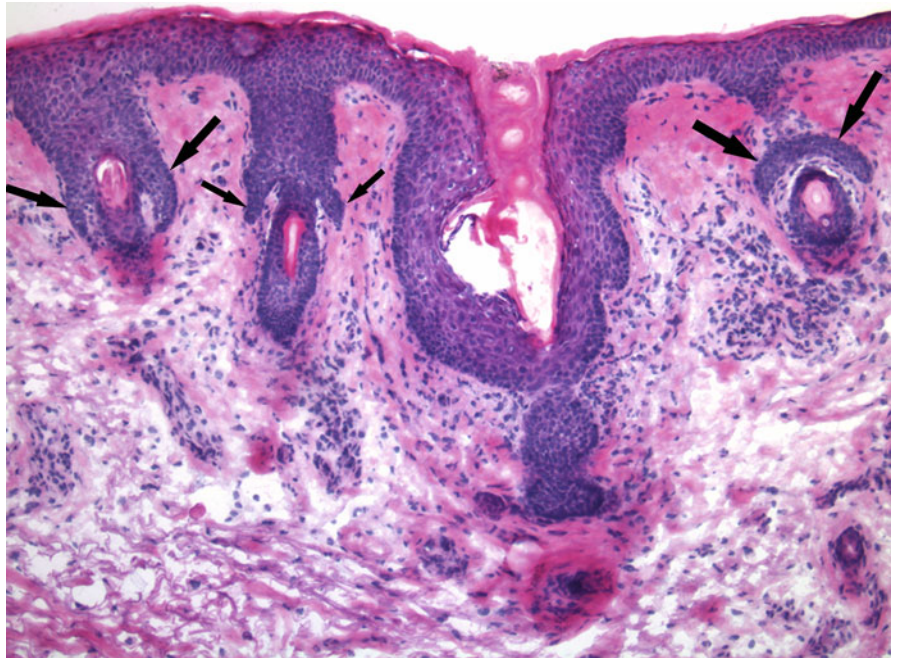
Fig. 2.4 A cross-section of a follicular bulb and a centrally placed papilla (*P*). Numerous melanocytes are admixed with matrix cells



Hair follicles undergo periods of growth and rest, which is reflected in changes in their microscopic appearance. Actively growing follicles penetrate deeply in the subcutaneous fat and demonstrate a prominent hair bulb. On the scalp and face, particularly in bearded areas of

men, terminal hair follicles are deeply rooted in the subcutaneous fat. In other areas of the face vellus hairs predominate, which are much smaller and superficially located. Their bulbs are present in either the superficial or mid reticular dermis.

Fig. 2.5 Vellus hair follicles on the face with prominent mantles (*arrows*)



The hair follicle consists of a series of concentric layers that form in the bulb and move progressively upward. These layers are often most obvious in the anagen growth phase. The outermost layer is a highly vascularized fibrous sheath. Immediately medial to that is a basement membrane followed by the outer root sheath. The cells of the outer root sheath are large, monomorphous, and with clear cytoplasm. Immediately medial to that area is the inner root sheath of the hair follicle consisting of a Henley's layer (which is the first of the lower follicle layers to keratinize), followed by the Huxley's layer (which also keratinizes and contains trichohyalin granules). The inner most layer is the hair shaft itself.

A sebaceous unit consists of a mature sebaceous gland comprised of several discrete sebaceous lobules and a sebaceous duct. The glands often appear clear or empty because they contain lipids that dissolve away during processing.

A sebaceous duct is a channel with thin, crenulated cornified epithelial lining that connects one or more sebaceous lobules to an infundibulum of the hair follicle. Each sebaceous lobule has a single row of immature sebocytes at the periphery and mature sebocytes in the center, which undergo complete disintegration and thus form the sebum in a process known as holocrine secretion. Sebocytes have scalloped nuclei and vacuolated, foamy cytoplasm.

Fig. 2.6 (a, b) Terminal hair follicles in anagen with follicular bulbs, papillae, and discernable follicular epithelial layers

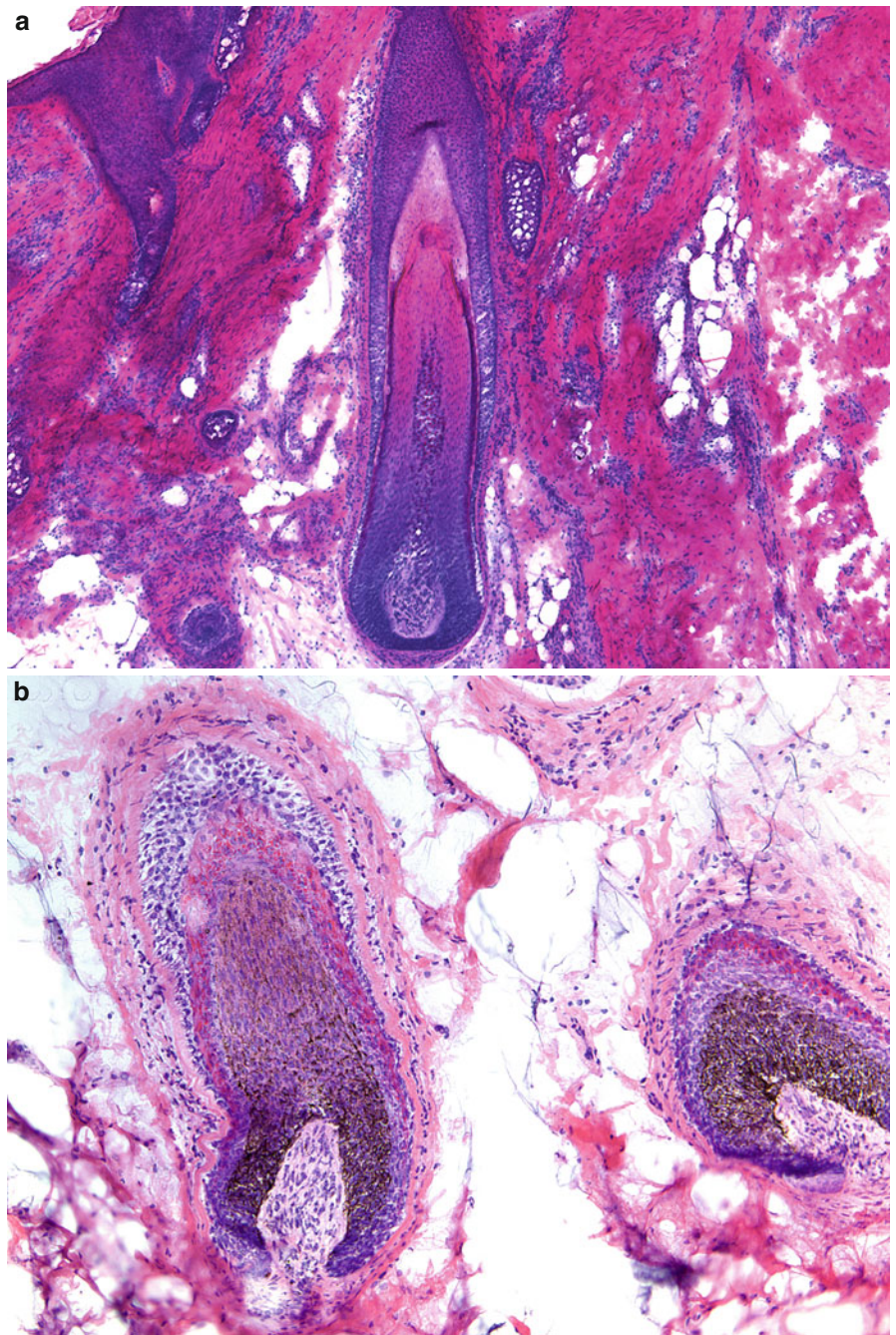


Fig. 2.7 Cross-section of hair follicles in anagen with hair shafts in the center and one miniaturized hair follicle (*arrow*)

