Human odors—what can they tell us?

John N. Labows, Jr.
Monell Chemical Senses Center, Philadelphia, PA

Natural human body odors may be an important source of information about body processes and may also provide an additional communications channel. Initially, our research efforts have been directed at chemically characterizing the odors which normally emanate from the body. This information is used in an attempt to diagnose disease states, sexual receptivity, and stress. We are not involved in creating new odors but in knowing the chemical nature of the human odor bouquet. An understanding of these natural odors from different parts of the body will allow the perfumer to create other odors which will blend with or mask the natural ones. In addition, there is a real possibility that skin odors—axillary odors in particular—may be involved in a human communication system.

Present analytical methods such as headspace concentration, gas chromatography, and the combination of gas chromatography/mass spectrometry (GC/MS) have made it possible to separate and identify submicrogram quantities of organic compounds. GC/MS profiling of the small organic compounds present in body secretions, such as blood serum, cerebrospinal fluid, and urine of diseased and healthy individuals, provides useful diagnostic information. In some cases, complete metabolic profiles are obtained and qualitative or quantitative changes in individual components are noted with the onset of disease processes or across the female reproductive cycle. In the identification of the chemicals responsible for skin odors or for the odors produced in cultures by microorganisms, GC/olfactory analysis is used to determine which components of these complex mixtures contribute to the observed odor.

Odor and disease

The most important use of body odors in disease diagnosis relates to the infant diseases involving errors in amino acid metabolism. Strong and unusual odors are manifest in the breath, sweat, and urine of these infants. Table I summarizes the various known acidurias, the amino acids that are not properly metabolized, and the odors associated with the compounds which accumulate and can be detected in the urine.

Table I. Metabolic disorders in infants

	Amino acid(s)	Enzyme defect	Compound(s) accumulated
MSUD	leucine, valine isoleucine	branched chain decarboxylase	2-hydroxy acids 2-keto acids (maple syrup)
Oasthouse	methionine	methionine utilization	2-keto-butyric acid 2-hydroxy-butyric acid (celery, yeast)
PKU	phenyl alanine	phenyl alanine hydroxylase	phenyl pyruvate phenyl acetic acid (mousy, horsey)
Sweaty feet	leucine	isovaleryl CoA dehydrogenase	isovaleric acid (sweaty)

In the case of the Maple Syrup Urine and Oasthouse syndrome, the keto- and hydroxy-acids which have been identified may not be responsible for the observed maple and celery/yeast odors. The odors could be the result of conversion of 2-keto-butyric acid to methyl-ethyl-tetronic acid (Slusser's lactone) which is used as an extender in maple and celery flavors and has a maple syrup-like odor (R. Soukup, personal communication). With these acidurias it is imperative that an immediate diagnosis be made, since corrective diet can prevent the brain damage that results from the diseases. Diagnosis is most readily made on an olfactory basis which can subsequently be supported by gas chromatographic analysis of the urine. It is accepted procedure for the pediatrician to "smell his patient" and at least one medical school uses odors as a part of its lecture material. As we understand which odors are associated with various disease processes, it would be appropriate to make perfumer training available to physicians or even to have perfumers who could work with physicians in olfactory diagnosis.

We are investigating the relationship between various oral pathologies and the chemicals found in human saliva. Various volatile compounds such as skatole, indole, sulfides, and long chain alcohols have been identified in the headspace of saliva samples. These materials increase in both a quantitative and qualitative fashion with varying degrees of periodontitis. Specifically, alkyl pyridines appear to be present in the saliva only in individuals with periodontal disease. Our hope is that by monitoring these compounds we will be able to detect early stages of this problem which affects 60-70% of the popu-

 0361-8587/79/0004-1201$02.00

lation.

Systemic disease processes such as gastrointestinal disorders and diabetic keto-acidosis (acetone breath) also manifest themselves in odors associated with breath and/or saliva. The classic uremic breath odor has been described as "fishy" or "ammoniacal" and involves the presence of dimethylamine and trimethylamine in the breath. In addition, other illnesses such as skin ulcers, gout, typhoid, diphtheria, smallpox, and scurvy have been reported to have distinct odors.

