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Review Article

A short history of sweat gland biology

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Synopsis

The axilla, especially its microflora and axillary sweat glands as well as their secretions, is the main target of cosmetic compositions such as deodorants or antiperspirants. There are three types of sweat glands present in the axillary skin, namely apocrine, eccrine and apoeccrine sweat glands. Here, we provide an overview of the morphological, structural and functional characteristics of the different gland types and present techniques that allow their clear distinction. Moreover, we describe different forms of perspiration as physical reactions to external and internal stimuli.

Résumé

Les glandes sudoripares axillaires et leurs sécrétions sont les points d'application principaux des produits antitranspirants et déodorants. Dans la peau axillaire, il y a trois formes différentes de glandes sudoripares appelées apocrines, eccrines et apoeccrines. Nous donnons une vue d'ensemble des propriétés fonctionnelles, morphologiques et structurelles des différentes glandes et présentons des techniques qui permettent leur distinction. Nous décrivons également les différents modes de transpiration corporelle entant que réactions physiques aux stimuli externes et internes.

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Introduction

Skin is not only the largest, but also, functionally, the most versatile organ of the human body. A vast amount of research has been published on different key functions of the skin, e.g. its barrier function or its role as a first-line immune response system.

Although the regulation of body core temperature by sweating is one of these key tasks, comparatively few studies are available focussing on sweat glands or their biology. Moreover, the information from different research teams is often rather controversial, among the literature published on the molecular mechanisms of sweating. These data include findings from patch clamp studies on isolated cells, as well as conclusions from analogy. So far, to our knowledge, besides micropuncture studies on sweat glands, no work has been carried out with sweat glands or parts of them. Thus, we have decided not to include these data as they might rather confuse the reader than inform. We hope that, in the near future, there will be an opportunity to put together a clear-cut review on these mechanisms as well.

Physiology of perspiration

The regulation of body core temperature is crucial for survival; constant body core temperatures above 40°C result in protein denaturation and cell death, finally leading to multiple organ failure. Thus, the down-regulation of body core temperature under conditions of high environmental temperature or under physiological stress is the most important role of perspiration. With the onset of

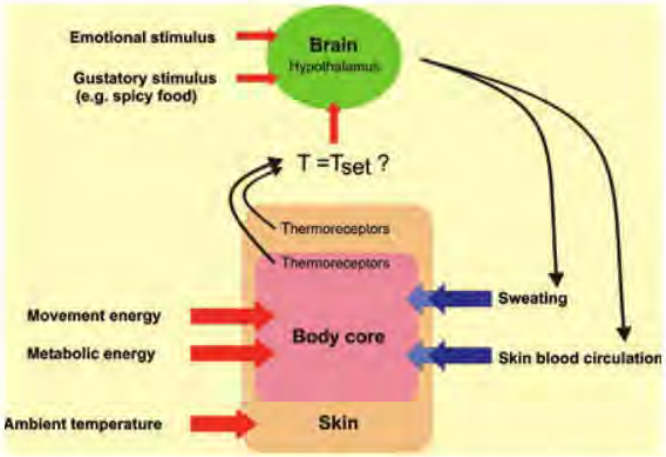

Figure 1 Control cycle of thermoregulation in humans. Changes in body core temperature and skin temperature are driving forces for thermoregulation. These changes, caused by physical exercise/movement energy, metabolic rates and ambient temperature, are detected by local thermoreceptors and further processed in the hypothalamus as the principal centre of thermoregulation. This brain region is also influenced by emotional and gustatory stimuli like, e.g. stress or spicy food. Thermoregulatory sweating and skin blood circulation finally lead to the reduction of skin temperature as well as body core temperature.

sweat secretion, thermal energy is released by the evaporation of water from the skin surface, and skin and body core temperatures are lowered. Other stimuli for perspiration, which are less well understood, are emotional stress or consumption of spicy food (Fig. 1).