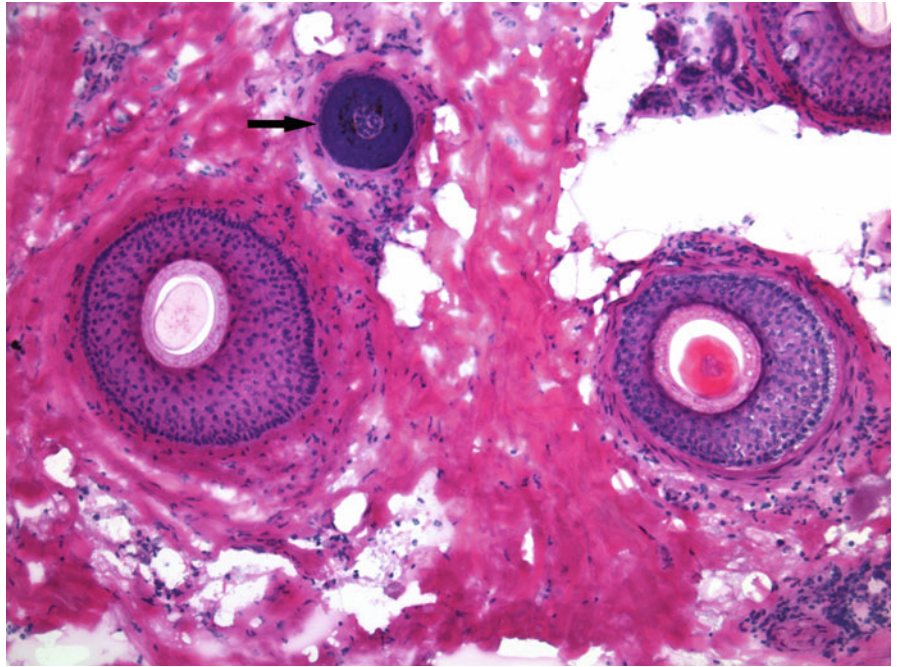


Fig. 2.8 Cross-section of hair follicles at the level of the sebaceous glands

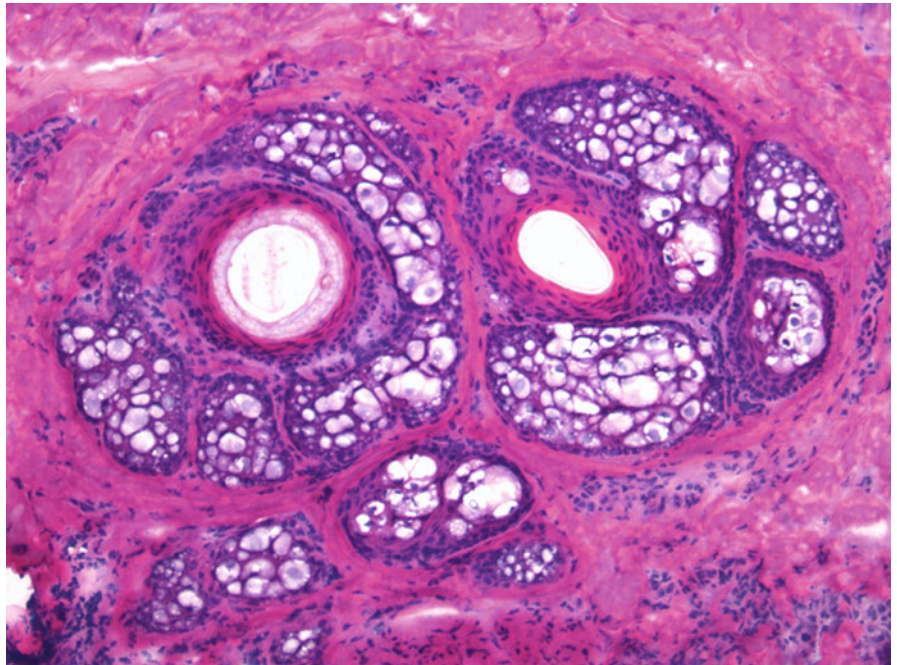
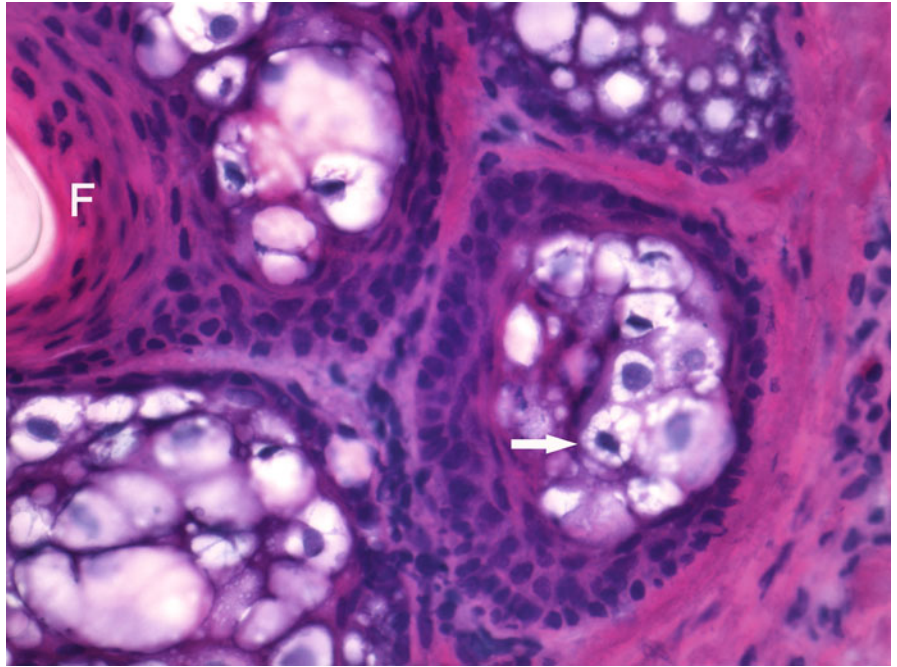


Fig. 2.9 Sebaceous glands surrounding a hair follicle (*F*), comprised of sebocytes, which have scalloped nuclei and vacuolated clear cytoplasm (*arrow*)



Nerves

Nerves are often seen in association with blood vessels as part of a neurovascular plexus. Nerves can be seen throughout the reticular dermis as well as in deeper tissues such as within subcutaneous fat and in between skeletal muscle fibers. The “basic unit” is a nerve fiber, which consists of an axon and the

surrounding Schwann cells. Multiple nerve fibers form nerve fascicles, which are surrounded by a sheath, called a perineurium. The space within the perineurium is called endoneurium. The endoneurium also contains fibroblasts, capillaries, and mast cells. Numerous nerve fascicles are grouped together into nerve bundles and are “held together” by a protective sheath referred to as epineurium. Often nerves are seen

Fig. 2.10 A medium sized longitudinally sectioned nerve (*N*) with surrounding collapsed blood vessels (*arrows*) and eccrine glands (*EG*) and ducts in the vicinity, all situated within the subcutaneous fat and adjacent to skeletal muscle (*SkM*)

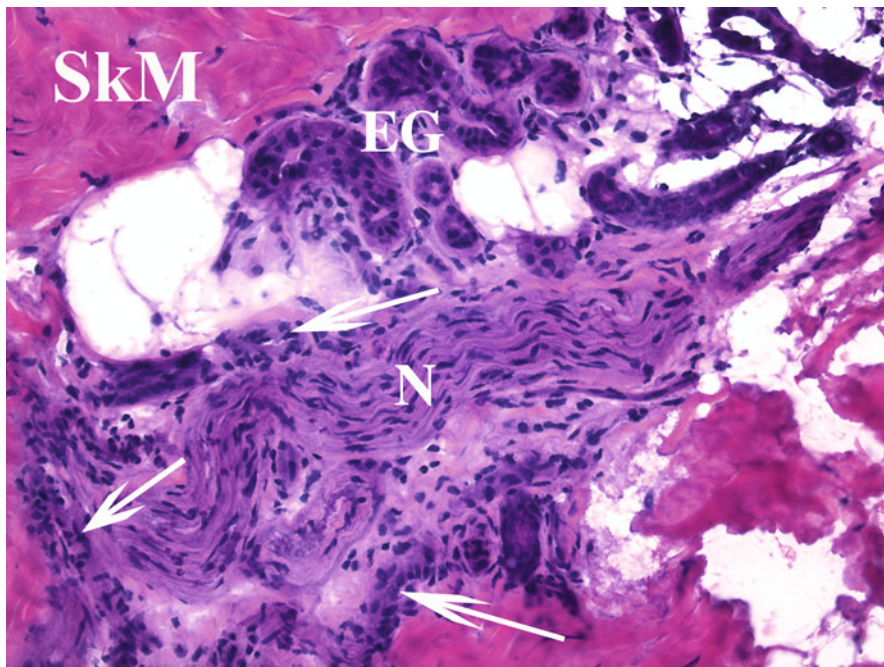


Fig. 2.11 Two longitudinally sectioned small nerves (*arrows*) surrounded by dense collagenous fibrous tissue called perineurium

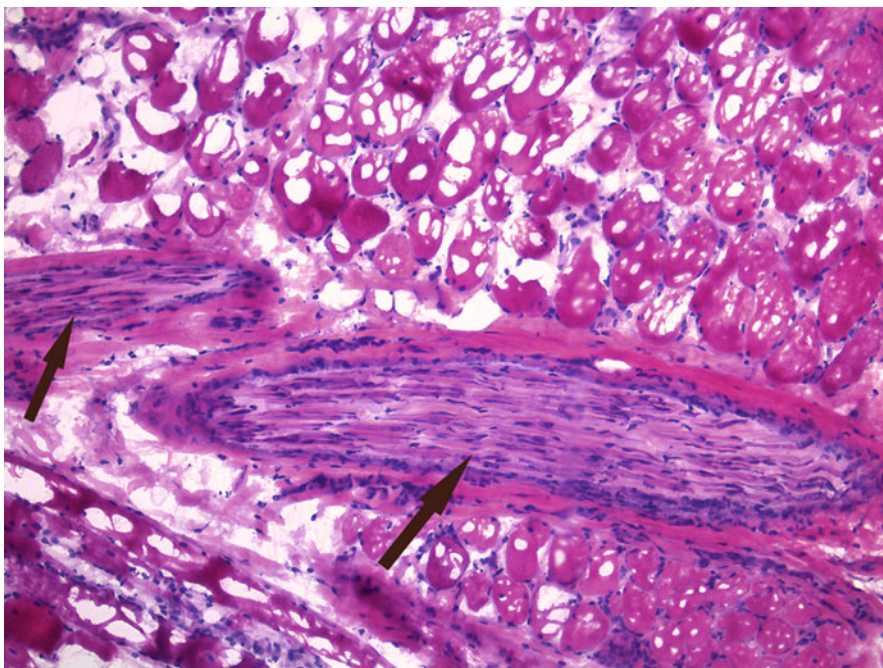


Fig. 2.12 Longitudinal zigzag alignment of nerve fibers with wavy, pointed nuclei

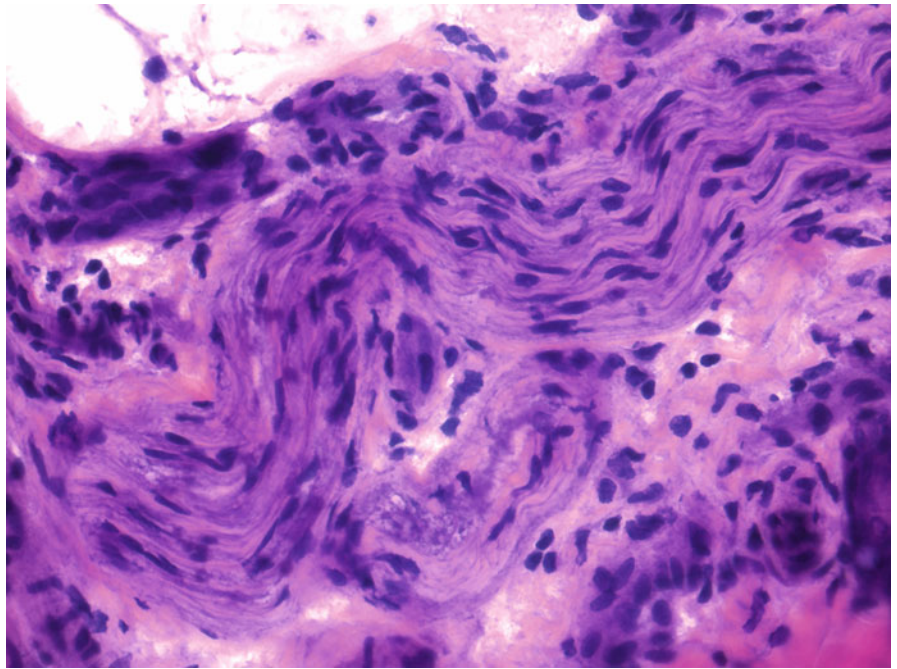
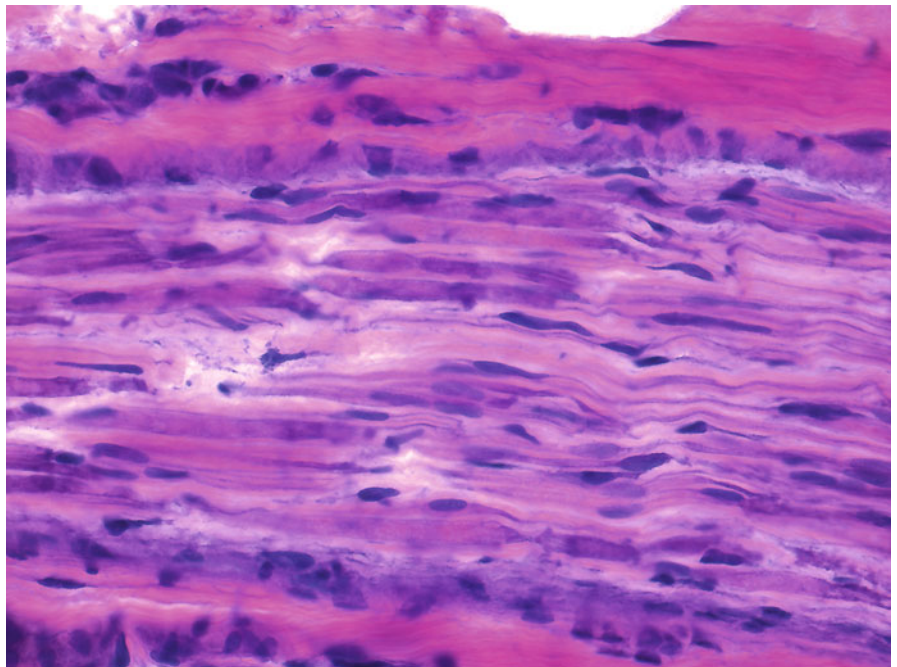


