Scent glands in mammals: social functions and implications of apocrine gland odours

F. JOHN G. EBLING, D.Sc., Ph. D., University of Sheffield, Sub-Department of Dermatology, Academic Division of Medicine, Royal Hallamshire Hospital, Sheffield, S10 2JF (Great Britain).


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Synopsis
The human apocrine glands and associated structures are scent organs, just as are similar complexes in many other orders of mammals. The units of the axillary organs are precisely equivalent to, for example, those of the oral glands of ground squirrels or the chin glands of rabbits. The rabbit glands are androgen-dependent; clinical and other evidence suggests that this is equally true of the human axillary glands. Amongst other substances, the axilla produces 16-androstenes, the same volatile steriods which emanate from boars and induce sexual receptivity in sows. Production of 16-androstenes by the axilla involves the activity of bacteria, particularly of diphtheroids. The recent demonstration that axillary secretions of both men and women can affect the timing of the menstrual cycle clearly establishes the existence of true human pheromones and adds verisimilitude to the numerous entertaining anecdotes on the role of odour in human behaviour and history.

Riassunto
Le ghiandole apocrine umane e le relative strutture sono organi sebacei, proprio come lo sono complessi simili in altri ordini di mammiferi. Le ghiandole ascellari, per esempio, sono esattamente equivalenti a quelle oralì degli scoiattoli o a quelle del mento dei conigli. Queste ultime sono androgeno-dipendenti; prove cliniche e non fanno supporre che ciò sia altrettanto vero per le ghiandole ascellari umane. Oltre ad altre sostanze, le ascelle producono 16-androstene, lo stesso steroide volatile secreto dai cinghiali e che produce lo stimolo sessuale nelle scrofe. La produzione ascellare di 16-androstene è legata all'attività di batteri, in particolare di dipheroidi. Di recente è stato dimostrato che le secrezioni ascellari di uomini e donne possono influire sulla regolarità del ciclo mestruale e ciò prova inequivocabilmente l'esistenza di autentici feromoni umani e dà verosimiglianza ai numerosi e divertenti aneddoti storici sul ruolo degli odori nel comportamento umano.
Résumé
Les glandes apocrines humaines et ses structures sont des organes olfactifs qui présentent une parfaite ressemblance avec les organes de beaucoup d'ordres de mammifères. Les unités des organes axillaires par exemple, sont identiques à celles des glandes orales d'une espèce d'écureuil (lat. citellus) ou aux glandes du menton des lapins. Parmi d'autres substances, la glande sudoripare axillaire produit des 16-androstènes, c'est-à-dire les mêmes stéroïdes volatils qui sont émis par les sangleis et qui provoquent ainsi la réceptivité sexuelles des laies. La production des 16-androstènes, émis par l'axille, implique aussi une activité de bactéries, en particulier des diphtéroïdes. Récemment on a démontré que les sécrétions axillaires masculines et féminines peuvent peser sur la régularité du cycle menstruel; cela prouve l'existence de véritables phéromones humains et rend aussi plus vraisemblable la floraison d'amusants anecdotes à propos du rôle de l'odeur dans le comportement et l'histoire de l'homme.

Resumen
Las glándulas apócrinas humanas y las relativas estructuras son órganos sebáceos, precisamente como complejos semejantes en otros muchos ordenes de mamíferos. Las glándulas de los sobacos, por ejemplo, son exactamente equivalentes a las orales de las ardillas de tierra o a las de la barbilla de los conejos. Las glándulas de los conejos son andrógeno-dependientes; hay pruebas clínicas y de otro tipo de que esto es verdadero también para las glándulas de los sobacos. Entre otras sustancias, los sobacos producen 16-androstenes, el mismo esteroide volátil que producen los jabalíes e induce la receptividad sexual en las cerdas. La produccion de 16-androsten por los sobacos comporta la actividad de bacterias, en particular de difteroides. La reciente demostración que la secreción en los sobecos de hombres y mujeres puede afectar la regularidad del ciclo menstrual establece de manera clara la existencia de verdaderos feromonos humanos y añade verosimilitud a las numerosas anécdotas cerca el papel del olor en el comportamiento humano y en la historia.

