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Anatomy of Sweat Glands

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Sweat glands are widely distributed over the skin. The total number lies between 2 and 4 million. Each gland weighs approximately 30–40 μg. The aggregate weight of all sweat glands is roughly 100 g, i.e. almost equivalent to that of a kidney. Thus, sweat glands form the largest exocrine gland of the body.

At least 2 types of sweat glands are distinguished concerning development, morphology and function: *eccrine sweat glands* forming the majority and *apocrine sweat glands* which are present just in limited areas. However, there is increasing evidence that further types of sweat glands exist in distinct body regions.

Eccrine Sweat Glands

Eccrine sweat glands are distributed over nearly the entire body surface. They are most numerous on the sole of the foot ($620 \pm 20/cm^2$) and the forehead ($360 \pm 60/cm^2$) followed by the palms ($300 \pm 50/cm^2$) and the cheek ($320 \pm 60/cm^2$) and are rare on the back ($65 \pm 20/cm^2$), the thigh ($120 \pm 30/cm^2$) and the scrotum ($80 \pm 30/cm^2$) [1]. They are absent from the tympanic membrane, margins of the lip, nail bed, nipple, inner preputial surface, labia minora, glans penis and glans clitoridis. However, there exist large variations in the number of eccrine sweat glands between different ethnic groups. Recently, eccrine sweat gland density has been found to be higher in Caucasians compared to Orientals in all regions apart from the back and buttocks [2].

Eccrine sweat glands have an important thermoregulatory function, but they also respond to emotional and gustatory stimuli. The secretory rate is far greater than that of other exocrine glands. Under severe heat stress, they are capable of producing up to 10 liters of sweat per day. The sweat is a clear, hypotonic and odorless fluid which contains mainly sodium and chloride but also potassium, urea, lactate, amino acids, bicarbonate and calcium. Proteins such as immunoglobulins make up less than 1% of sweat by weight.

Prenatal Development

The development of human eccrine sweat glands starts around the third month [3, 4]. The first anlagen are detectable in the palmar finger skin of 12- to 13-week-old embryos and few weeks later in the foot, axillary skin and other areas of the body. The density of sweat glands during early fetal life appears to be higher than in the adult. In the thigh of 24-week-old fetuses, a density of about 3,000/cm^2 sweat gland anlagen has been measured. The number at birth is about half, and at 18 months the density has been reduced further by about two thirds. The adult density of approximately 120/cm^2 does not change throughout the remaining life.

Each eccrine sweat gland arises from an epidermal ridge as a small epithelial downgrowth [5]. The sweat gland precursor cells form a solid epithelial cord which elongates in the dermis. The lower end of the anlage becomes a secretory coil. Between the fourth and eighth fetal months, the lumen is formed by fusion of intracytoplasmic vacuoles at the luminal cells and by dissolution of desmosomal contacts. Early mature sweat glands are visible at approximately 32 weeks, but the glands have apparently no significant function before birth.

Histology

Eccrine sweat glands are long-branched tubular structures with a highly coiled secretory portion and a straight or slightly helical ductular portion [6] (fig. 1a). The *duct* fuses with the base of epidermal papillae and the lumen passes between the keratinocytes to open via a rounded aperture onto the skin surface. In thick hairless skin, regular series of puncta – sweat pores – are visible along the center of friction ridges.

The *secretory coil* of about 0.5 mm in diameter is situated deep in the dermis or hypodermis. It is lined by a simple or pseudostratified epithelium resting on a basal lamina and enclosed by a thin fibrous sheath (fig. 1c). Within the epithelium, *clear* and *dark cells* which occur in approximately equal numbers as well as myoepithelial cells are distinguishable [7, 8] (fig. 2a).