Fig. 2.13 Spindled pointed nuclei and long cytoplasmic processes oriented parallel to the long axis of the nerve fascicle



clumped together, some cut longitudinally and others cut transversely, but in close proximity to each other and each encased in a very thin fibrous sheath. When longitudinally sectioned, nerves show fascicles of spindled cells with

S-shaped nuclei and long thin cytoplasmic processes. Very often fine purple granules of different sizes are seen within the cytoplasm of the nerves. Small vacuoles are also noted in both longitudinal sections and cross sections.

Fig. 2.14 Three small nerves between skeletal muscles. The nerve on the right is longitudinally sectioned and the two nerves on the left are transversely cut

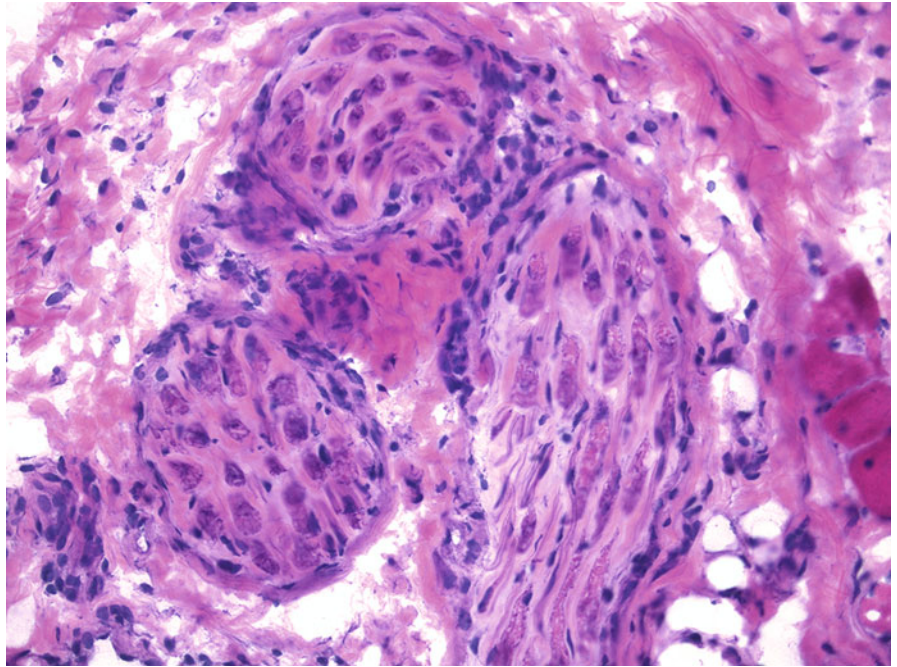
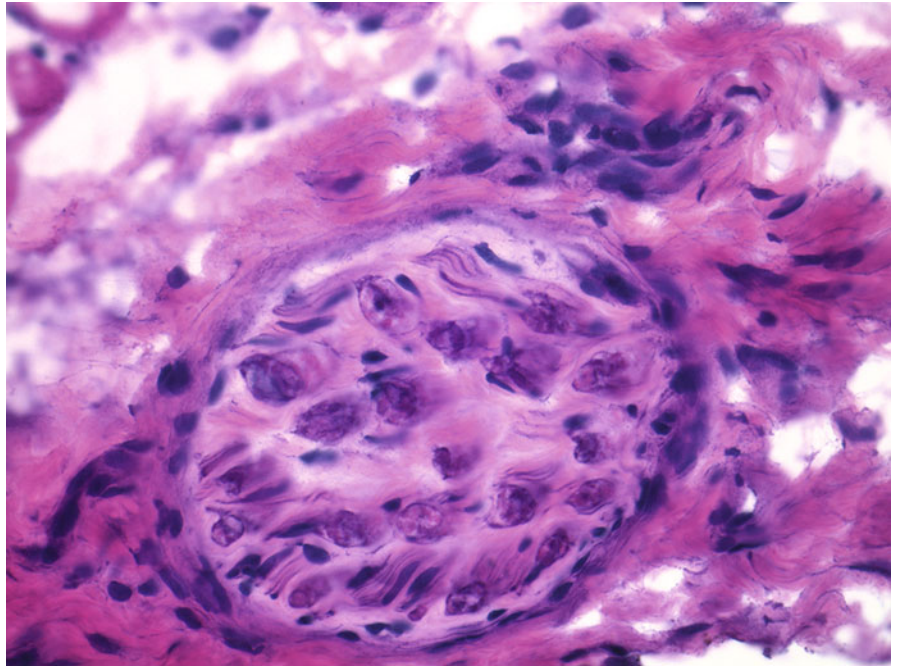


Fig. 2.15 Small nerve in a transverse section showing nerve axons in the center with a surrounding bubbly purple ring of myelin



Skeletal Muscle

Skeletal muscle fibers are typically located deep beneath the subcutaneous fat; however, depending on body site, they can be seen more superficially. The lip and eyelid are regions where skeletal muscle appears relatively superficially because of the lack of substantial subcutaneous adipose tissue in these areas. Skeletal muscle fibers are usually arranged in

large aggregates and fascicles. When longitudinally cut, the fascicles show a syncytium of cells with elongated blunt ended nuclei usually seen at the periphery, dense pink cytoplasm, and no distinct borders between the cells. In cross sections, skeletal muscle fibers are round, oval, or slightly angulated, containing round nuclei that are situated at the periphery. Dense pink non-vacuolated cytoplasm sometimes showing cross striations is seen in the center of the syncytium.

Fig. 2.16 Large fascicles of transversely cut skeletal muscle fibers, surrounded by a rim of fibrous tissue

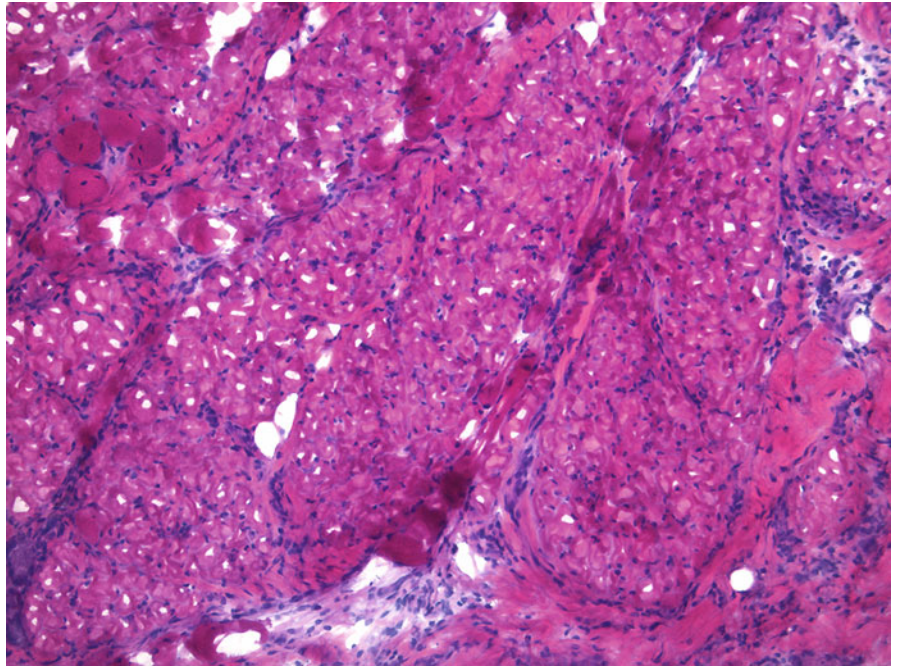


Fig. 2.17 Skeletal muscle fibers are a syncytium of cells without distinct borders

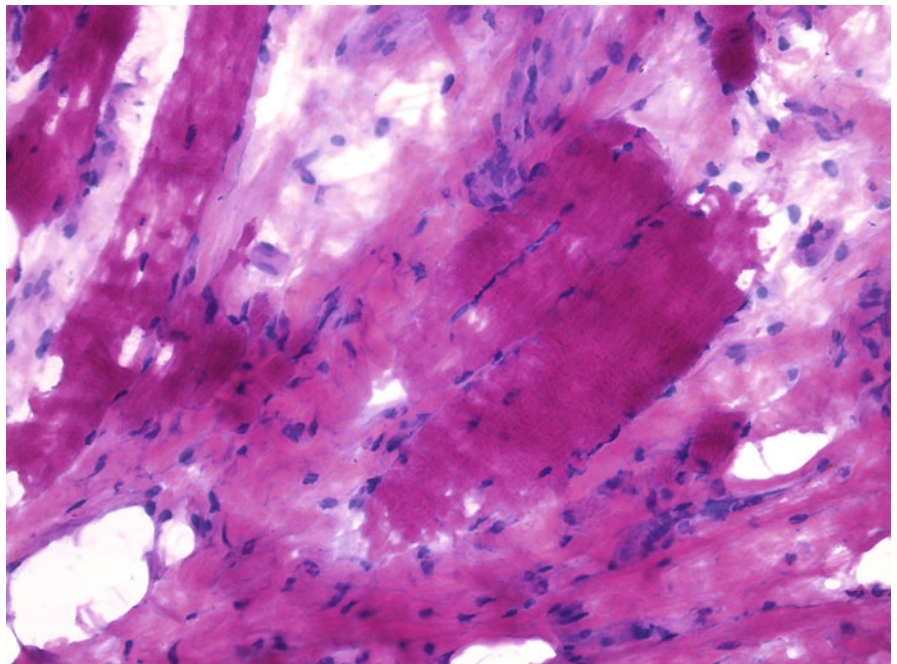


Fig. 2.18 The cells have elongated blunt ended nuclei and dense pink cytoplasm without vacuoles, distinguishing them from nerve fibers. Cross striations can be appreciated on high power (*arrows*)