Odor and reproductive state

Dramatic chemical and psychological changes take place within the female body throughout the menstrual cycle. These are the result of variations in hormone levels and include changes in olfactory acuity as well as cyclic changes in numerous biochemical processes. The latter may be reflected in cyclical variations in body odors as is the case in many mammalian species where information on female receptivity is transmitted to the male through various odors from body secretions.

Odors from the mouth and vagina have been examined as possible sources of chemicals which undergo cyclical changes. Preliminary work with female breath samples has centered on three volatile sulfur compounds (hydrogen sulfide, methyl mercaptan, and dimethyl sulfide) which are primarily responsible for endogenous bad breath ("halitosis"). These three compounds were found to change in a cyclical fashion increasing at the time of ovulation and again during menstruation. With a gas chromatograph adapted for the detection of sulfur compounds, these materials can be quantitated at the low nanogram levels. Their increase corresponds to increases in both bacterial counts and in exfoliation of cells in the oral cavity.

Olfactory analysis of vaginal odors has shown that human observers rate the odor least unpleasant and less intense at the time of ovulation. However, the large variations in response on individual subjects suggests that this is not a useful predictive approach.

Detailed chemical profiling of vaginal secretions has led to the identification of a variety of low molecular weight organic compounds. Lactic acid concentrations did rise at midcycle and this information may be useful in predicting the time of ovulation. Short-chain aliphatic acids were present in only six of fourteen women and did not vary in concentration in a cyclical manner. These aliphatic acids, referred to as *copulins,* were found originally in rhesus monkey vaginal secretions. However, their pheromonal effects have been questioned.

Odor and communication

It is of interest, in the context of human olfactory communication, to consider the chemical odorants present in animal skin glands, urine, and saliva which have pronounced physiological and behavioral effects. The scent-marking skin glands are either apocrine-like and analogous to the human apocrine gland or are a combination of apocrine and sebaceous glands. A variety of these glands present in the rabbit and deer convey alarm and fright messages as well as information on individual identity. The isolated boar pheromones, androst-16-en-3-ol and androst-16-en-3-one, secreted by the submaxillary gland, have a direct effect on the sexual receptivity of the sow and are used commercially to assist in artificial insemination. The fact that estrus can be determined in the sow by her response to these compounds suggests that there is a heightened acuity for these compounds at the time of ovulation. This is similar to the increase in olfactory acuity prior to ovulation noted in human females. A somewhat unique but analogous situation is the elephant temporal gland which is an apocrine gland that is active under stress and possesses an "elephanty" odor. Table II summarizes some of the mammalian communication systems that have been studied. In many cases there are unique odors such as rab-

Table II. Mammalian chemical communication

Animal	Chemical (source)	Behavior
Boar	*androstenol and androstenone* (submaxillary gland)	induces lordosis
Deer	unsaturated lactone (urine)	sniffing licking
Marmoset monkey	butyrate esters of long-chain alcohols (circumgenital gland)	individual identity
Hamster	dimethyl sulfide (vagina)	elicits attraction
Rhesus monkey	*short-chain aliphatic acids* (vagina)	sexual activity not reproducible
Elephant	phenol, m,p-cresol (temporal gland)	---------
Dog	methyl p-hydroxybenzoate (vagina)	attraction and arousal

bit odor, monkey odor, and deer odor which are associated with specialized skin glands.

The characterization of a behaviorally active chemical is a tedious task and may involve isolation and structural identification of numerous constituents from a secretion. This is followed by a bioassay in which the chemical(s) are presented to the animal in a natural context and behavioral response is measured. Though many mammalian secretions have been found to give behavioral responses, few chemicals with definitive effects have been characterized (Table II). The best example is the two androgen steroids used by the boar. Recently, methyl p-hydroxybenzoate has been isolated from the vaginal secretions of female dogs and shown to be a highly effective sexual excitant to males.

Psychologists and poets have long commented on the ability of human odors to communicate sexual and social information. Odor control of endocrine states is suggested by the work on the synchronization of cycles of females living together. Other researchers in limited studies have attempted to demonstrate that subjects can detect sexual differences and individual identity using axillary odors (Table III).