Clear cells have a pyramidal shape and rest with a broad basal region on the basal lamina or myoepithelial cells. The apical membrane is rarely exposed directly to the lumen because the luminal surface is mainly occupied by dark cells. Clear cells have a round, large, moderately euchromatic nucleus. The cytoplasm is devoid of secretory vesicles and contains only few organelles. Between adjacent cells, distinct intercellular canaliculi are present which emerge immediately above the basal lamina or myoepithelial cells and open directly into the

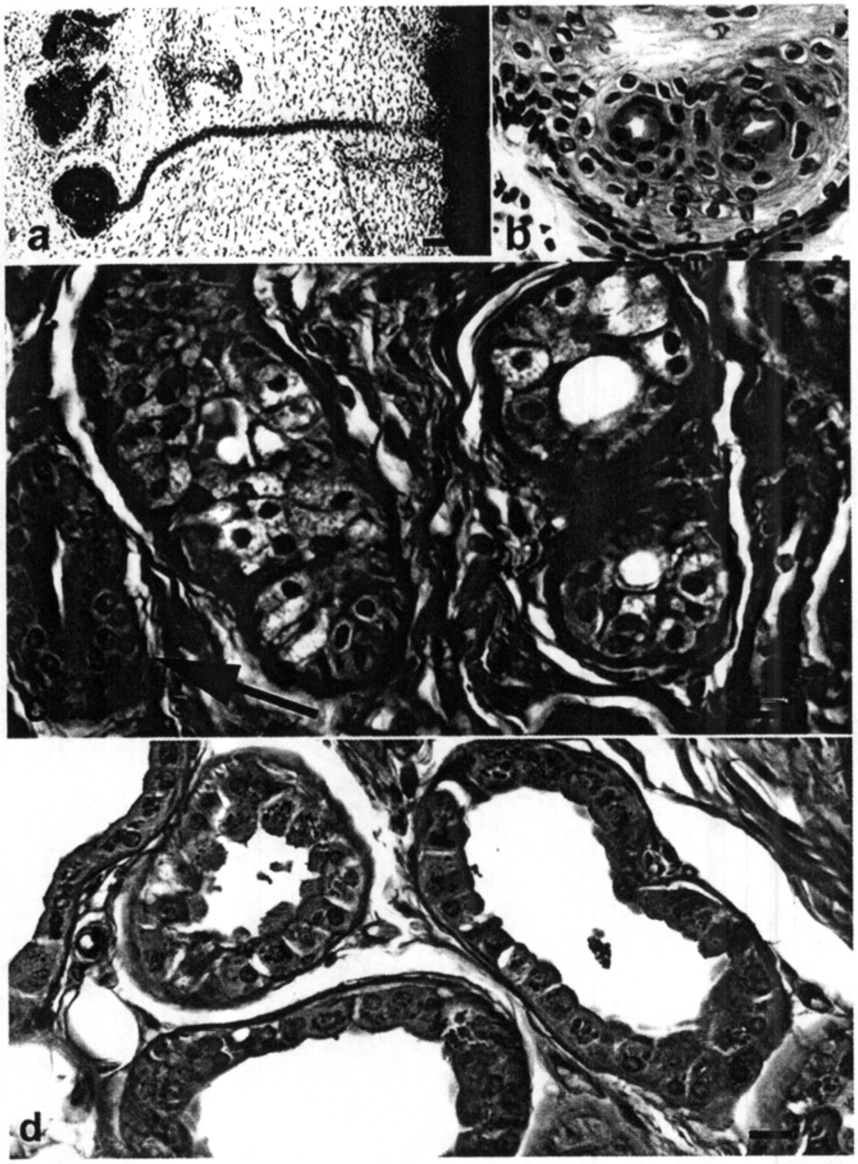

Fig. 1. Light microscopy of sweat glands. ***a*** Thick section (30 μm) of finger pad skin showing secretory coils and straight ducts of eccrine sweat glands. Bar = 500 μm. ***b*** Intraepidermal portion of two eccrine sweat gland ducts. Bar = 20 μm. ***c*** Oblique and transverse section of an eccrine sweat gland coil with typical single-layered and pseudostratified epithelium. Note the excretory duct (arrow) lined by a double-layered epithelium. Bar = 5 μm. ***d*** Secretory coil of an apocrine sweat gland. Note the varying shape of the epithelial cells and the cytoplasmic caps projecting into the lumen. Bar = 5 μm.

