Behav Ecol Sociobiol (2003) 54:89–97
DOI 10.1007/s00265-003-0613-4

REVIEW

Warren S. T. Hays

Human pheromones: have they been demonstrated?

Received: 27 November 2002 / Revised: 22 March 2003 / Accepted: 22 March 2003 / Published online: 30 April 2003

Abstract Efforts to collect evidence of human pheromones have focused on three partly overlapping classes of possible human pheromones: (1) axillary steroids, (2) vaginal aliphatic acids, and (3) stimulators of the vomeronasal organ. Examples of each of these classes have been patented for commercial use, and in some cases aggressively marketed, but there is only incomplete evidence supporting any particular claim that a substance acts as a human pheromone. The large axillary scent glands found in humans appear to be well adapted for the production of pheromones, but may actually be used for non-pheromonal odor communication, such as the sharing of information about the immune system. Putative menstrual synchronization within social groups of women and putative acceleration of the menstrual cycle caused by men's odors may suggest the existence of human pheromone systems, but evidence in both cases is still inconclusive.

Keywords Human pheromone · Androstenone · Copulin · VNO · Vomeropherin

Communication odors in humans and other primates

Pheromones are defined as "substances which are secreted to the outside by an individual and received by a second individual of the same species, in which they release a specific reaction—for example, a definite behavior or a developmental process" (Karlson and Luscher 1959, p 55). Two varieties are generally acknowledged: releaser pheromones, which cause an immediate behavioral response, and primer pheromones, which initiate a long-term physiological response (e.g., puberty). The entomologists who coined the term noted that the scent marks of mammalian Carnivora might be an example. By the early 1970s, the word "pheromone" was being used widely to describe a variety of signal smells in many taxa, including mammals. Some authors have felt that the word is too broadly used by mammalogists (Beauchamp et al. 1976). In this review, I will assume a liberal interpretation of the original definition.

This review explores the possibility that humans use pheromones of some sort. It is important to remember that if this is the case, then this communication almost certainly takes place within the context of a hugely complex array of physiological, psychological, and sociological factors. As one study succinctly expressed the matter: "We cannot expect humans to behave like moths flying up the concentration gradient toward the desirable source" (Jacob and McClintock 2000, p 59).

Hominoids (including humans) and Old World monkeys typically have far fewer scent glands on their bodies than New World monkeys, but social sniffing is nonetheless a common aspect of behavior in many Old World primates. The few known scent glands in these species include those found in the axillae of African hominoids [humans, gorillas (*Gorilla gorilla*), chimpanzees (*Pan troglodytes*) and bonobos (*P. paniscus*)], on the chest of orangutans (*Pongo pygmaeus*) and mandrills (*Mandrillus leucophaeus*) and on the forehead of stump-tailed macaques, (*Macaca arctoides*; Albone and Shirley 1984).

Among these examples, human axillary scent glands are particularly large, and also contain an unusually high density of apocrine glands (Montagna 1964). These apocrine glands make a nutrient-rich sweat that feeds coryneform and coccal bacteria, which produce a variety of odorous molecules. This system is similar to that used by some Carnivora to produce their scent marks (Gorman et al. 1974). There are substantial differences between men and women in the structure and flora of the axillary scent glands. Women have 75% more apocrine glands in their armpits than men do (Brody 1975), and men's apocrine glands are larger than women's (Doty et al. 1978). Women typically have more coccal bacteria

Communicated by A. Cockburn

W. S. T. Hays (✉)
Department of Biology,
Hawaii Pacific University,
Honolulu, HI 96815, USA
e-mail: whays@hpu.edu
Tel.: +1-808-2565842