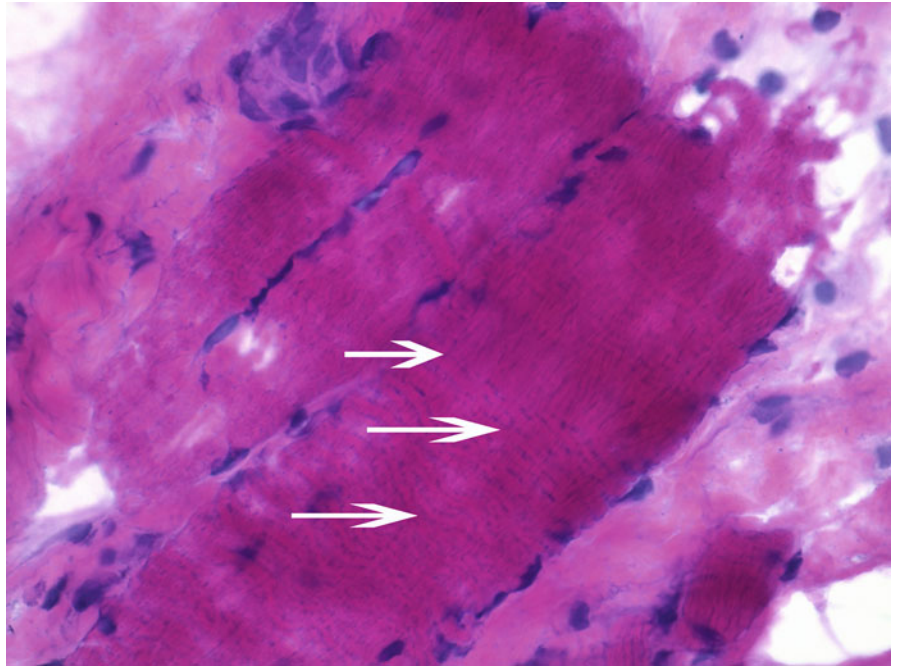
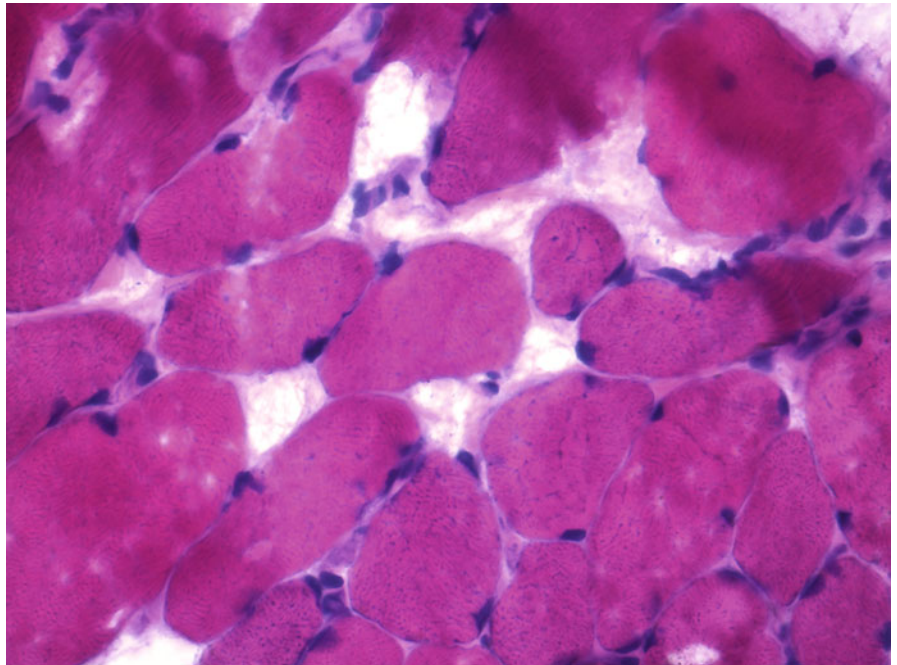


Fig. 2.19 Cross section of skeletal muscle fibers with round, oval, and slightly angulated contours



Smooth Muscle

Two types of smooth muscle are present in the skin: one is associated with hair follicles and the other is found in vessel walls. The muscle of hair erection (arrector pili or pilar muscle) is attached at a 45° angle in the mid-portion of the hair follicle, in the region of the mantle. Its upper portion attaches within the papillary dermis. When the pilar muscle contracts, it pulls the skin surface around the hair, which

elevates the hair shaft and produces what is known as “goose bumps.” Fascicles of pilar muscle can vary in shape and appear elongated, oval, or sometimes round. On longitudinal sections they reveal a syncytium of cells without distinct cellular borders, with elongated blunt ended nuclei, often oriented parallel to each other, and surrounded by eosinophilic cytoplasm. When cut transversely the nuclei appear round.

Fig. 2.20 Smooth muscle of hair erection (*arrows*) running at a 45° angle toward the mid portion of a hair follicle

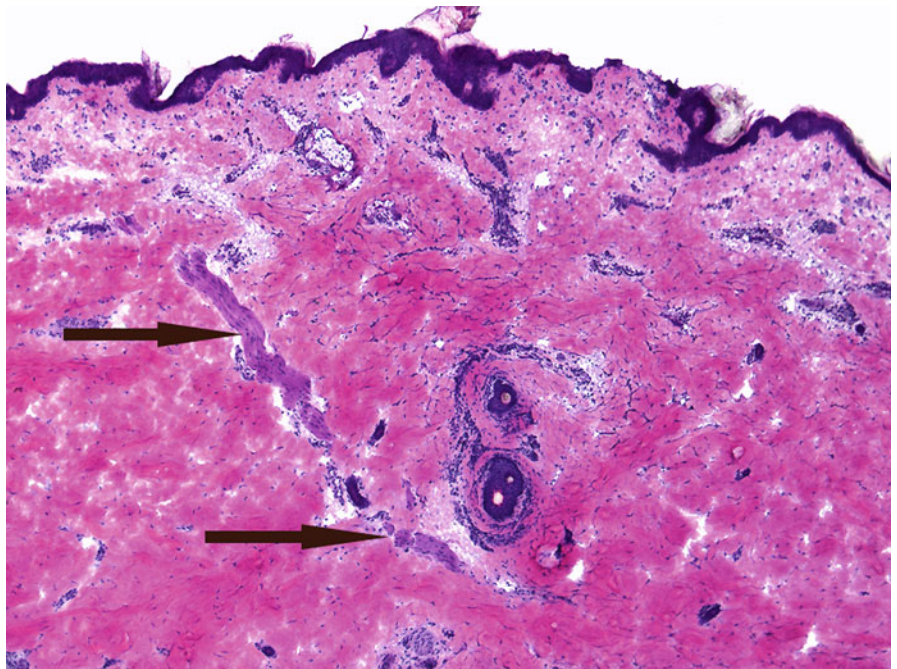
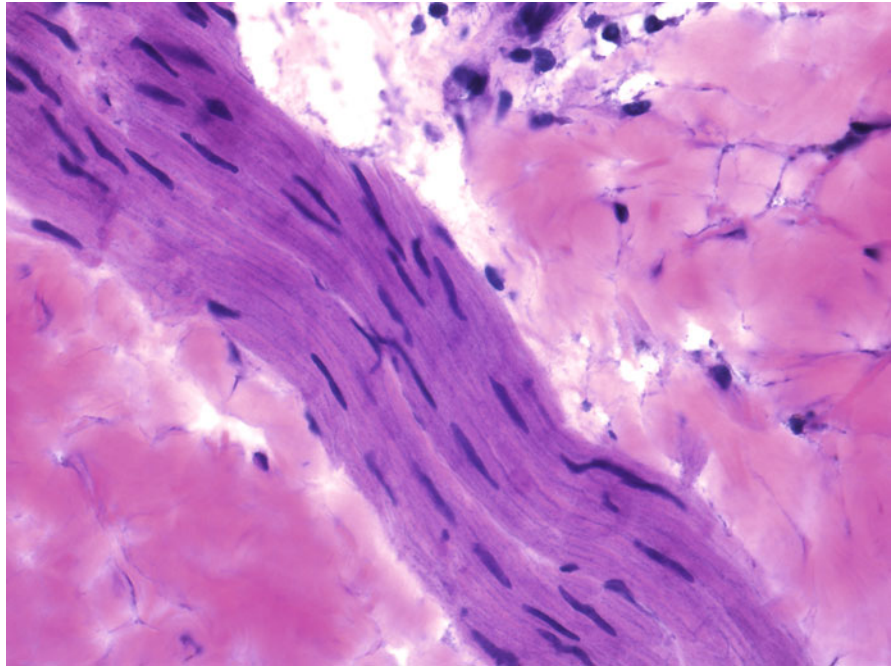


Fig. 2.21 Longitudinal section of smooth muscle with blunt ended elongated nuclei dispersed throughout the abundant eosinophilic cytoplasm that lacks cross striations



Nerves and smooth muscle can sometimes be difficult to differentiate for the novice. Aggregates of smooth muscle fibers are usually quite large as opposed to nerves especially in the superficial portion of the dermis. Large nerves are not seen there because they branch into smaller nerve fibers and present as nerve twigs in the most superficial portion of the dermis. Aggregates of pilar muscle have irregular shapes as opposed to nerves, which are either round, oval, or slightly elongated and encased in a thin fibrous sheath. Purple

granules seen within the cytoplasm of nerves are not observed within smooth muscle fibers. Smooth muscle fibers that are associated with a hair follicle and have as a main function erection of hair follicles are always seen in the upper, mid and, extremely rarely, in the lower reticular dermis. They are never present in the subcutaneous fat or in deeper soft tissues even when associated with terminal hair follicles deeply rooted in the subcutaneous fat as seen on the scalp and in bearded areas of the face in men.