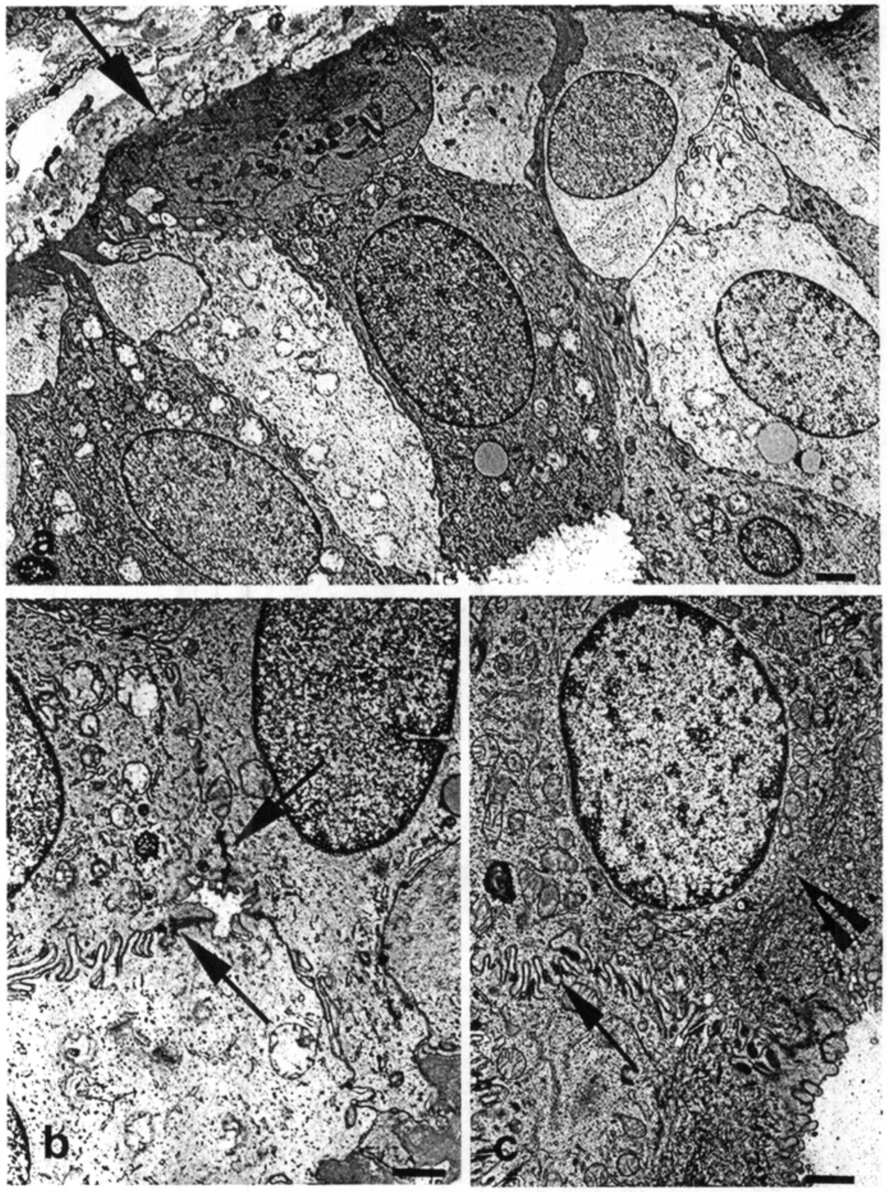

Fig. 2. Transmission electron microscopy of eccrine sweat glands. ***a*** Secretory coil lined by clear and dark cells. The arrow points to a myoepithelial cell. Bar = 1 μm. ***b*** Intracellular canaliculus running between adjacent secretory cells. Note the junctional complexes (arrows) and the abundant interdigitating microvilli. Bar = 0.5 μm. ***c*** Intradermal portion of an eccrine sweat gland duct. The inner epithelial cell displays numerous desmosomes (arrow) and a distinct terminal web in the apical cytoplasm (arrowhead). Bar = 0.5 μm.

lumen of the gland (fig. 2b). The basal and lateral plasmalemma is often elaborately folded indicating high activity in transepithelial fluid and electrolyte transport. The major part of sweat, in particular water and electrolytes, is formed by clear cells.