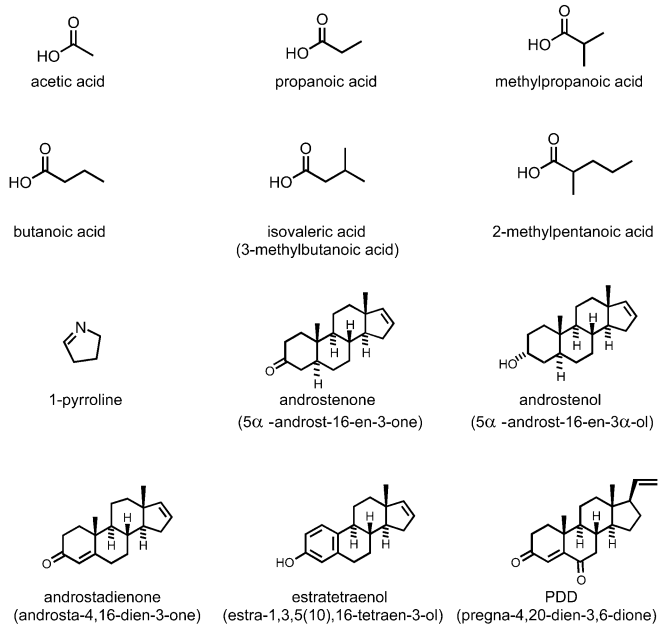

Fig. 1 Chemicals proposed as human pheromones or as synthetic equivalents

among their flora, and men more coryneform (Jackman and Noble 1983). The sexual dimorphisms of the axillary scent glands and the fact that they only become active at puberty support the hypothesis that they play a role in sexual communication.

Humans also have large apocrine glands around the genitals and nipples, and on the cheeks (Albone and Shirley 1984), some of which may be involved in scent production. Women's nipples appear to produce smells that can be detected by newborn infants (Porter and Weinberg 1999), as has been demonstrated in domestic rabbits (*Oryctolagus cuniculus*; Hudson and Distel 1984).

Several other sources of pheromones on the human body have been proposed, without substantial evidence. Albone and Shirley (1984) suggested that male pubic sweat may contain 1-pyrroline (Fig. 1), the main odorous molecule found in semen. Twenty percent of people lack the ability to smell 1-pyrroline, a specific anosmia that may indicate that the ability to smell 1-pyrroline is a special adaptation (Albone and Shirley 1984). Immerman and Mackey (1997) proposed that smegma, a substance produced by the Tyson's glands found under the prepuce of the penis, contains pheromones. Berliner et al. (1991) proposed that pheromones are carried in cells that slough from the epidermis.

Saliva carries pheromones in at least one mammal species, the pig (*Sus scrofa*). Doty et al. (1982) found that human subjects have some ability to discern whether a hidden person is male or female by sniffing his or her breath through a tube. However, these authors also found that male subjects typically had greater reported strength of breath odor, and that subjects tended to guess that anyone with strong breath odor was male. This might merely reflect culture-specific sexual differences in, for example, diet or hygiene.

Non-pheromonal scent communication in humans

The fact that humans have large axillary organs with an anatomy typical of mammalian scent glands may be the strongest evidence that our species communicates via odor. However, at least one non-pheromonal purpose has been proposed for human axillary scent glands: the creation of odors used in individual assessment of the immune systems of potential mates. Some researchers regard such odors as examples of human pheromones, but they will not be treated as such in this review because they do not "release a specific reaction", as stipulated in the original definition of the term.

A similar system has been evidenced in laboratory mice, which avoid potential mates that have major histocompatibility complex (MHC) genetic patterns that are similar to their own (Jordan and Bruford 1998). In choice tests, mice also prefer the smell of conspecifics that have MHC different from their own (Penn and Potts 1998). One possibility is that individual mice may have different odors because they carry different bacterial flora, which may reflect differences in the genetic constitution of their immune systems (Howard 1977). By selecting mates with odors that differ from their own, mice may enhance the genetic diversity of immune systems among their offspring, raising their collective resistance to disease.

Similar evolutionary pressures acting on humans appear to favor dissimilar MHC patterns among mated pairs. Couples with similar MHC typically have babies with lower than average birth weight (Reznikoff-Etievant et al. 1991). Couples suffering from frequent spontaneous abortions are more likely than usual to share similar patterns in their MHC (Beer et al. 1985; Wedekind et al. 1995; Weetman 1999). Married couples of Hutterites, a North American religious sect, typically share greater similarity in their MHC patterns than non-Hutterite couples, and also have low fertility, possibly suggesting poor survivorship of embryos (Ober et al. 1988).