Vessels

Dermal vasculature consists of superficial and deep vascular plexuses. The upper plexus is beneath the papillary dermis and the deep plexus is in the lower part of the reticular dermis. The arteries in the subcutaneous fat and larger arterioles

in the deep reticular dermis have three layers. The internal layer or “intima” contains endothelial cells and an internal elastic membrane. The second layer or “media” contains collagen, elastic fibers, and several concentric layers of smooth muscle cells. In muscular arteries, there is also an external elastic membrane. The outer layer is “adventitia”

Fig. 2.22 Nerves (*N*) and vessels (*V*) often run together

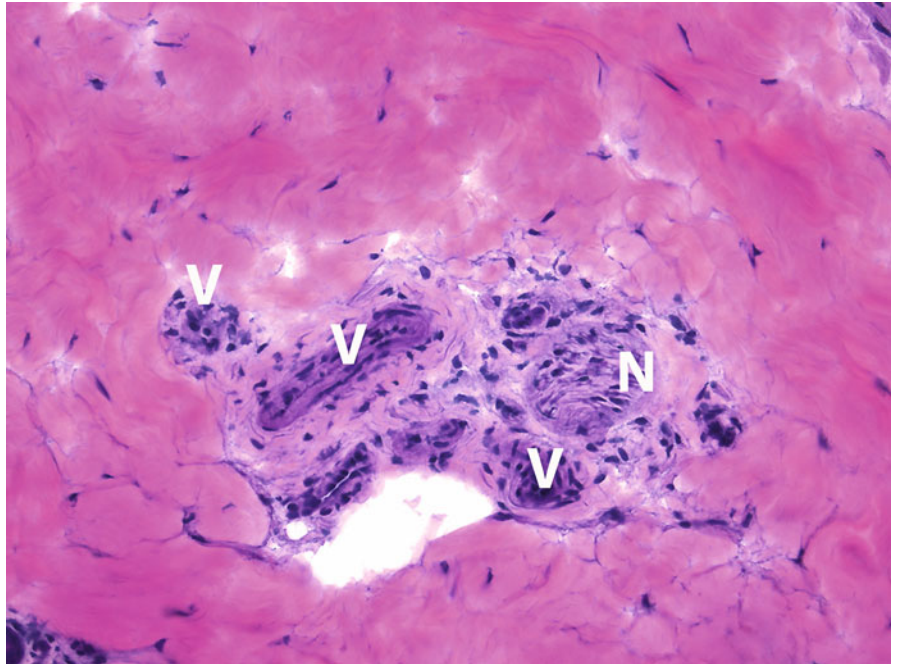
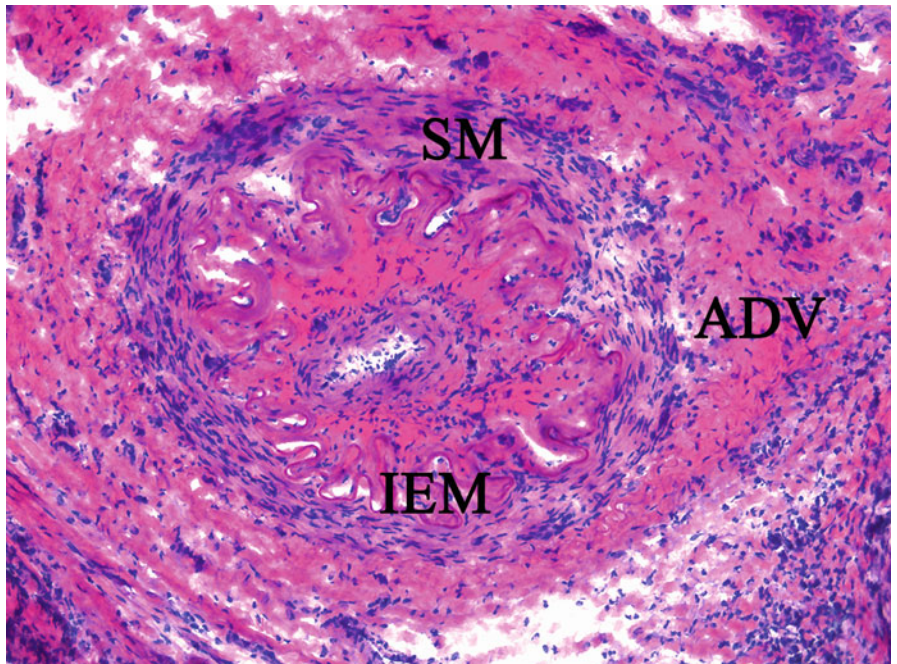


Fig. 2.23 A medium size artery with a small open lumen in the center, internal elastic membrane (*IEM*), smooth muscle layers (*SM*), and adventitia (*ADV*)



composed of fibrocytes, collagen, and elastic fibers. Small arterioles have only a single layer of smooth muscle cells. Capillaries are composed of a single layer of flattened

endothelial cells without a muscular or adventitial layer. Veins are distinguished by their thinner walls, wider lumina, and the presence of valves.

Fig. 2.24 A small artery (A) with a narrow lumen and a vein (Vn) with widely open lumen

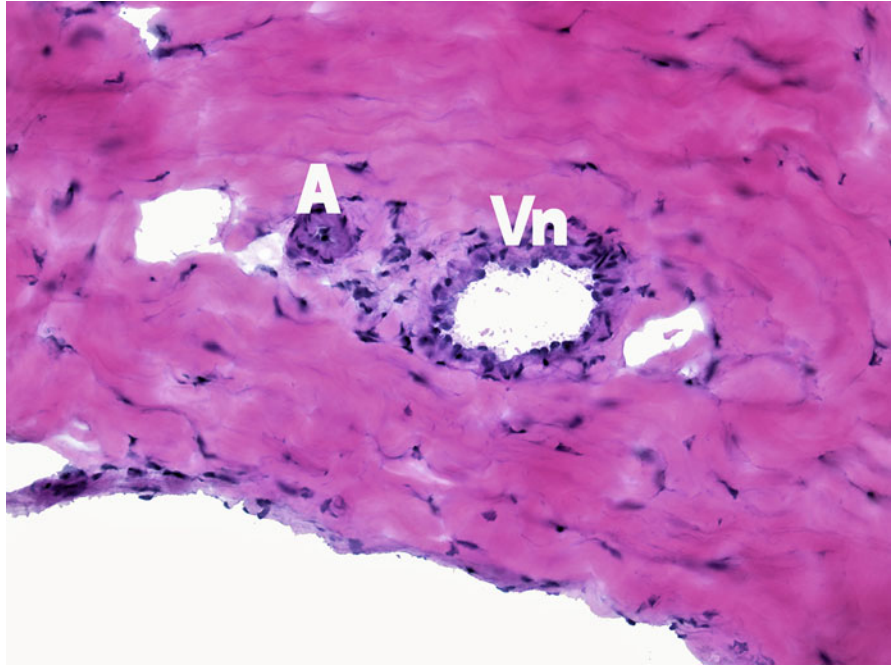
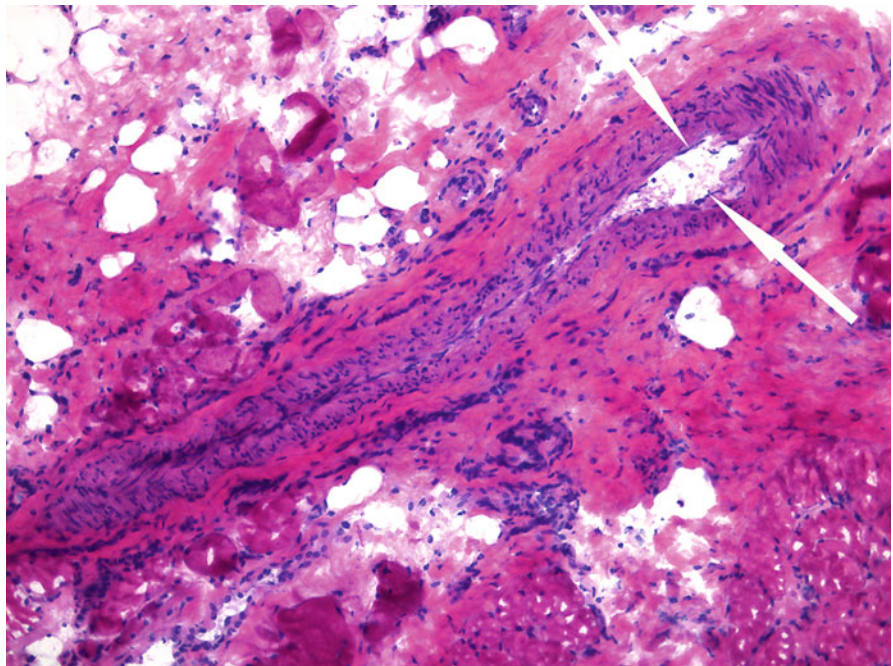


Fig. 2.25 A medium to large vein in longitudinal section with a patent partially collapsed lumen lined by flat endothelial cells (arrows)



Eccrine Glands

Sweat glands are unbranched, tubular structures that are composed of three segments: the intraepidermal duct (also known as the acrosyringium), the intradermal duct, and the secretory portion. The secretory portion of the gland forms a compact coil deep in the dermis and upper subcutaneous fat. In histologic sections, the glands appear as a mass of tubules cut in various planes. Eccrine glands are interspersed with

sections of the proximal part of the excretory duct. The eccrine glands consist of a single layer of large cuboidal or columnar cells surrounded by myoepithelial cells. The intradermal duct consists of a single layer of luminal cells and two or three rows of outer cells. The intraepidermal duct is composed of two layers of small, cuboidal basaloid cells. Unlike the secretory portion of the eccrine gland, the duct does not have a peripheral hyaline membrane zone but the lumen is lined with an eosinophilic cuticle.