Table III. Possible information content of human odors

Human odor sources	Information content	References*
Urine	Sex discrimination	Beauchamp (1976)
Axillae (T-shirt)	Sex discrimination Individual recognition	Russel (1976) Hold (1977)
	Personality traits	McBurney (1976)
Axillae (pads)	Sex, pleasantness, intensity	Doty (1976)
Hand	Sex discrimination	Wallace (1976)
Vagina	Odor change with menstrual cycle	Doty (1975)
Breath	Odor change with menstrual cycle	Tonzetich (1978)
Androstenol copulins	Assessment-of-people Test in presence of odorants	Cowley (1977)

* References in "Chemical Signals in Vertebrates" article by Doty, p. 273.

Odor perception and preference

The primary odors, as elaborated by Amoore and based on specific human anosmias, include spermous, musky, fishy, urinous, malty, and sweaty. Most of these can be related to observed human odors. Thus, Amoore suggests that if we have a specific olfactory receptor for a given odorant, that odorant might be naturally given off by the body. The sweaty odor of isovaleric acid is probably part of the foot odor and is also produced by the action of skin bacteria on apocrine secretion (see below). Pyrolline, the spermous odor, has been shown to be produced by enzymatic breakdown of the polyamines in semen. Androst-16-en-3-one, the urinous odor, also has axillary-like odor and may be formed as a result of the metabolism of apocrine secretion; the related androstenol is found in urine. Chemicals which fit the musky or malty anosmias have not as yet been reported from human odor sources; but the natural musks, such as cycloheptadecenone (civet), were first obtained from animal scent glands. The observed odorants are in most cases metabolic by-products of human secretions rather than odorants which were directly secreted. The same situation may be true in a number of mammalian species where bacteria may be involved in the eventual formation of chemicals used in odor communication.

Our olfactory preference appears to change with sexual maturity from sweet, fruity odors to heavier, musky odors. This preference alteration parallels a marked change in body odors due to the increased activity of the sebaceous glands and the initial activity of the apocrine glands. The apocrine odor which is subsequently produced is a secondary sexual characteristic, a sign of sexual maturity, and a heavy odor not unlike that of androstenone. It has been variously described in the literature as goat-like, ammoniated valerian, chlorinated urine, cumarone, overripe peaches, heliotrope, lamb, and burnt coffee-beans. In some cultures where human odors are not taboo, the apocrine odor is a preferred odor and may represent a source for olfactory communication.

Odor sampling

There has been an interest in developing techniques for sampling total body odors. Dravnieks' group has placed an individual in a large glass cylinder and sampled the volatiles by passing a gas stream through the tube and concentrating the volatiles. He has also developed systems for sampling skin and axillary odors. Another group used a telephone booth-like chamber in which human volatiles were sampled. Here approximately 300-400 individual chemicals were detected and 135 identified. The object of these trials was to explore the possibility that body odors might be unique to a given individual or a given race and serve as a personal signature. Room air also has been sampled in the presence and absence of individuals in an attempt to determine what contaminants are added to the environment by body volatiles. This is particularly relevant to restricted environments such as submarines and space cabins where air recirculation is a necessity. The thermally induced total body sweat of schizophrenic patients was collected for analysis of unique odorants by the use of large plastic bags. In all of these collections, including one on axillary odor using cotton pads, no volatile chemicals which represent specific human odors were identified.

Skin glands and odor

Three separate glandular systems are responsible for secreting chemicals to the skin surface. The eccrine glands which are present over most of the body are thermoregulatory sweat glands which respond to physical activity. The eccrine

secretion has been well characterized and consists of an aqueous solution of inorganic salts and amino acids which has no significant odor. The sebaceous glands which are located primarily on the forehead, face, and scalp are under hormonal control and secrete lipid materials such as triglycerides and esters. This secretion has a slight pleasant odor but can be readily metabolized by skin microorganisms. The third glandular system is that of the apocrine glands which are located primarily in the genital and axillary areas. They become active at puberty because of the presence of androgen steroids from the adrenal glands, testes, and ovaries and secrete in response to emotional situations. Our analysis has shown that the secretion contains protein (10%), cholesterol (1%), and steroids (~0.02%).