Thermal sweating

Thermoregulatory sweating involves eccrine sweat glands that are distributed over almost the whole body surface. Along with vasodilatation in the skin, thermoregulatory sweating serves as a system for temperature reduction under heat stress conditions. Failure of this mechanism can lead to hyperthermia and death. Sweat gland activity is directly controlled by the central nervous system with the hypothalamus as the principal centre of thermoregulation. This centre responds not only to changes in core body temperature but also to hormones, endogenous pyrogens, physical activity, and emotions [1]. The central drive for thermoregulatory sweating is described as the sum of internal body temperature and mean skin temperature, whereas the influence of the first exceeds the second by a factor of 10 [2, 3]. Moreover, the sweat rate is affected by local thermal skin conditions – an augmentation of local skin temperature leads to increased sweating. However, the mechanism by which this reaction is controlled remains unclear; it could be explained with both, a greater release of neurotransmitters and an increased sensitivity of sweat glands to a given neurotransmitter during conditions of higher local skin temperature [4–6]. In addition to skin and body temperature, thermoregulatory sweating is affected by many other internal factors like gender, physical fitness, menstrual cycle and circadian rhythm as well as external factors like air humidity [7–9].

Emotional sweating

Emotional sweating is a physical reaction to emotive stimuli like stress, anxiety, fear and pain that can occur over the whole body surface, but is most evident on palms, soles and in the axillary region [10–12]. Unlike thermoregulatory sweating, emotional sweating arises independently of ambient temperature and decreases during sleep and relaxation.

Emotional sweating of palms and soles already occurs in babies [13]. Evolved as a fleeing reaction in different mammals, palmoplantar sweating increases friction and thus prevents slipping during running or climbing in stressful situations [14]. Investigations of Kerrassidis [15] indicate that sweating of palms and soles is mainly induced by emotive stimuli, not by high ambient

temperature. Like thermoregulatory sweating, emotional palmar and plantar sweating involves eccrine sweat glands that are typically activated by cholinergic fibres of the sympathetic nervous system. However, recent investigations in subjects suffering from anhidrosis due to deficits in cholinergic transmission indicate that adrenergic stimulation is also present in palms and soles [16]. Moreover, several authors demonstrated the pharmacological responsiveness of eccrine sweat glands to adrenergic stimuli, supporting the hypothesis that this type of sweat gland is, beyond cholinergic innervation, to a certain degree under adrenergic control. Compared to cholinergic stimulation, the adrenergically induced sweat rate is clearly decreased [17–19]. The central pathway of emotional eccrine sweating remains unclear. Yet, there is evidence that a centre in the premotor cortex, as well as the amygdala as a part of the limbic system, is involved [20, 21].

Emotional sweating in the axillary region, as well as axillary hyperhidrosis, does not occur before the onset of puberty. This may lead to the assumption that apocrine and apoeccrine sweat glands play an essential role in emotional axillary sweating, as they are activated during this developmental stage [22, 23]. Apocrine sweat glands respond vigorously to emotive stimuli and are physiologically activated by adrenergic stimulation [16, 24, 25]. The function of apocrine sweat secretion has not been completely elucidated until now. Still, there is evidence that apocrine odours exhibit a pheromone-like effect [26, 27]. Apoeccrine glands, which contribute notably to axillary secretion by emitting high amounts of watery fluid, show strong cholinergic sensitivity, but can also be activated by adrenergic stimulation [28].

Gustatory sweating

Under certain conditions, sweat secretion can be induced by ingestion, which can be explained by a direct or indirect thermal effect. First, ingestion causes an increase in metabolism, leading to elevated body temperature and thermal sweating. Second, hot and spicy food is able to induce a mild form of gustatory sweating, which is confined to the face, the scalp and the neck. This reaction is believed to be driven by the substance capsaicin, which binds to warmth sensors in the oral cavity leading to a thermoregulatory response [29–31]. On the other hand, gustatory sweating describes a pathological state, referred to as *Frey's syndrome*, which follows parotid surgery and affects the area of the cheek. It is assumed that this unilateral form of gustatory sweating results from disruption of parasympathetic secretomotor fibres. These later anastomose with sudomotor sympathetic fibres of the skin, thereby gaining control of sweat gland activity [32, 33]. Aside from *Frey's syndrome*, gustatory sweating is a rare complication in diabetic patients with autonomic neuropathy [34].

Sweat glands

Sweat glands are cutaneous appendages like hair follicles or sebaceous glands. Cutaneous glands are exocrine glands, as the secretion is released via a duct to the outer skin surface. The embryonic development of the glands begins with an ingrowth of the epithelial surface, when the epithelial cells begin to form the duct and the gland with differentiated cells.