There is, however, less matching of MHC types among Hutterite couples than expected by chance (Ober et al. 1997), suggesting some mechanism that allows individuals to obtain information about the MHC pattern of potential mates. There is evidence that humans can accomplish this by smell, as seen in mice. Both men and women prefer the axillary odors of people whose MHC pattern is dissimilar to their own (Wedekind et al. 1995; Wedekind and Furi 1997). Although humans in many societies replace their natural odors with artificial ones, their personal selection of these replacement odors is also significantly determined by their MHC combination (Milinski and Wedekind 2001). It is possible, then, that axillary scent glands evolved in humans to display olfactory information about the immune system, which may be regarded as a non-pheromonal role.

Airborne odor detection

Humans have a number of sensory organ systems that may be involved in the detection of airborne chemicals. In addition to the olfactory epithelium and the trigeminal nerves (which detect irritants on the nasal mucosa), two other such systems have been proposed. These are the terminal nerves and the vomeronasal organs (VNOs).

Wysocki and Meredith (1987) proposed that adult humans may have functioning terminal nerve systems, a cranial nerve pair found in many vertebrates, but there appears to be little supporting evidence. Terminal nerves are known to be involved in pheromone detection in hamsters (*Mesocricetus auratus*; Wirsig and Leonard 1985) and Atlantic stingrays (*Dasyatis sabina*; Moeller and Meredith 1998).

VNOs are found in many mammals, including humans. In mammals with well-developed VNOs, each organ is connected by a nerve to an accessory olfactory bulb (AOB) in the brain. In some species such as hamsters, the VNOs are found at the bottom of tubes in the wall of the nasal cavity, surrounded by muscular tissues that actively pump odors onto the receptor cells (Meredith 1994). The VNOs, like the olfactory epithelium, are used in many species as pheromone receptors. Horses (*Equus caballus*), dogs (*Canis domesticus*), cats (*Felis catus*) and many other mammal species perform flehmen (wrinkle their upper lips) when they are sniffing the urine of a conspecific, as a method of drawing odors up into their VNOs through the nasopalatine duct in the palate. Chemicals detected by the VNOs have been called both vomodors (Cooper and Burghardt 1990) and vomeropherins (Monti-Bloch et al. 1994), but the former term has precedence.

Although the VNO is traditionally regarded as vestigial in humans and is known to degenerate in late fetal development, several studies have found that at least 90% of adults have visible VNOs on their nasal septa (Garcia-Velasco and Mondragon 1991; Moran et al. 1991; Stensaas et al. 1991; Bhatnagar and Smith 2001). The human VNOs appear as a pair of tiny dead-end tubes, a few millimeters long (Garcia-Velasco and Mondragon 1991). This is similar to the state of the VNOs of other hominoids and Old World monkeys, but far smaller and less elaborate than the VNOs of New World monkeys (Wysocki and Meredith 1987).

Human VNOs have epithelia with an appearance consistent with the hypothesis that they serve as a chemical sensory organ (Moran et al. 1991). However, all of the 34 putative human VNO receptor genetic loci that have been identified have turned out to be pseudogenes, suggesting that they are nonfunctional (Kouro-Mehr et al. 2001). Human VNOs also contain cells that appear to be sensory neurons (Stensaas et al. 1991), but attempts to find neural connections between the human VNO and the central nervous system have not been successful (Witt et al. 2002). The adult human brain lacks AOBs, though they do begin to form in the fetus.

If the human VNO is an active organ, then its effects are apparently subtle. Both VNOs are often accidentally removed from patients during routine nasal surgery, but so far there have been no reports of anyone suffering ill effects from this loss (Wohrmann-Repenning 2000). The evidence for functional human VNOs is further reviewed and critiqued by Wysocki and Preti (2000).