Fig. 2.26 A longitudinally cut eccrine duct spiraling in its lower portion and leading to a group of eccrine glands located in the subcutaneous fat

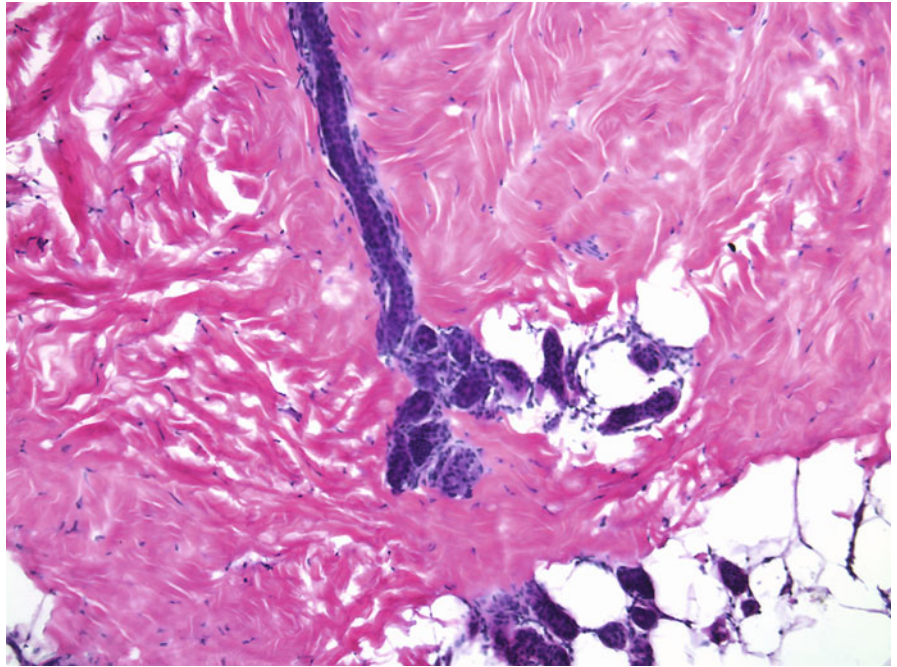
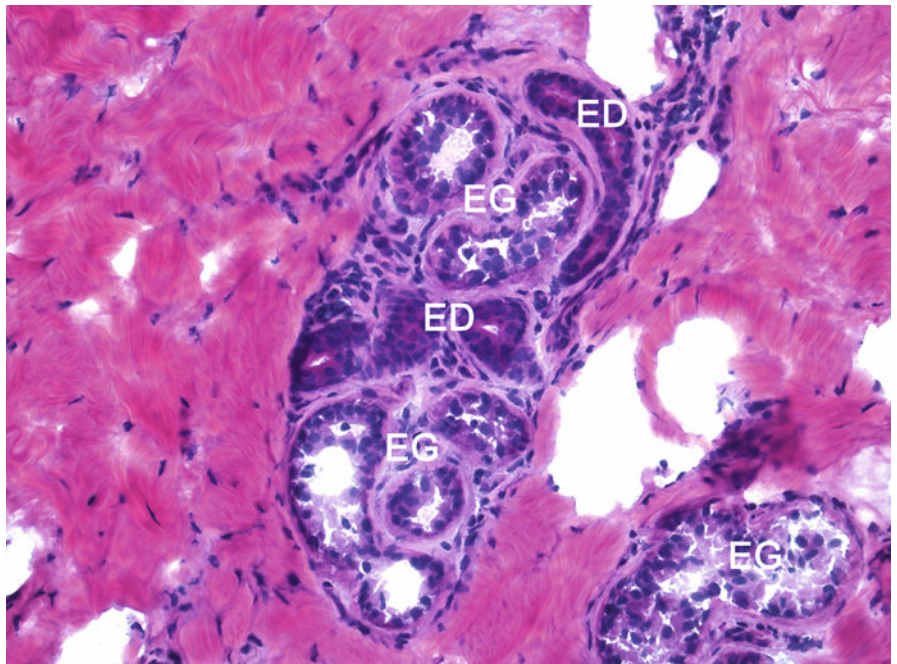


Fig. 2.27 A group of eccrine ducts (ED) with a lumen covered by a pink cuticle and eccrine glands (EG), which are lined by cuboidal cells and filled with pink secretion



Salivary Glands

Salivary glands are divided into numerous lobules each containing many secretory units. The glands consist basically

of ductal and acinar portions. Large excretory ducts have dilated lumina filled with secretions.

Fig. 2.28 A scanning magnification of a salivary gland comprised of lobules each containing many secretory units and excretory ducts

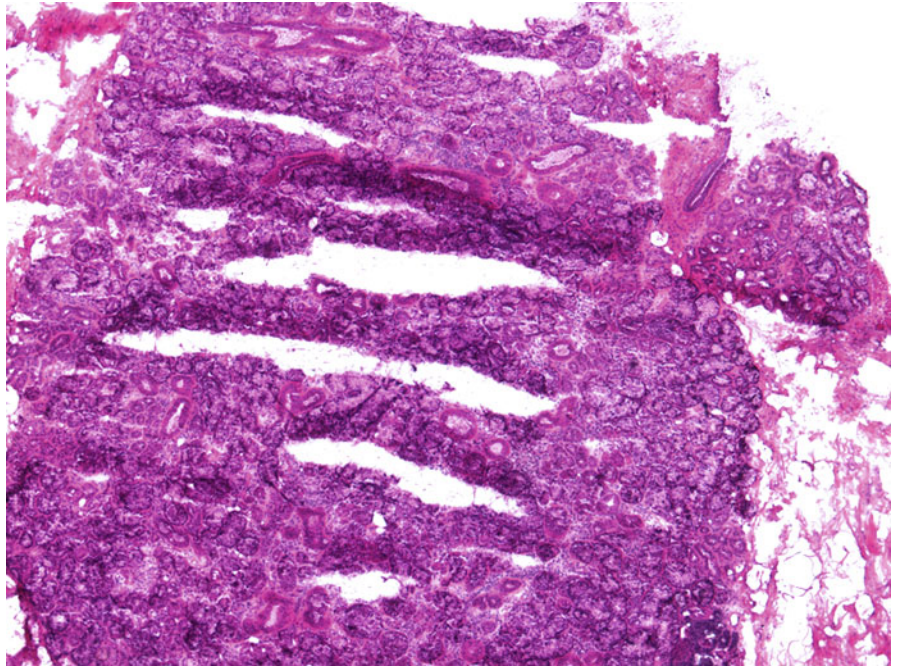


Fig. 2.29 The secretory units (*SU*) of the salivary glands are round and lined by cells that disintegrate to form holocrine secretions. The cell nuclei are positioned at the periphery of the glands. A thin rim of fibrous tissue (*arrow*) surrounds the entire glands. The salivary ducts (*SD*) are lined by two layers of cuboidal cells with eosinophilic cytoplasm. A thin layer of myoepithelial cells encircles the ducts. Pink amorphous secretions are seen in their patent lumina

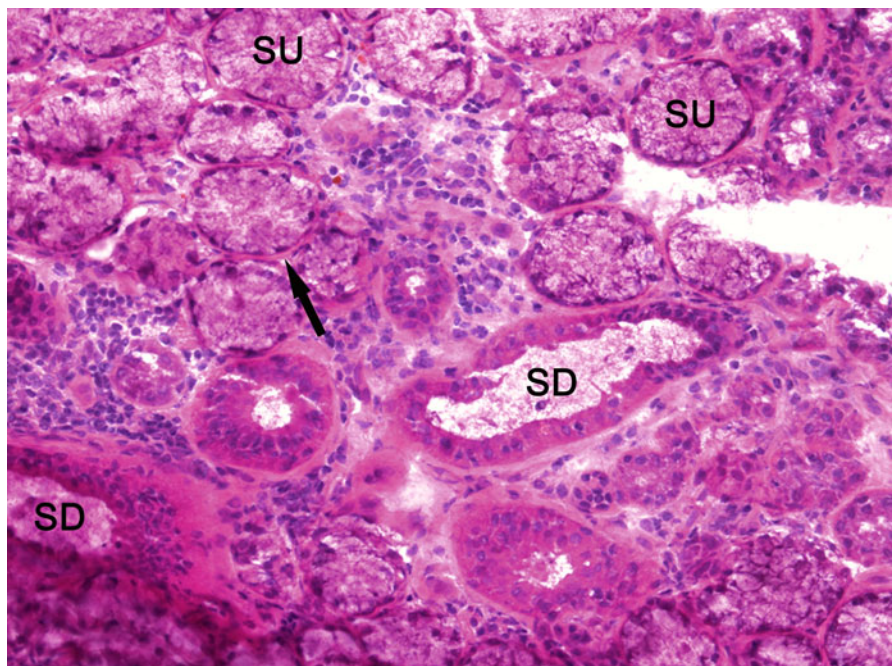


Fig. 2.30 Minor salivary gland: low power view of aggregates of a portion of minor salivary gland (*thin arrows*) deep in the subcutaneous tissue. Three large nerves in longitudinal sections are also seen (*thick arrows*)

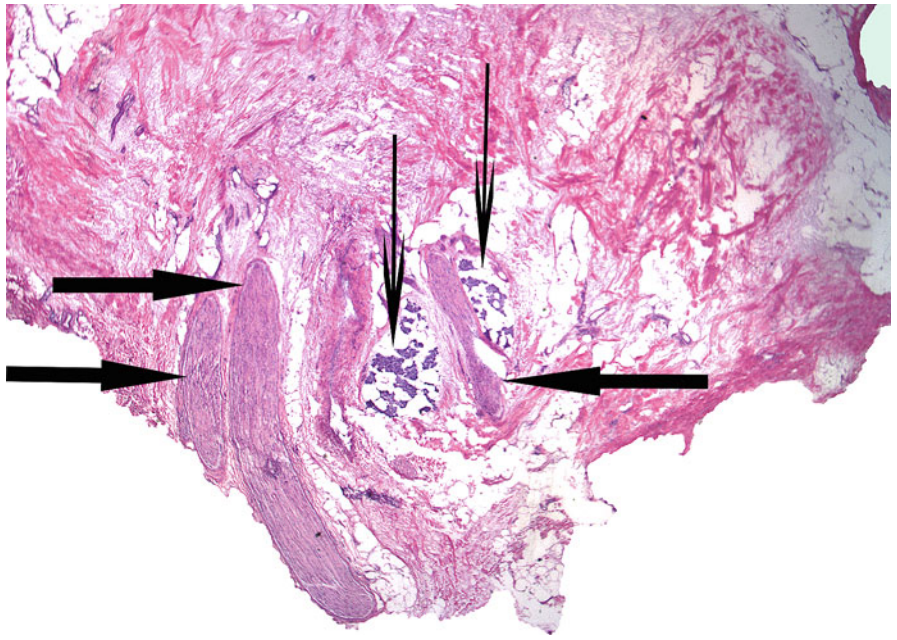


Fig. 2.31 Minor salivary gland: closer examination reveals that these are acini of a minor salivary gland with glandular structures organized in lobules with small lumina seen in the center of the acini

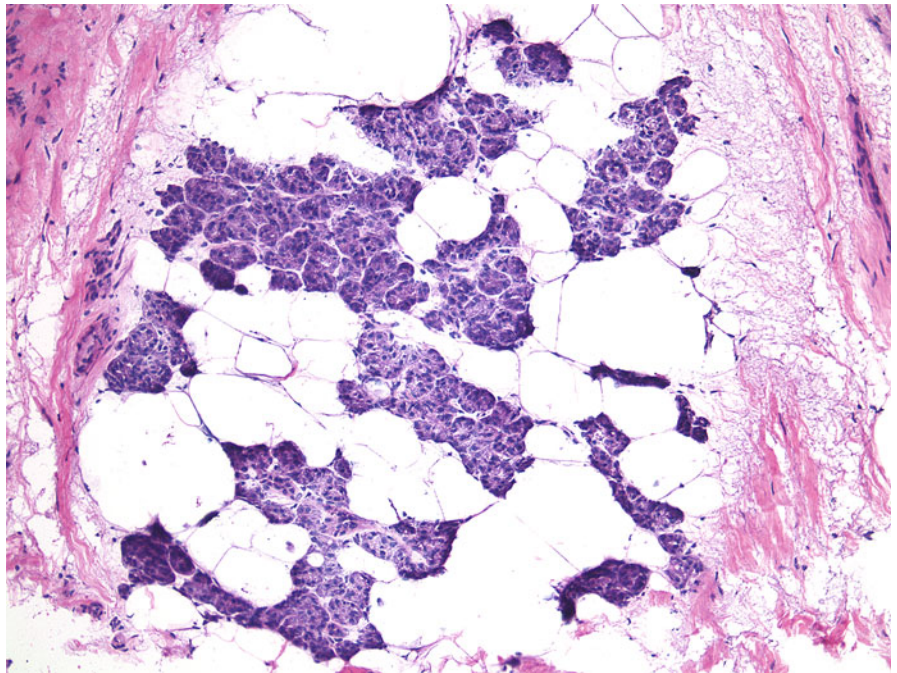


Fig. 2.32 Parotid gland: sheets of basophilic staining cells organized in clusters/groups