Synopse
Introduction

Dermatologists and cosmetologists often regard the human skin glands as an embarrassment rather than a physiological advantage. Sebaceous glands have no obvious single function except the provision of a site for acne, and though sweat is a proper accompaniment to violent exercise, it must subsequently be removed or deodorized without delay, as must all other potentially odoriferous material. Especially unpopular, at least in theory, are the glandular areas of the axillary and genital regions, which have been and still are subjected to a barrage of cosmetic assaults. Other mammals are less self-conscious; a wide variety of them have scent glands which are overtly utilized in a range of behavioral interactions such as, for example, the establishment of individual identity, social dominance or territory, and sexual attraction. This paper will review some of this phylogenetic background and the evidence that human apocrine glands are, as in other mammals, under hormonal control and have social or sexual functions.

Skin glands

There are two main kinds of glandular unit in the skin of mammals: sebaceous, which secrete lipid, and tubular, with an aqueous product. The first type form their secretion by complete disintegration of the cells in which it is made and are known as holocrine. In the second type, known as merocrine, the cells are not destroyed, but extrude their product into a lumen. Schiefferdecker (1917); who invented the terminology, further divided merocrine glands into eccrine, in which the cells remain completely intact, and apocrine, in which he believed secretion involved decapitation of the terminal projections of some, at least, of the cells. Eccrine glands are not associated with hair follicles, and they are found in hairy skin only in some primates and in man, where they function in sweating. In many other mammals, for example in rats and mice, similar glands are found in the footpads and help the animal to grip the substrate. So-called «apocrine glands», whether or not their mode of secretion is truly apocrine, are connected to the ducts of hair follicles and occur in almost all mammalian orders, excepting only whales, sea cows and scaly anteaters. In some large mammals, notably in horses, oxen and camels, apocrine glands are present throughout the hairy regions and function as sweat glands to control body temperature. In a wider range of species, however, apocrine units are aggregated to form scent glands, sometimes, though not always, in association with sebaceous units. For example, the chin and anal glands of the rabbit contain only tubular units, whereas the anal glands in group squirrels contain both apocrine and sebaceous units, and the well-known flank organs of the golden hamster are purely holocrine. Both types of scent gland occur in primates; for example lemurs have «antebrachial» glands, composed of tubular units, on the inner forearms, and paired «brachial» glands, composed of sebaceous units, on the anterior chest. A comprehensive account of scent glands and their function has been compiled by Brown and Macdonald (1985).

The glands of ground squirrels and of rabbits may be considered as model structures. The oral glands of ground squirrels (Kivett, 1978) have several lobes, each composed of branched tubules which coalesce to open into the canal of a hair follicle (Fig. 1). Small sebaceous glands are also present. The anal glands consist of three masses with both apocrine and large sebaceous units, each ope-
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Rabbits have three pairs of apocrine glands: anal, inguinal and submandibular. Mykytowycz (1965, 1966a, 1966b) has described their structure in detail and shown that their development is inhibited by castration in early life. There is clear experimental evidence (Ebling, 1977; Strauss and Ebling, 1970; Wales and Ebling, 1971) that the growth of the glands is stimulated by testosterone and inhibited by oestradiol (Fig. 2).

Chin glands are used for marking vegetation or the ground (Mykytowycz, 1968), and for nose to chin postures in social encounters. Anal glands scent the faeces which are also used for territorial purposes. The inguinal apocrine glands differ from the chin and anal glands, in that they are associated with a pair of discrete glands composed of holocrine units. Their secretion appears to be chemically different, and is probably concerned with sexual encounters.

**Human apocrine glands**

In man, rudiments of tubular glands are formed in most embryonic hair follicles.