Glands can be either characterized by their morphology or by their mode of secretion. Sebaceous glands can be classified as holocrine (i.e. the whole secretory cell is secreted) whereas sweat glands secrete either apocrine (secretion occurs via pinch-off of outer cell parts) or eccrine (secretion is released from the cell as a liquid without disintegration). This distinction of sweat glands into eccrine and apocrine sweat gland was introduced in 1922 by Schiefferdecker [35]. For this reason, most of the literature refers to sweat glands as eccrine or apocrine. In 1987, Sato and co-workers found sweat glands which could not be classified as either eccrine or apocrine and showed the characteristics of both glands. Hence, this third type of sweat gland was called apoeccrine [23, 28]. Recent studies confirmed the existence of this type of gland [36, 37] although further studies are needed to understand fully the development of these glands as well as their contribution to sweating.

However, as this third type of sweat gland makes a clear-cut structural and functional differentiation much more complicated, a discrimination of sweat glands into epitrichial and atrichial was suggested, i.e. the differentiation by their opening either into the hair follicle or freely onto the epidermal surface [38, 39]. Earlier literature may also refer to the eccrine sweat gland as the small sweat gland and to the apocrine sweat gland as the big or scent gland. The apoeccrine gland may also be called the mixed-type sweat gland. In the

following, however, axillary sweat glands will be referred to by the most commonly used terms eccrine/apocrine/apoeccrine.

Eccrine sweat glands

Eccrine sweat glands already exist at birth and can be found over the whole body surface with only two exceptions: lips and glans penis [40]. Sweat glands (1.6–5 million) are distributed over the whole body surface with an average density of 200 sweat glands per square centimetre (see Table I). According to the literature, the highest sweat gland density (i.e. 700 sweat glands cm^{-2}) can be found on the palms and soles and the least (i.e. 64 sweat glands cm^{-2}) on the back [40–42]. However, data on sweat gland density from different studies diverge quite severely [43]. This may be due to the different techniques used for its determination. Some methods refer only to active sweat glands and are often based on indirect measurements, e.g. by counting sweat drops instead of sweat glands. Other methods use direct counting of sweat glands by, e.g. histological assays, but with a preparation-dependent change in skin surface area. Ethnologic or gender differences have only rarely been studied and taken into account as most of the studies were carried out with only a few subjects [44] and carried out in Japan [38]. Moreover, some data were falsely converted from inches to the metric system [45].

Sweat glands are coiled tubular systems. Although they are usually perceived as distinct single entities, there is evidence that the coils of two eccrine glands may also occur convoluted within each other; these structures might easily be mistaken as one large coil with two or more ducts to the surface [43, 46]. An eccrine gland consists of a single tubule ranging from about 4 to 8 mm in total length. The intra-epidermal part of the sweat gland is called the *acrosyringium* followed by the *dermal duct* with a straight and a coiled part, and a coiled, *secretory portion*, which is found in the deep dermis (see Fig. 2).

The *acrosyringium* consists of epithelial cells with no clear distinction or border to the epidermis. The epithelial cells differentiate towards the lumen and cornified cells can be found inside the lumen. The luminal diameter is between 20 and 60 μm.

The *dermal duct*, whether straight or coiled, has a smaller inner diameter of only 10–20 μm, the outer diameter is about 50–80 μm. The dermal duct is described as an epithelium of two to three layers of epithelial cells [47, 48]. These epithelial cells are connected at numerous sites by desmosomes and intercellular junctions. It has been shown that they constitute a functional barrier between the luminal and extracellular compartments [49]. The inner cells are rich in tonofilaments, building a thick terminal web or cortical zone called cuticula. The outer or basal cells are surrounded by a continuous basal membrane which, in turn, is surrounded by a collagenous and fibrocyte sheath [50].

The basic function of the sweat duct is the reabsorption of ions from primary sweat, having an almost isotonic sodium chloride concentration when entering the duct. During the process of reabsorption, sodium moves passively into the ductal cells via sodium channels on the apical membrane. This process is driven by a Na/K-ATPase on the basolateral membrane, pumping sodium from the ductal cells into the interstitial fluid. The chloride channel cystic fibrosis transmembrane

Region	Wilke *et al.* [38]	Sato *et al.* [35]	Fiedler *et al.* [37]	IFSCC Monograph [79]
Palms	644	600–700	620 ± 120	370
Forearm	134	108	225 ± 25	155
Abdomen	127	–	190 ± 5	–
Upper arm	90	108	150 ± 20	–
Armpit	68	~100	400 ± 50	90–200
Thigh	57	–	120 ± 10	80
Face	59	181	360 ± 20	175
Chest	20	–	175 ± 30	–
Back	–	64	160 ± 30	60–100