Dark cells have either a cuboidal or an inverted pyramidal shape with a broad adluminal end and a narrower abluminal portion. They border on nearly all the apical surface of the epithelium and usually do not reach the basal lamina (fig. 2a). The cytoplasm contains a well-developed Golgi complex, long mitochondria, few cisterns of rough endoplasmic reticulum, abundant free ribosomes as well as numerous vesicles and dense granules which contain a huge amount of glycoproteins. Dark cells secrete PAS-positive glycoproteins which are the most prominent protein constituents in the sweat, but the real function of dark cells is not known.

The spindle-shaped *myoepithelial cells* form an incomplete layer along the basal lamina [9] (fig. 2a). They are arranged more or less parallel to the course of the secretory coil. The organelles are found mainly superiorly and laterally of the nucleus whereas the infranuclear region of the cytoplasm is occupied by densely packed microfilaments. Coexpression of keratin and α-smooth-muscle actin is a hallmark for myoepithelial cells. Furthermore, nitric oxide synthase type I and choline acetyltransferase have been found exclusively in myoepithelial cells [6]. The function of myoepithelial cells is not fully understood. They may protect the secretory cells against overdistention when large volumes of fluid are secreted or move the cells, thus exposing a larger surface of clear and dark cells to the basal lamina.

Within the *ducts,* secretory and myoepithelial cells are replaced by a double layer of small cuboidal cells (fig. 1c). The *intradermal portion* of the ducts has an outer basal layer with a comparatively large dark-staining heterochromatic nucleus and abundant mitochondria. The inner layer of luminal cells is connected with numerous desmosomes and the apical regions contain a conspicuous terminal web-like cuticular border (fig. 2c). The *intraepidermal portion* of the duct is lined by 2 layers of cells which are different from the surrounding keratinocytes (fig. 1b). The outer cells contain keratohyalin granules and lamellar granules and undergo keratinization. The inner cells display numerous vesicles and microvilli at the luminal portion. They undergo incomplete keratinization and are shed into the lumen of the stratum corneum.

Along the duct, the primary secretion which is the same as that of blood plasma is modified by the action of basal cells whereby the proximal dermal portion appears to be functionally more active than the distal part. The basal cells exhibit distinct Na-K-ATPase activity and resorb most of the sodium, potassium and chloride of the primary secretion.

Recently, transitional cells have been described between clear and dark cells as well as between clear cells and myoepithelial cells [6]. Thus, there may exist a stem cell population within the coil epithelium with the ability to differentiate into various directions.

Innervation

The eccrine sweat glands are innervated by sympathetic nerve fibers which arise from the intermediolateral cell nucleus of the spinal cord [10, 11]. The myelinated axons (preganglionic fibers) pass the anterior roots of the spinal nerves to reach the sympathetic trunk via the white ramus communicans. From the sympathetic ganglion, unmyelinated class C axons (postganglionic fibers) arise which enter the spinal nerve via the gray ramus communicans and end around the sweat glands.

Nerve cells from spinal cord segments Th_2 to Th_8 supply the skin of the upper limbs, from Th_1 to Th_4 the face and eyelids, from Th_4 to Th_{12} the trunk and from Th_{10} to L_2 the lower limbs.

Periglandular nerve endings release acetylcholine as major neurotransmitter. In addition, catecholamines as well as several neuropeptides including S-100 protein, substance P, neuron-specific enolase, vasoactive intestinal polypeptide, calcitonin gene-related peptide, synaptophysin and galanin have been detected in the periglandular nerves by immunohistochemistry [12, 13]. It is suggested that sweat glands are capable of some intrinsic regulation in addition to that mediated by the nerve supply, but the real significance of these peptides or neurotransmitters for sweat gland function remains unclear.