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Figure 1
They become canalized and functional in any numbers, however, in only a few areas, including notably the axilla, the perineum, and the areola (Montagna and Parakkal, 1974). The fact that apocrine glands function as sweat glands in some other large mammals, and the evidence from comparative anatomy that eccrine glands appear to have gradually replaced apocrine glands in the hairy skin of non-human primates, has engendered a view that apocrine glands were once sweat glands but are now vestigial. It is more appropriate, however, to stress that human apocrine glands are survivors of an archaic system of scent organs which occurs in nearly all mammals and of which the oral glands of ground squirrels and the chin glands of rabbits are appropriate anatomical and physiological models. Each unit of the human axillary organ (Fig. 3) consists of a large coiled tubular gland opening into a hair follicle. The secretory segment is large and compact, with adjacent loops often fusing together and joined by shunts, and extending deep into the subcutaneous fat. There are modest sebaceous glands. The complex is remarkably similar to that of the oral gland of the ground squirrel; the axillary organ differs only in that eccrine sweat glands are also present and contribute substantially to the output.

Figure 2
Endocrine control of human apocrine glands

The hormonal dependence of the axillary organs is indicated by the fact that they do not become fully developed and functional until puberty (Hamilton, 1958). Since the pubic hair develops around the same time, it seems virtually certain that apocrine glands in this region also are hormone-dependent as, indeed, are sebaceous glands throughout the body. The role of androgen appears to be firmly established by the demonstration that hidradenitis suppurativa, an inflammatory condition of the apocrine glands and associated structures in the axillary and perineal regions, is ameliorated by treatment with the antiandrogen cyproterone acetate (Ebling, 1986; Ebling et al., 1980; Mortimer et al., 1986a; Sawers et al., 1986). The overall pattern of plasma androgen levels suggests that this disease has an androgenic basis (Mortimer et al., 1986b). These conclusions are not contradicted by a reported failure to show any effect of implantation of testosterone into the axilla (Shelley and Hurley, 1957), since like the sebaceous glands (Strauss et al., 1962) the apocrine glands of adult males may already be maximally stimulated by endogenous androgens. It is also worthy of note that the maximal rate of eccrine sweating is greater in men than in women and that this difference starts at puberty (Rees and Shuster, 1980). Mo-
reover, the sweat rate in eunuchs and in females can be increased to the normal male range by treatment with androgen (Walton et al., 1983).

**Composition of axillary secretion**

Human odour is usually ascribed to caprylic and similar volatile free fatty acids, which can be obtained from the genital and axillary and some other areas. Such secretions collected from the skin surface may, however, contain material from sebaceous and eccrine as well as from apocrine glands. Pure human apocrine secretion, obtained by cannulating tubules of the axillary glands has been described as a milky fluid containing proteins, reducing sugars and ammonia (Robertshaw, 1983).

Of particular significance is the demonstration that both 5α-androst-16-en-3-ol (Brooksbank et al., 1974) and 5α-androst-16-en-3-one (Bird and Gower, 1981) occur in human axillary secretion. These are the steroids (Fig. 4) which are produced by the boar and induce the sow to adopt a rigid stance, the so-called «standing reaction», in response to his attentions (Booth, 1980; Sink, 1967). 5α-Androstenone levels are higher in men than in women (Bird and Gower, 1981). In tests with alcoholic extracts of axillary secretion, that of males was considered to have a «strong» or «muskly» odour,
whereas that of women was more generally rated as «sweet» (Gower et al., 1985). The smell of pure 5α-androstenone was described as «strong», «musky» or «urinous» by men and «repellent» or «unpleasant» by 90% of women. The evidence thus suggests that the musky or strong smells of male axillary extracts, as compared with the sweeter smell of those from women, are related to production of 5α-androstenone.