The observed skin odors result from a breakdown in these secretions, principally from the sebaceous and apocrine glands. Bacterial lipases can hydrolyze the triglycerides to glycerol and fatty acids which may be further metabolized to odorous compounds. Our approach has been to attempt to duplicate the natural odors *in vitro* by incubating the normal skin microorganisms with these secretions. For example, the yeast *Pityrosporum ovale,* the major scalp resident, is able to metabolize lipid substrates to 4-hydroxy-acids which readily undergo ring closure to the volatile and odorous γ-lactones. We have used the technique of headspace concentration on Tenax followed by GC/MS analysis to profile all the volatiles produced by Pityrosporum (fig. 1). These compounds include pentanol, benzyl alcohol, phenyl ethanol, and several lactones, including γ-octalactone (coconut flavor), γ-nonalactone (cream, fruity), and γ-decalactone (peach, pear). The odor of the culture is similar to that of unwashed hair and closely matches that of γ-decalactone, the major lactone component. Because of the compounds it produces, this scalp microorganism has the potential to be used for the natural formation of flavor additives.

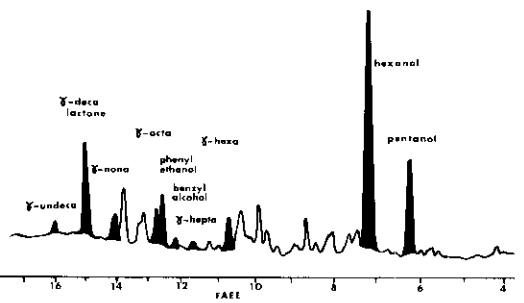

Figure 1. Odor profile of Pityrosporum ovale. (Reproduced with permission of Applied and Environmental Microbiology.)

This odor profile may also be used for the detection of the Pityrosporum genus since other yeasts grown on the same media failed to yield any lactones. In addition, when sebum is the major substrate and longer incubation times are used, a scalp odor is generated. Our preliminary headspace analysis suggests that this odor contains short-chain aliphatic acids in addition to the lactones. The formation of odors on the scalp may be a cooperative effort of *Propionibacterium acnes*, which readily hydrolyzes triglycerides, and *Pityrosporum ovale*, which can metabolize the resultant fatty acids and/or glycerol to various odorants.

The unique human axillary odor is also the result of microbial action on an odorless secretion. The two major residents of the axillae are the diphtheroids (lipophilic and large colony) and the micrococci bacteria. Specific odorants can be produced by incubating these bacteria with apocrine secretion either on a cleansed forearm (fig. 2) or in a test tube. The micrococci produce a sweaty, acid odor which has been shown by headspace analysis to be isovaleric acid (fig. 3). The diphtheroids also produce this acid but its odor is masked by other odor components which impart a heavier apocrine odor to the incubated sample. Addition of sebum increases the growth and odor of the lipophilic diphtheroids. Bacterial sampling, along with olfactory analysis of individual subjects, further demonstrates that the apocrine odor is associated with the diphtheroid bacteria (fig. 4). These odorants, which represent a unique human odor in analogy to the animal scents, are presently being investigated. However, the following experimental observations relate to the possible identification of these odorants.

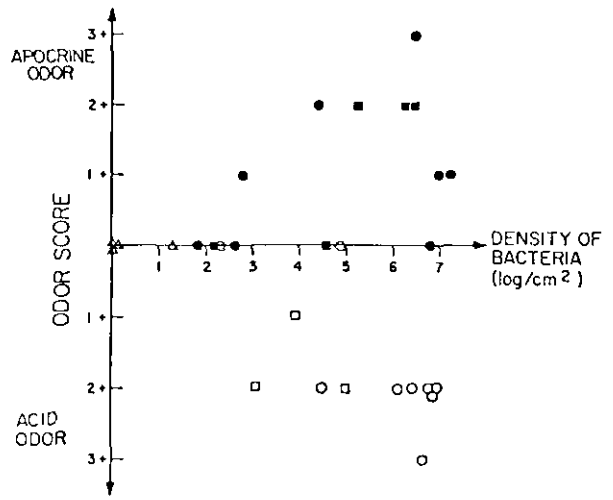

Figure 2. In vivo generation of apocrine odor under occlusive patches on the forearms inoculated with various bacteria and sterile apocrine secretion. △ Mg-Omadine, ○ COCCI, □ GNB, ● LIPO, and ■ LCD.