Table I Sweat gland density for different body parts. This synopsis shows sweat gland density (in cm^{-2}) for different body regions that have been assessed by direct [38] and indirect [37, 79] counting techniques in the 1970s [37], 1980s [35], 1990s [79], and recently [38]. Note the broad variations of sweat gland numbers, e.g. in the armpit, the face or the chest

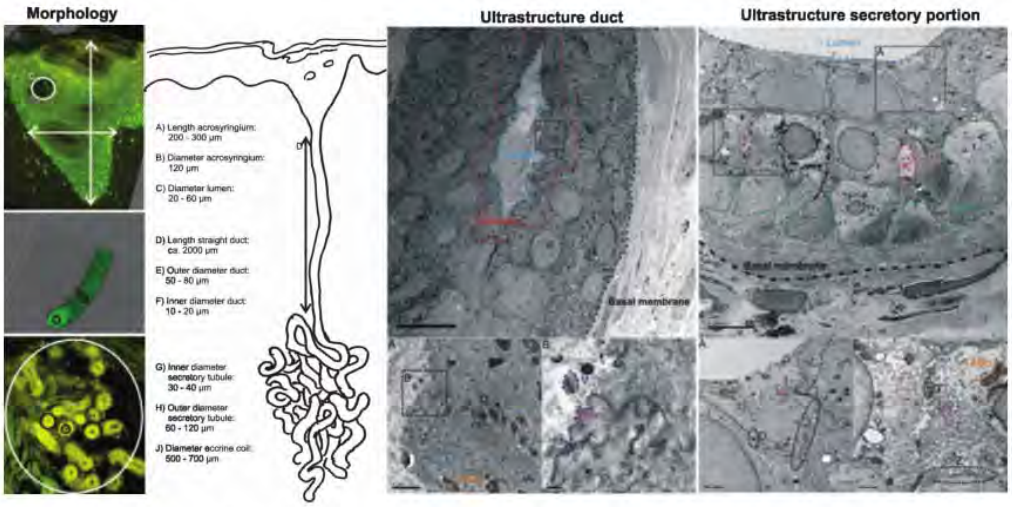

Figure 2 Morphometry of the eccrine sweat gland. In this synopsis dimensions and morphology (left and middle) as well as ultrastructure of the different segments of the eccrine sweat gland (right) are shown. The *sweat gland dimensions* have been determined in plastic-embedded, fluorescence-labelled skin biopsies (3D image data) and cryostate sections of skin (2D image data); for each dimension, at least 10 different samples have been examined (for further technical details about the images, please refer to Ref. [43]). The *duct ultrastructure* shows two to three cell layers. The basal cell layer is surrounded by a basal membrane; the luminal cell layer forms a cuticula towards the lumen. Inset A shows that the membranes between adjacent cells are heavily folded and linked by desmosomal contacts (D). Inset B shows luminal cells, forming microvilli (MV) towards the lumen; vesicles (V) can be found within the lumen near to the cuticula. The basal cells show a strinking number of mitochondria (Mito). The basal cell layer of the eccrine *coil* is surrounded by myoepithelial cells (Myo). Basal and luminal cells show a lot of mitochondria (Mito), and in the luminal cell layer also many vesicles (V) are present. The membranes between adjacent cells are again heavily folded and interconnected by Zonulae occludentes are located (Z) and desmosomal contacts (D). Intercellular canaliculi (IC) can be found between adjacent cells with formed microvilli (MV) towards the intracellular space.

conductance regulator (CFTR), which is abundantly expressed in the human reabsorptive duct, is composed of a major part of the electrical conductance for chloride and is acutely regulated by protein kinase A-dependent phosphorylation [51]. Mutations in the CFTR gene lead to cystic fibrosis (CF), a clinical condition in which ductal electrolyte reabsorption is highly affected, leading to increased sweat chloride levels. This is why sweat testing is a relevant tool for CF diagnosis [52]. Recent studies led to the identification of anion exchangers, carbonic anhydrases II and vacuolar proton pumps ($V\text{-}H^+$-ATPase) in ductal cells, providing evidence for the existence of a second chloride reabsorption mechanism that proceeds as proton-driven active transport, allowing chloride reabsorption also under low luminal chloride concentrations [53–55].