Apocrine Sweat Glands

In adult humans, apocrine sweat glands are present just in limited areas: the axilla, perianal region, areolae, periumbilical skin, prepuce, scrotum, mons pubis and labia minora [6]. The ceruminous glands of the external auditory meatus and the ciliary glands of the eyelids are often included in this category, but they are quite different concerning secretion and regulation and should therefore be considered as distinct subtypes. The ratio between apocrine and eccrine sweat glands is 1 : 1 in the axilla but 1 : 10 in other regions.

The secretory product of apocrine sweat glands is a sterile, thick, milky and odorless fluid containing protein, carbohydrate, ammonia, lipids, ferric ions, chromogranins such as indoxyl as well as fatty acids. The secretion undergoes bacterial decomposition which generates potent odorous compounds with a characteristic smell. In nonhuman species, the secretory product mediates potent pheromone signals important in courtship, parental and territorial behavior, but its role for modern humans is not certain.

Prenatal Development

The anlagen of apocrine sweat glands are formed at the same time as those of eccrine glands. They arise as a solid epithelial bulge along one side of the pilosebaceous apparatus. Initially the anlagen are widely distributed over the body, but their number diminishes from the fifth month of gestation. At birth, well-defined glands are found in specific areas (see above), but they do not start secretory activity until puberty. The maturation of the apocrine sweat glands is apparently dependent on sex hormones but not their maintenance since gonadectomy in adults does not affect their function.

Histology

Apocrine sweat glands consist of a basal secretory coil and a straight duct which opens above the sebaceous gland into the pilary canal or occasionally directly onto the skin surface [7, 8]. The secretory region which is approximately 2 mm wide, is situated in the deep dermis or hypodermis. The coils often anastomose with each other forming a labyrinthine network. They are limited by a thick basal lamina and covered by a connective tissue capsule rich in capillaries and nerve terminals.

Each *coil* is lined by a single-layered epithelium of varying shape [14] (fig. 1d). The secretory cells are cuboidal or low columnar but may be squamous when the gland is distended with secretory product. They rest upon a well-defined basal lamina or a discontinuous layer of myoepithelial cells. The cells often display apical caps of cytoplasm projecting into the lumen which determine the apocrine or pinching-off character. The cytoplasm contains vacuoles, vesicles and granules of varying size which are separated from the apical membrane by a conspicuous terminal web and whose number appears to depend on synthesis and discharge.

The *ducts* of apocrine glands are morphologically most like the eccrine ducts. They are lined by a double layer of cuboidal cells which – though unlike eccrine duct cells – have not been shown to modify apocrine secretions.

The mechanism of secretion of apocrine sweat glands is still not entirely clear. It may involve a number of different processes including eccrine secretion, detachment of apical caps or complete holocrine disintegration of cells.

Innervation

Apocrine sweat glands are innervated by sympathetic nerve fibers coming from the same spinal segments as those of eccrine glands [6]. However, catecholamines and not acetylcholine are the major neurotransmitter for the apocrine glands whereby the cells appear to be more sensitive to epinephrine than norepinephrine. The vast majority of unmyelinated nerve fibers ends in closer proximity to capillaries than to secretory or myoepithelial cells suggesting that there exists a form of neurohumoral regulation of apocrine sweat glands.

Modified Sweat Gland Types

There is increasing evidence that besides eccrine and apocrine glands further types of sweat glands exist. Recently, apoeccrine or mixed sweat glands have been detected in the human axillary and perianal skin [15, 16]. They develop during puberty from eccrine-like precursor glands. The secretory coil of apoeccrine glands consists of two segments which are connected to each other: a dilated segment which is very similar to that of apocrine glands and an undilated segment indistinguishable from that of an eccrine secretory coil. The duct of apoeccrine sweat glands opens onto the nonfollicular skin surface.

A further sweat gland type with unique morphology has been identified in the human anogenital region [17]. It is characterized by a long excretory duct and a wide coiled secretory part which has the tendency to develop diverticula and short branches and is lined by tall columnar luminal cells with conspicuous 'snouts'. They are clearly distinguished from eccrine, apocrine and apoeccrine glands and are more reminiscent of mammary glands.

The function of both apoeccrine and anogenital sweat glands remains obscure.

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