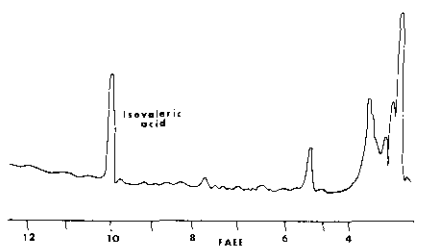

Figure 3. Micrococci on apocrine secretion.

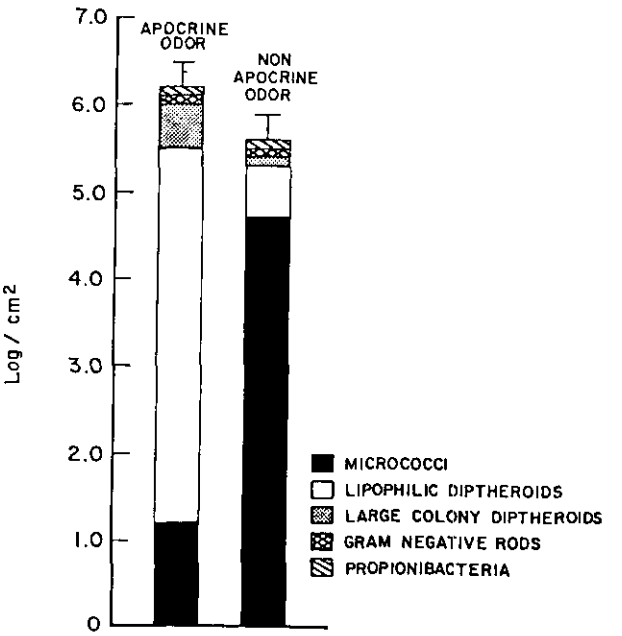

Figure 4. Relationship of bacteria and odor.

The boar pheromone androstenone, and its precursor androstadienone, both have intense odors which closely resemble the apocrine odor. Trace amounts of androstenone and androstenol as well as other steroids have been reported to be present in human axillary sweat (Table IV).

Table IV. Steroids found in human axillae

Steroid	Sample
Androst-4-ene-3, 17-dione Androsterone (sulphate) DHA (sulphate) Cholesterol	Axillary hairs and sweat
Androst-4-ene-3, 17-dione Pregn-5-en-3β-ol-20-one	Axillary sweat
5α-Androst-16-en-3α-ol	Axillary sweat
5α-Androst-16-en-3-one	Axillary sweat
Androsterone (sulphate) DHA (sulphate) Cholesterol	Apocrine secretion

More recently we have found that heated apocrine secretion (>150°) gives an apocrine-like odor. The major contributors to this odor are isomeric androstadien-17-ones and androst-2-en-17-one which arise from the thermal breakdown of dehydroepiandrosterone and androsterone sulfates, respectively. Thus the apocrine secretion contains specific steroid materials in addition to cholesterol which may be metabolized to the odorous Δ^{16}-androgens by the diphtheroid bacteria. Whether this actually occurs remains to be demonstrated. However, if it is the case, the fact that about 50% of the population is anosmic to these odorants suggests that

axillary odor would be perceived as a sweaty odor by anosmic individuals whereas others would perceive an apocrine odor. This may be of importance to physicians with an unrecognized specific anosmia when confronted by patients with unusually strong axillary or pubic odors. Finally, the fact that these steroids have demonstrated sexual effects in one animal suggests that they might also be physiologically active in other species.

The apocrine secretion and the resultant odor are normal responses to emotional stimuli. The recognizable odor of schizophrenic patients is believed to be associated with an altered axillary odor. Thus, a sensitive method for monitoring of the activity of the apocrine gland could provide information relative to the emotional state of an individual.