Fresh axillary secretion is generally considered to have little odour. The pungence appears to develop as a result of the action of anaerobic diphtheroid bacteria on the native secretion. Leyden et al. (1981), while unable to detect differences in the skin surface lipids between smelly and non-smelly axillae, found clear bacteriological differences. Odour was associated with lipophilic diphtheroids. In an experiment, they first sterilized volar forearms of human subjects with compresses of 70% ethanol for two minutes. After evaporation, 3 µl of sterile apocrine sweat, collected after local injection of adrenalin, was spread over a small area. This was then inoculated with 0.1 ml of a suspension of one or other strains of bacteria isolated from human axillae. Odour was produced only by diphtheroids, not by micrococci (Fig. 5). Subsequently, Bird and Gower (1982) have produced evidence that 5α-androst-16-en-3-one is, indeed, a product of the bacterial action.
Biological and social functions of human odour

If the role of odour in human behaviour is sparsely documented in science, it is richly illuminated by anecdote. Female odour has, indeed, affected the course of history. King Henry III, while at the betrothal feast of the King of Navarre and Margaret of Valois, is said to have dried his face with a garment which was wet with the perspiration of Maria of Cleves, for whom he developed an irresistible passion, notwithstanding that she was the bride of the Prince of Condé (Doty, 1976).

Havelock Ellis (1905), in his book on the psychology of sex, laid stress on the sexual aspects of odour. He points out that the characteristic body odours develop at puberty and may become exaggerated in sexual and other emotional states. Men frequently, if not normally, emit an odour during sexual excitement which may last for several hours. So do women. According to the ancient medical writers, this phenomenon was especially marked in harlots and in the newly married. A case has been recorded of a woman who emitted a rose odour for two days after coitus, and it is said that there was a monk in Prague in the seventeenth century who could recognize which women were chaste by their smell. A somewhat more practical use of female odour was that of Asiatic princes who sometimes «caused a number of ladies to race in the seraglio garden until they were heated; their garments were then brought to the prince, who selected one of them solely by the odour». Ellis quotes other authors as attributing the source of the female sex attractant to the glands at the vulvar orifice.

Iwan Bloch (1934) has surveyed the field, with many historical references, in his book «Odoratus Sexualis». Bloch was particularly intrigued by the belief that the natural odour of the body becomes more intense immediately before, during, and after sexual intercourse, and he attributed this mainly to secretion from the axillae. According to Bloch, the philosopher Democritus was well acquainted with this odor voluptatis. «When Hippocrates visited him once, the physician was much surprised that the sage greeted a female who was accompanying the father of Greek medicine, one day as a virgin, and the next as a woman. La Motte le Vayer regards it as highly probable that in these judgments Democritus was following not his eye, as Diogenes Laertius supposes, but his nose. Ever so often we hear the story of the blind man who, upon his return home, recognized that in his absence his daughter had suffered herself to be seduced».

If Bloch paid most of his attention to female odours, Ellis was well aware of the possible effects of male odour on the female. He refers to an Austrian peasant who found that he was aided in seducing young women by dancing with them and then wiping their faces with a handkerchief he had kept in his armpit, and he mentions also the case of a young lady, not usually sensitive to body odours, who on one occasion «when already in a state of sexual erethism, was highly excited on perceiving the odour of her lover's axilla».

The historical evidence thus suggests that odour, especially that from the axillary and genital regions, plays a part in social and sexual communication in man, just as it does in other animals. It is important, however, to recognize that the associations of odour may be cultural rather than biological or, at least, that any biological mechanisms may be heavily overlaid by cultural tradition. Ellis (1905) clearly recognized this. He pointed out that axillary odours are anathema to the
Japanese and that at one time an odorous axilla constituted a disqualification for military service. He illustrates the ambivalence of reactions to axillary odour by relating a story about a man who on a hot day entered a steamboat with a woman to whom he was attached and seated himself between her and a male stranger. He soon became conscious of an axillary odour which he concluded to come from the man and which he felt was disagreeable; but a little later, when he realized it proceeded from his own companion, the odour at once lost its disagreeable character.

How far are these beliefs of history justified by experimental evidence? It seems clear that individual axillary odours can be recognized by their owners, and that discrimination can be made between male and female odours. Russel (1976), for example, had 13 women and 16 men wear T-shirts for 25 hours without bathing or using deodorants. The subjects were then asked to sniff the armpit regions of his or her own shirt, a strange male's shirt, and a strange female's shirt. They were each asked to identify their own shirt and to report which of the other two shirts came from a male. Nine out of the 13 females and 13 of the 16 males correctly made both judgments.