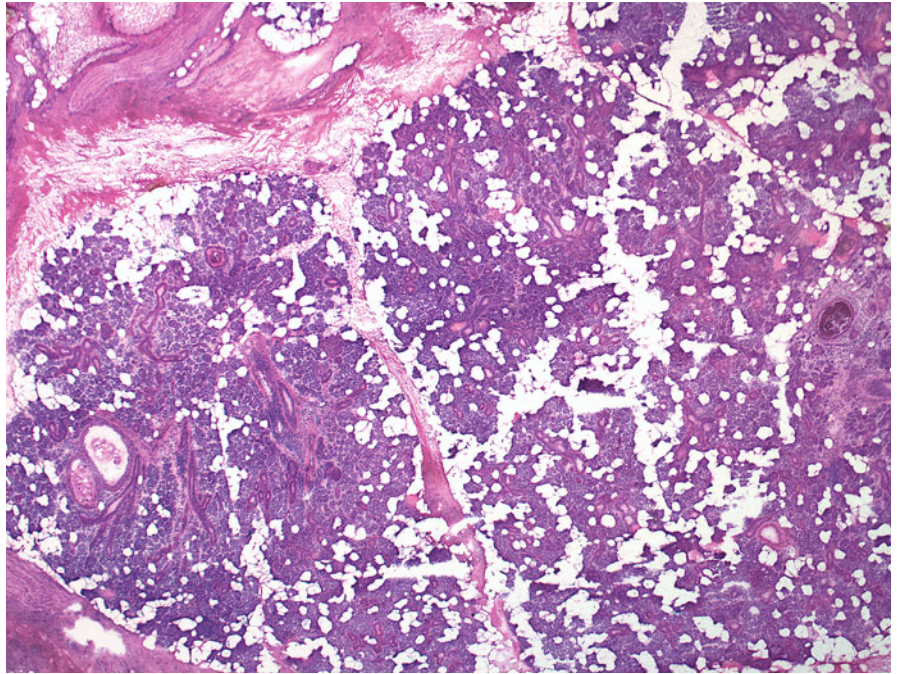
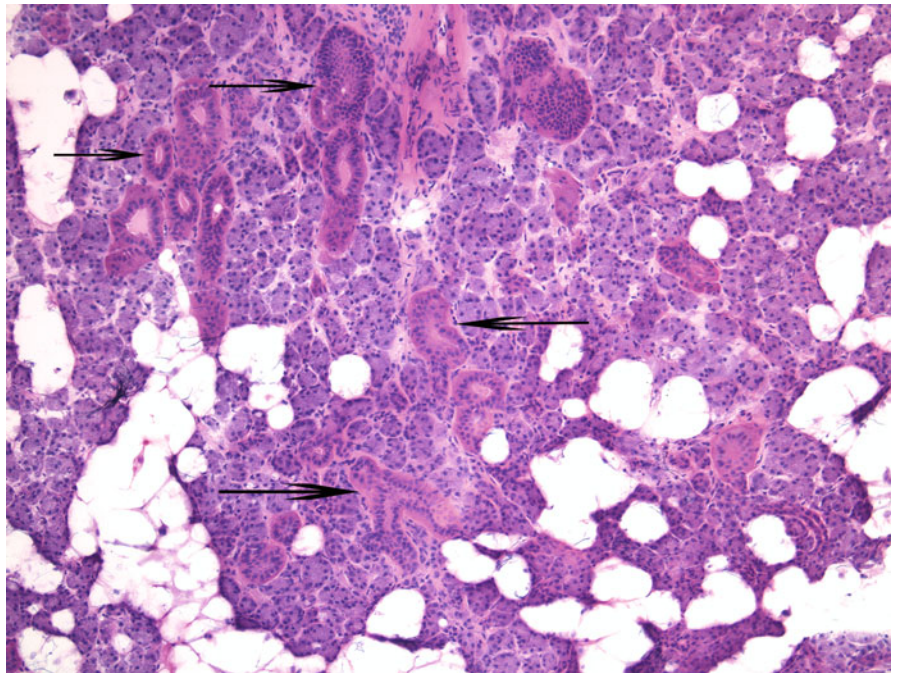


Fig. 2.33 Parotid gland: higher magnification reveals glands and ducts (arrows)



Apocrine Glands

Apocrine sweat glands are mainly confined to the axillae and the genital regions where they produce a viscid milky secretion. They can also be present on the forehead/scalp, areolae, as well as the periumbilical region. Apocrine glands are situated in the subcutaneous fat and their secretions are discharged into an adjacent hair follicle via a duct. Like eccrine glands, apocrine glands also consist of three segments: the intraepidermal duct, the intradermal duct, and the secretory portion. The secretory portion of

the gland is of the coiled, tubular type with widely dilated lumina. This portion of the apocrine glands consists of a single layer of cuboidal cells that have eosinophilic cytoplasm and are surrounded by a layer of myoepithelial cells. The snouting or budding of the apical portion of the cytoplasm is characteristic of the apocrine type of decapitation secretion. Like the eccrine duct, the apocrine duct is often lined by two layers of basophilic cuboidal cells with a periluminal eosinophilic cuticle, and an outer layer comprised of circumferentially arranged elongated myoepithelial cells.

Fig. 2.34 Apocrine glands: scanning magnification showing apocrine glands in the axilla

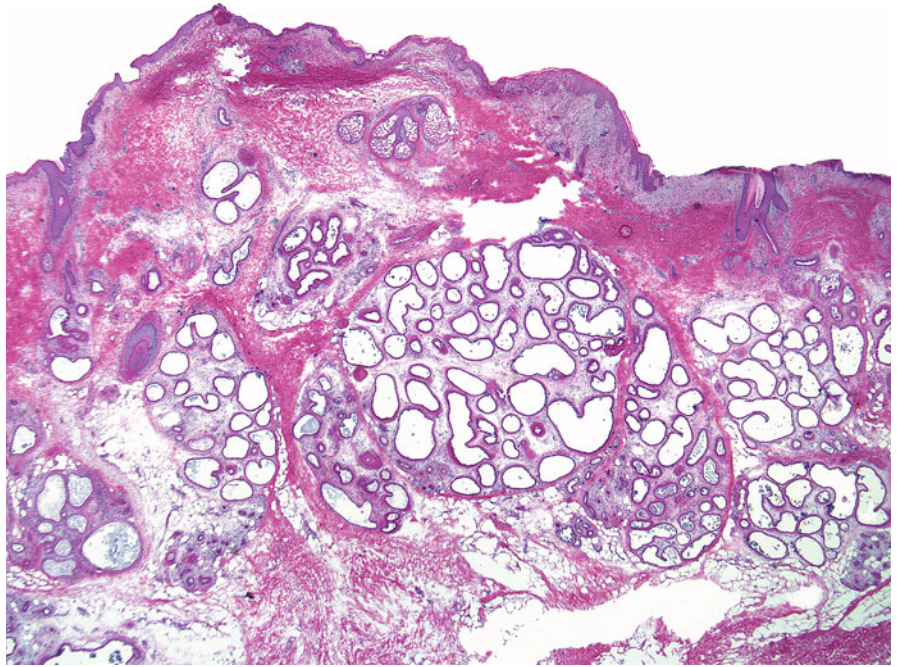
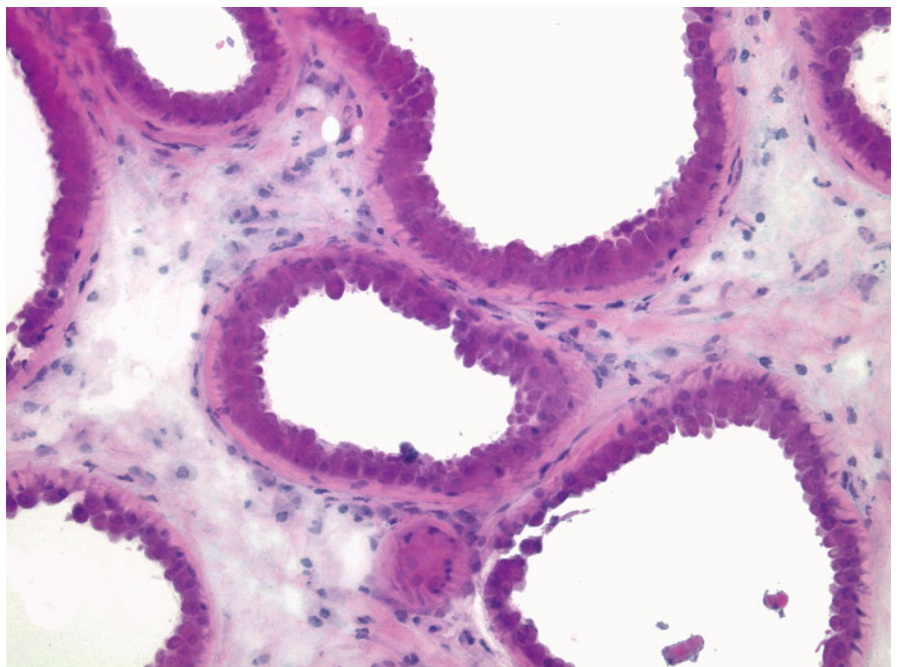


Fig. 2.35 Apocrine glands: widely dilated lumina of apocrine glands lined by two layers of cuboidal cells demonstrating decapitation secretions