The *secretory portion* consists of a tubule with an outer diameter of 60–120 µm and an inner diameter of 30–40 µm. The overall diameter of the coil is around 500–700 µm. Three different cell types can be found within the secretory portion: clear cells, dark cells and myoepithelial cells. The function of the myoepithelial cells remains unclear. Dark cells, in contrast to clear cells, can be intensely stained with eosin, toluidine blue and methylene blue [56]. They are also osmophilic and appear to be denser due to their abundant granules. The dark cells dominate the luminal surface of the coil, whereas the clear cells are located basally. Clear cells contain many mitochondria. Between adjacent cells, intercellular canaliculi can be found which are specific to eccrine secretory cells [57]. Their role in secretion together with convoluted cell membranes of adjacent cells is not fully understood [58].

Eccrine sweat glands are innervated by postganglionic sympathetic fibres. As an exception to the general rule of sympathetic innervation, in which noradrenalin is the peripheral neurotransmitter, the innervation of the eccrine sweat gland

is via acetylcholine. Spinal cord segments from T2 to T8 provide innervation to the skin of the upper limbs, from T1 to T4 to the skin of the face, from T4 to T12 to the skin of the trunk, and from T10 to L2 to the skin of the lower limbs [59].

Eccrine sweat glands express various muscarinic acetylcholine receptor subtypes in myoepithelial cells (m2–m5 ACh-R) as well as in acinar cells (m1, m3, m4-AChR) [60]. As eccrine sweat secretion can be blocked effectively by anti-muscarinic compounds, it can be assumed that this receptor type acts as a main switch in primary eccrine sweat secretion. The subsequent secretory process is assumed to be driven by an electrochemical gradient. Several ion transporters and ion channels like CFTR, Na^+–K^+–2Cl-cotransporter 1, Na^+/H^+ exchanger 1, V-H^+-ATPase as well as Na/K-ATPase have been shown to be localized in the secretory portion of sweat glands and probably contribute to the electrochemical driving of sweat secretion. However, the overall mechanism of the formation of an electrochemical gradient as the driving force for sweat secretion is still unclear. Additionally, a recent investigation on aquaporin 5 (AQP5)-null (−/−) mice discusses a role of this water channel in sweat secretion as the mice showed a decreased number of active sweat glands in this study. However, the exact role of AQP5 in the sweat secretory process needs to be further elucidated [58, 60–64].

Beyond cholinergic innervation, eccrine sweat glands have been shown to respond to adrenergic stimulation, whereas the induced sweat rate is weaker than the one triggered by cholinergic stimulation [17–19]. Reddy and co-workers were able to attribute β-adrenergic responsiveness of eccrine sweat glands to a certain cell type, the β-adrenergic-sensitive cell, and presumed that β-adrenergic secretion is controlled by the cAMP-mediated opening and closing of CFTR chloride channels [61, 62]. Accordingly, a β2-adrenoceptor has been shown to be localized in the secretory portion of sweat glands [63]. These findings suggest a contribution of adrenergic stimulation to the process of primary sweat secretion, though the physiological significance remains to be clarified. Apart from the mentioned components shown to be localized in the secretory portion of the human sweat gland and presumed to play a role in the primary sweat secretion, several other receptors like Vasoactive intestinal polypeptide receptor [64], epidermal growth factor receptor [65], vanilloid receptor-1 [66] and nicotinic acetylcholine receptor [60] are also expressed in eccrine sweat glands. However, their significance for sweat gland function remains to be elucidated.

Eccrine sweat can vary in composition, depending on hydration, exercise, state of health and region of the body [67–69]. Besides water, which accounts for 99% of eccrine sweat, further components are sodium, chloride, potassium, calcium, magnesium, lactate, ammonia, amino acids, urea and bicarbonate [59, 68, 70]. In addition, several proteins and peptides, e.g. cysteine proteinases [71], DNAse I [72], lysozyme, Zn-α2-glycoprotein [73], cysteine-rich secretory protein-3 [74] and dermcidin [75] have been identified in eccrine sweat. Some of these, like dermcidin (DCD), an antimicrobial peptide, that is expressed constitutively in eccrine sweat glands, are believed to play a role in innate host defence mechanisms [75, 76]. Recently, it was shown that sweating leads to a reduction in bacteria on the skin of healthy subjects, but not in patients with atopic dermatitis having reduced DCD concentrations in eccrine sweat [77].