Profiling of human odors represents a noninvasive technique which might provide information for the detection of many metabolic and infectious disorders. Knowledge of the composition of natural odorants specific to different body areas could also provide the perfumer with an *in vitro* method for testing the effects of odor-masking compounds or for the blending of perfumes with natural odorants.

Acknowledgements

The work described on scalp and axillary odors is part of a cooperative research program with the Duhring Laboratories of the Department of Dermatology, University of Pennsylvania, and is supported in part by a grant from the National Institute of Arthritis, Metabolic, and Digestive Diseases.

Selected references

J. Amoore, Specific anosmia and the concept of primary odors, Chemical Senses and Flavor, **2,** 267 (1977)

J. E. Amoore, P. Pelosi and J. L. Forrester, Specific anosmias to 5α-androst-16-en-3-one and ω-pentadecalactone: The urinous and musky primary odors, Chemical Senses and Flavor, **2,** 401 (1977)

B. Brody, The sexual significance of the axillae, Psychiatry, **38,** 278 (1975)

A. Comfort, The likelihood of human pheromones, in Pheromones, p. 386-396, M. C. Birch, ed., North-Holland Publishing Co., (1974)

R. L. Doty, ed., Mammalian, olfaction, reproductive processes and behavior, Academic Press, 1976

A. Dravnieks, Evaluation of human body odors: Methods and interpretations, J. Soc. Cosm. Chem., **26,** 551 (1975)

R. L. Ellin, et al., An apparatus for the detection and quantitation of volatile human effluents, J. Chromatogr., **100,** 137 (1974)

S. K. Freeman, Pheromones (olfactory communication), J. Soc. Cosm. Chem., **29,** 47 (1978)

D. A. Goldfoot, M. A. Dravetz, R. W. Goy and S. K. Freeman, Lack of effect of vaginal lavages and aliphatic acids on ejaculatory responses in rhesus monkeys: Behavioral and chemical analyses, Horm. and Behav., **7,** 1 (1976)

M. Goodwin, K. M. Gooding and F. Regnier, Sex pheromone in the dog, Science, **203,** 559 (1979)

D. B. Gower, 16-Unsaturated C_{19} steroids—A review of their chemistry, biochemistry and possible physiological role, J. Ster. Biochem., **3,** 45 (1972)

R. L. Henkin, Olfaction and its relationship to the sexual function in men and women, Perf. and Flavor., **1,** 19 (1976)

E. Jellum, Profiling of human body fluids in healthy and diseased states using gas chromatography and mass spectrometry, J. Chromatogr., **143,** 427 (1977)

E. Johnson, Steroids and specialized skin secretions in mammals, Biochem. Soc. Trans., **4,** 602 (1976)

K. Liddel, Smell as a diagnostic marker, Postgrad. Med. J., **52,** 136 (1976)

J. W. Mace, S. I. Goodman, W. R. Centerwall and R. F. Chinnock, The child with an unusual odor, Clin. Pediat., **15,** 57 (1976)

R. P. Michael, R. W. Bonsall and D. Zumpe, Evidence for chemical communication in primates, Vitamins and Hormones, **34,** 137 (1976)

R. W. Moncrieff, Odour preferences, Grampian Press, London, 1966

W. Montagna and P. Parakkal, Structure and function of skin, Academic Press, 1974

D. Muller-Schwarze and M. M. Mozell, eds., Chemical signals in vertebrates, Plenum Press, New York, 1977

R. Mykytowycz and B. S. Goodrich, Skin glands as organs of communication in mammals, J. Invest. Derm., **62,** 124 (1974)

G. Preti and G. R. Huggins, Organic constituents of vaginal secretions, in The Human Vagina, E. Hafez and T. Evans, eds., Elsevier/North-Holland Biomedical Press, (1978)

R. Soukup, personal communication

J. Tonzetich, G. Preti and G. R. Huggins, Changes in concentration of volatile sulfur compounds of mouth air during the menstrual cycle, J. Int. Med. Res., **6,** 245 (1978)