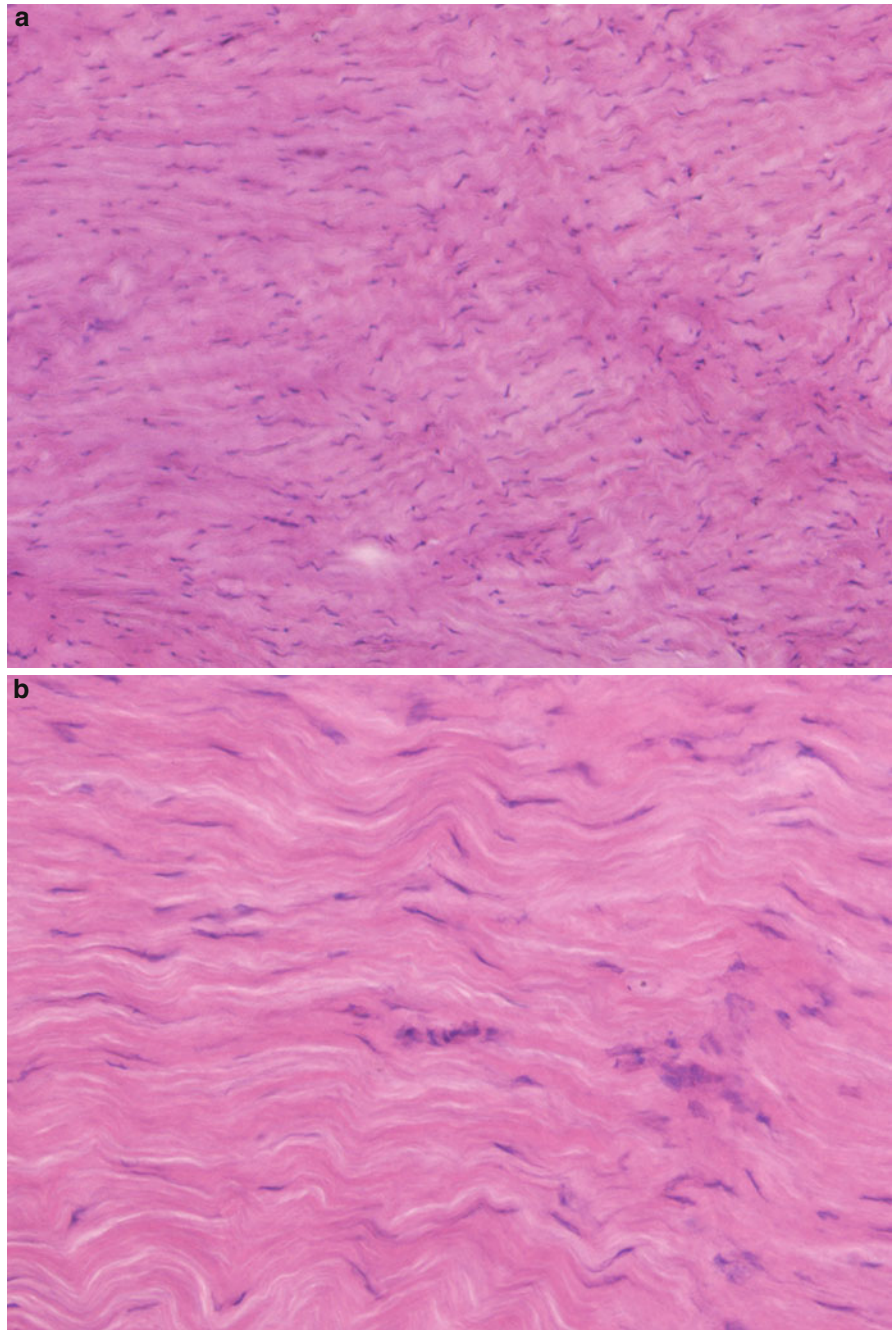


Periosteum

Periosteum is a layer of condensed fibrous tissue that covers the bone. It is comprised of cells arranged parallel to each

other that closely resemble fibroblasts with thin elongated nuclei embedded in dense eosinophilic fibrous stroma. The periosteum is richly supplied with blood vessels from adjacent connective tissue (Fig. 2.36).

Fig. 2.36 Periosteum: (a) Dense eosinophilic fibrous stroma with slender, wavy fibroblasts. (b) Higher magnification showing the compact nature of the eosinophilic stroma as well as the parallel arrangement of both the cells and the stroma



Scar Tissue

Immature (recent) scar tissue is composed of plump fibroblasts and slightly increased collagen bundles oriented parallel to the skin surface. There are vertically oriented,

newly formed blood vessels. As the scar matures, the fibroblasts become less discernable, slender, and fewer in number. The collagen fibers become more prevalent, thickened, and display horizontal orientation.

Fig. 2.37 Scar: a section taken from a recent biopsy, which shows significant scar tissue. There is epidermis on the left and a denuded area with immature scar underneath on the right

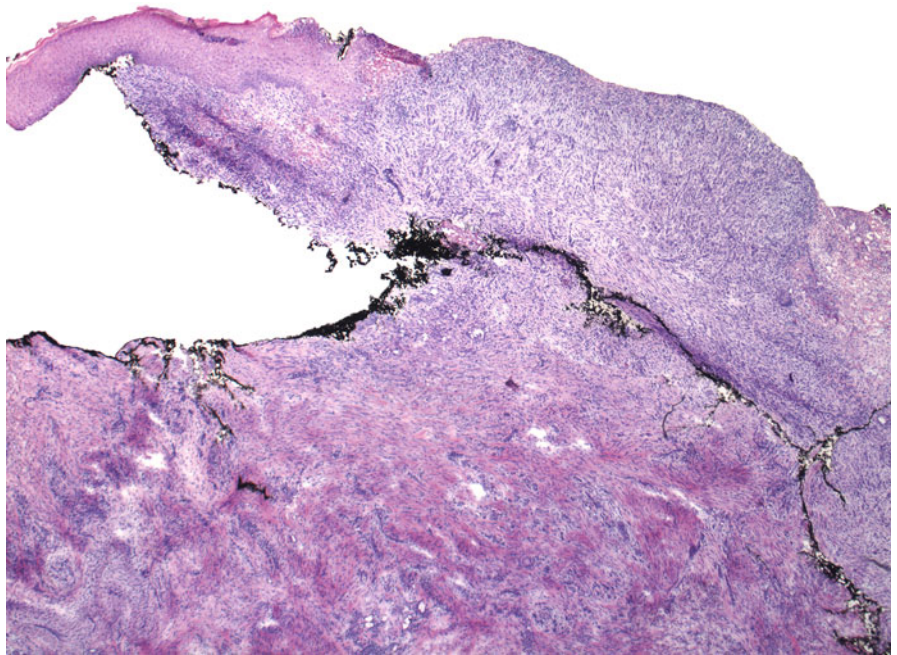


Fig. 2.38 Scar: a higher power view of immature scar tissue containing plump fibroblasts and numerous newly formed blood vessels lined by plump endothelial cells. Many vessels are aligned parallel to each other and perpendicular to the skin surface (*arrows*). Mild perivascular lymphocytic infiltrate is also seen. There is slight dermal edema

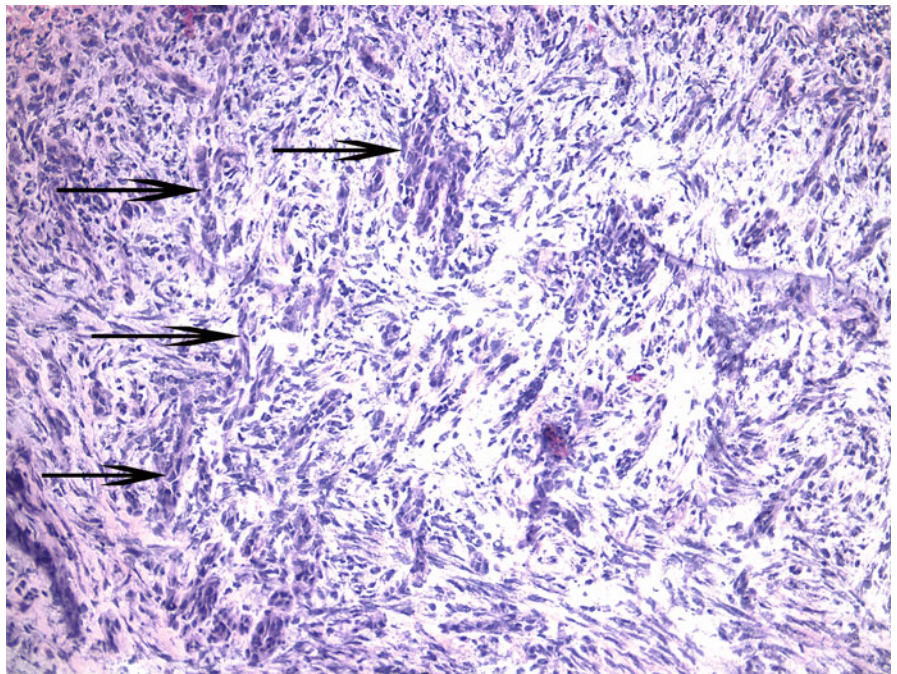
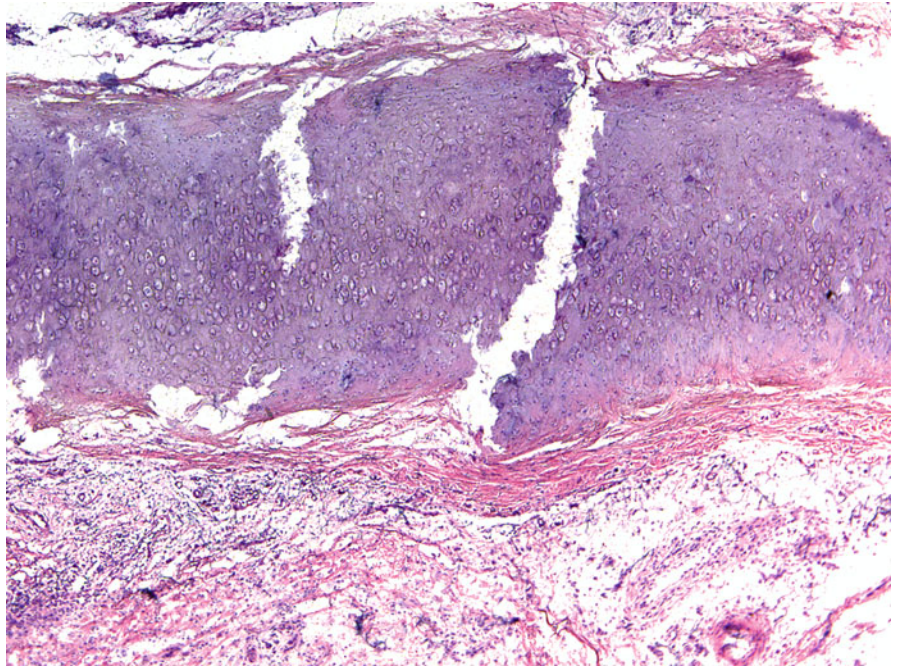


Fig. 2.39 Normal cartilage from the ear: cartilage is composed of chondrocytes positioned within lacunae



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