Apocrine sweat glands

Apocrine glands already exist at birth but do not become active until puberty. Apocrine glands are restricted to hairy body areas, as they open and secrete into the hair canal. For this reason, apocrine glands can only be found in the axilla, mammary, perineal and genital region. The occurrence or density of apocrine glands in the axillary region has been studied by Sato *et al.* [23], who found 8–43 clearly apocrine and up to 54 apoeccrine glands per square centimetre. However, Asians are supposed to have fewer apocrine glands than Caucasians [78], and men have fewer apocrine glands than women [79].

The morphology of apocrine glands is shown in Fig. 3. Apocrine glands open to the hair canal. The apocrine gland coil with an outer diameter of about 800 μm is bigger than the eccrine coil. The outer diameter of the apocrine gland tubule is about 120–200 μm, whereas the inner diameter is around 80–100 μm. It is hardly possible to differentiate between a duct and a secretory coil. The apocrine duct is very short and can be found in close vicinity to the hair follicle [80]. The secretory coil consists of two different cell types: secretory and myoepithelial cells. The myoepithelial cells are

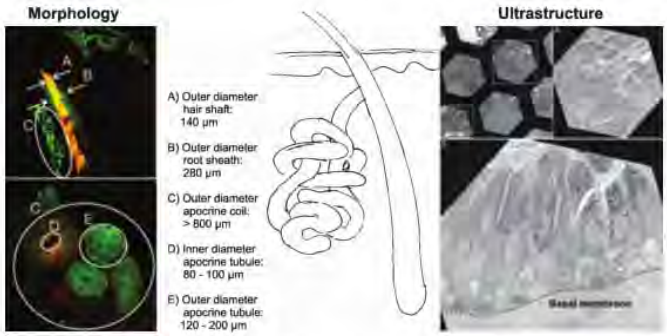

Figure 3 Morphometry of the apocrine sweat gland. In this figure morphology (left + middle) and ultrastructure of the apocrine sweat gland (right) are shown. The *sweat gland dimensions* have been determined in plastic-embedded, fluorescence-labelled skin biopsies (3D image data) and cryostate sections of skin (2D image data): for each dimension, at least 10 different samples have been examined (for further technical details about the images, please refer to Ref. [43]). Looking at the ultrastructure of the secretory portion, the apocrine *coil* consists of a single layer of tubular-shaped cells surrounded by myoepithelial cells (see inset B: Myo). The myoepithelial cells are bordered by the basal membrane. The tubular cells show many mitochondria, granules and vesicles (V). The membranes are folded and microvilli (MV) can be found between adjacent cells. The apocrine pinching-off (A) is frequently seen.

distinctly developed; their function remains unclear. The secretory cells can vary in shape because of their secretory activity. However, typical secretory cells are columnar shaped. The nucleus of the secretory cells is found near the basal membrane. The cells are full of mitochondria and different granules. The cell membranes are convoluted, and microvilli are present towards the lumen. Cells exhibiting the secretory pinch-off process can be observed at the ultrastructural level.

Apocrine sweat glands respond to emotional stimuli such as anxiety, pain or sexual arousal. Apocrine secretion takes place as apical budding-off from the luminal cells and is under adrenergic control, via adrenaline and noradrenaline [16, 22, 81]. It has not yet been proven, whether activation of apocrine glands takes place via innervation or via circulating catecholamines, and, until now, adrenergic receptors have not been identified in human apocrine sweat glands.

The fluid secreted by the apocrine sweat gland is an oily, odourless substance, containing proteins, lipids and steroids [82]. However, it cannot be excluded that apocrine secretions are mixed with sebum, as both, apocrine and sebaceous glands open into the hair follicle. Recently, it was shown that two apocrine proteins, referred to as apocrine secretion odour-binding proteins 1 and 2 (ASOB1 and ASOB2) function as carrier proteins for volatile odour molecules, e.g. (E)-3-methyl-2-hexenoic acid, which are linked as amino acid conjugates and are subsequently released by bacterial enzymes. ASOB2 was shown to be identical with the lipocalin apolipoprotein D [26, 83]. ASOB1 shares homology to the α-chain of apolipoprotein J [84]. As in other species, lipocalins serve as carrier proteins for pheromones; an analogous function has been suggested for ASOB1/2. Recent studies of Natsch *et al.* led to the purification of a Zn^{2+}-dependent aminoacylase from *Corynebacteria*, which was shown to mediate the release of (E)-3-methyl-2-hexenoic acid and 3-hydroxy-3-methylhexanoic acid, a chemically related compound, from their glutamine-conjugated precursors [85]. Moreover, several odoriferous sulfanylalkanols were identified as axillary odour components, that are presumably released from cysteine conjugates. A respective cystathione-β-lyase has been cloned from an axillary isolate of *Corynebacterium striatum* [86, 87].