Doty (1985) accepted that individual identification could be made on the basis of olfactory cues. (The conclusion, incidentally, adds verisimilitude to Ellis's report that Chinese can correctly sort items of laundry by their smell). However, Doty and his associates showed that there was a perfect correlation between perceived maleness and odour intensity. Thus discrimination may be based solely on intensity, not on any qualitative difference between males and females. Doty further found that, in American subjects at least, there were no differences between males and females in their ratings of the intensity and pleasantness of different odours, which would seem to vitiate against sex-specific roles in odour communication. However, regardless of their actual origin, odours which were believed to come from sexual partners were rated more pleasant than those believed to come from strangers. This finding clearly adds weight to the conclusion Ellis (1905) drew from the ambiguous reactions of a man to the odours of his girl friend on the steamboat trip.

Evidence about the effects of vaginal odour on behaviour is difficult to assess. Doty et al. (1975) took samples of vaginal secretions from women at different stages of the menstrual cycle and invited both male and female judges to rate the odours. Secretions from the preovulatory and ovulatory phases of the cycle were generally rated as weaker and less unpleasant in odour than those from the menstrual and luteal phases, but there was great variation.

One difficulty is that of identifying the nature and source of the important compounds, since a number have been isolated. For example, the view of several authors (for example, Curtis et al., 1971) that certain aliphatic acids are «pheromones» which elicit male attention is not, according to Doty (1985), satisfactorily established.

Another major question in all human studies is whether attitudes or responses to odour result from an underlying physiological mechanism or are culturally conditioned. Recent experimental evidence that human axillary secretions can affect the menstrual cycle appears to establish a clear biological as distinct from a psychological effect.

Ovulatory menstrual cycles of normal length (29.5 ± 3 days in North America) are known to be more frequent in women who have weekly coital activity than in those who do not. The act of coitus may
not be essential, provided a male is present and there is genital stimulation; self-masturbation is ineffective. Cutler et al. (1985) collected axillary secretions from males in which large numbers of lipophilic diphtheroids and micrococaceae were present. Fifteen women aged 19 to 22 and one aged 30, with cycles of less than 26 or more than 32 days were then used as test subjects. Each woman received either an alcoholic extract of male axillary secretion, or pure ethanol, on her upper lip three times a week, and was instructed not to wash the area for at least six hours. The study was double blind in the sense that neither the administrator nor the receiver knew whether extract or placebo was being used. The results (Fig. 6) showed unequivocally that male axillary extracts reduced the incidence of menstrual cycles of aberrant length.

In a somewhat similar experiment (Preti et al., 1986) axillary secretions were collected from female donors and applied to recipients with normal length menstrual cycles. The onset of menstrual bleeding in the recipients moved significantly towards synchrony with that in the donors within two cycles (Fig. 7). Moreover, frozen axillary secretions from a group of women were able to alter the menstrual cycles of another group when thawed one year later.

Whether or not these experiments lead to
advances in therapy, they appear for the first time to show that human apocrine glands produce a true pheromone, that is to say a substance which produces a biological response in another individual, as distinct from a scent which may have a culturally conditioned, purely psychological effect.

**Conclusions**

The apocrine glands of man are scent organs, as are those of many other mammals, and the human axillary organ closely resembles structures in, for example, ground squirrels and rabbits. Scent glands are, in general, androgen-dependent and the evidence suggests that the axillary organ is no exception. The glands of the axilla, with the aid of bacteria, particularly diphtheroids, produce androsteneone and androstenol, the same odoriferous steroids with which the boar induces sexual receptivity in the sow. The experimental demonstration that the human menstrual cycle can be affected by extracts of male and female axillary secretion, perceived by smell, suggests that a true pheromone is produced and adds weight to anecdotal beliefs that the axillary and other body odours have a functional role in behaviour. The suppression of copious eccrine sweating with antiperspirants may be rational, but should deodorization be the aim of cosmetology? Suppression of all odour certainly eliminates social risks, but a more subtle approach to the understanding of the ways in which natural odour might be modified rather than eliminated is worth consideration.

![Non-Weekly Subjects](image)
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