Apoeccrine sweat glands

The apoeccrine gland as a mixed type gland has been first described in 1987 by Sato *et al.* [23]. Like apocrine glands, apoeccrine glands can also be found in the anogenital region [88]. Therefore, it can be concluded by analogy that apoeccrine glands may also be restricted to hairy body regions. Apoeccrine glands are presumed to develop during puberty from eccrine glands as the proportion of eccrine glands decreases with age

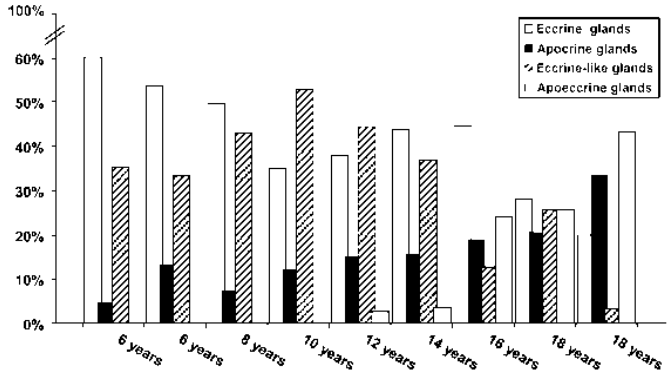

Figure 4 Percentage of different axillary sweat gland types in subjects of different age according to Sato *et al.* [23]. The amount of different sweat gland types in the armpit area was determined for individual subjects from 6 to 18 years and compared to the overall quantity of sweat glands (white: eccrine glands; black: apocrine glands; hatched: eccrine-like glands; grey: apoeccrine glands). According to this study, the proportion of apoeccrine glands increases with the onset of puberty and reaches almost 50% of the total sweat gland number. However, individual subjects show a high variation concerning the percentage of different sweat gland types in their armpit.

(see Fig. 4). However, up to 50% of the axillary glands can be apoeccrine.

A typical morphological characteristic is the irregular shape of the tubule itself as well as of the cells. The identification of apoeccrine glands is possible with specific markers, i.e. phalloidin, S-100 or CD15 [37, 89], as apoeccrine glands consist of myoepithelial cells, eccrine secretory cells and apocrine secretory cells.

Apoeccrine sweat glands exhibit continuous fluid secretion, comparable to eccrine sweat glands. *In vitro*, they show a very high cholinergic sensitivity, but can also be stimulated with β-adrenergic as well as α-adrenergic agonists in a pharmacologically specific way. Interestingly, apoeccrine glands show a greater responsiveness to cholinergic as well as adrenergic stimuli than eccrine glands. Moreover, the overall sweat rate of apoeccrine sweat glands is higher than that of other types of sweat glands suggesting that they contribute strongly to axillary sweating [23, 28].

Apoeccrine glands secrete an eccrine-like watery fluid. As they share multiple similarities with eccrine glands concerning morphology, marker proteins and mode of secretion [23, 28, 89], it is conceivable that the composition of apoeccrine sweat resembles that of eccrine sweat. Sato and Sato [28] determined sodium and potassium concentrations in the duct of isolated apoeccrine glands and found similar values as for eccrine sweat. However, until now the composition of apoeccrine sweat has not been elucidated, as it is not feasible to discriminate between eccrine and apoeccrine sweat during sweat collection in the axilla.

Summary and conclusions

Notable advances in the molecular understanding of the physiology of sweating have been made in the last decades. However, since the first detailed description of the different sweat gland types by Schiefferdecker in the 1920s, many of the questions raised by his studies have still not been answered. Besides very basic questions such as the real number and distribution of sweat glands in different body parts and especially the armpit, developmental aspects such as the role and function of apoeccrine sweat gland still need to be elucidated. Although the fear of excessive sweating and the resulting social embarrassment is an everyday problem, the biology behind is not well understood. To address this challenge in a reasonable way, an interdisciplinary approach including different histological and molecular biology techniques as well as sophisticated *in vivo* testing must be set up, ultimately leading to a deeper understanding of sweat glands as well as their development and physiology.

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