Efforts to collect evidence of human pheromones have focused on three partly overlapping classes of possible human pheromones: (1) axillary steroids, (2) vaginal aliphatic acids, and (3) stimulators of the vomeronasal organ. These are described in the following three sections.

Axillary steroids and other odorous axillary molecules

The main "sweaty" smell of axillary sweat comes from aliphatic acids (Gower et al. 1988). In addition, ten steroids are found in human axillary sweat (Labows 1988). Three of these have been described as human pheromones (Fig. 1): androstenone (5α-androst-16-en-3-one), androstenol (5α-androst-16-en-3-α-ol), and androstadienone (androsta-4,16-dien-3-one). The amounts of these steroids released into axillary sweat are too small to make a detectable odor, but axillary bacteria convert the less odorous steroids into more odorous ones (Gower et al. 1994), adding a "urinous" or "musky" component to the axillary odor. Larger molecules, mostly unidentified, are also present and add a pungent "burnt" component to the odor (Gower and Ruparelia 1993). One of these molecules is squalene, a major component of the pheromonal scent marks of saddleback tamarins (*Saguinus fuscicollis*), a New World primate (Smith et al. 1985).

Human axillary steroids are made by the testes, ovaries, and adrenal glands, and do not seem to be by-products of testosterone production (Gower and Ruparelia 1993). Young and middle-aged men produce much higher levels of some of these steroids, such as androstenone, than do women, pre-pubescent boys or elderly men (Gower and Ruparelia 1993). It has been proposed that some of these steroids may serve as male sexual pheromones in humans, as they do in pigs. Boars produce saliva with a high concentration of androstenone, and the smell of this steroid causes fertile sows to perform lordosis (Melrose et al. 1968). Commercial androstenone products are commonly used by pig farmers to determine if sows are fertile.

Axillary steroids and human behavior

Several experiments have tested androstenol and androstenone as possible agents influencing the affective and sexual reactions of human subjects, usually young women. It has been reported that the odor of androstenol improves women's feelings toward males (Cowley et al. 1977; Cowley and Brooksbank 1991) and causes ovulating women to feel more "submissive" (Benton 1982), and that androstenone attracted women in a blind choice test

(Kirk-Smith and Booth 1980). Other studies have yielded contradictory or negative results. It has been reported that androstenone worsens women's feelings toward males (Filsinger et al. 1985; Maiworm and Langthaler 1992) or has no effect on these feelings (Filsinger et al. 1984, 1990), that androstenol also has no effect on these feelings (Black and Biron 1982), that androstenol had no effect on women in a blind choice test (Gustavson et al. 1987), and that neither androstenone (McCullough et al. 1981) nor androstenol (Benton and Wastell 1986) affect women's reactions to erotic prose.

Gower et al. (1988) pointed out that both androstenone and androstenol smell similar to musks, and that if musky odors are not used as controls in these experiments then positive results might merely indicate affective reactions to familiar perfume odors. Only three of the studies listed above used musk controls (Black and Biron 1982; Filsinger et al. 1985, 1990), and none of these found axillary steroids to have a significantly stronger effect than musk.

Axillary steroids are widely and aggressively marketed as human sex attractants. Androstenol has been marketed in perfumes and colognes by the company Jovan since 1981. Both androstenol and androstenone are also sold by dozens of companies, generally with lurid claims, through sex-product stores and on the internet.

Cutler et al. (1998) reported that when heterosexual men wear an unidentified blend of chemicals derived from men's axillary secretions, they engage in more sexual activities with women. The senior author, Winifred Cutler, commercially manufactures a similar product, Athena 10X, and markets it as a sex attractant. Wysocki and Preti (1998) criticized Cutler et al. (1998), showing that the statistical methods used in this study were flawed, and most of the results were in fact non-significant. McCoy and Pitino (2002) recently reported that heterosexual women who wear Athena 10:13, a commercial women's fragrance also marketed as a sex attractant by Dr. Cutler's company, engage in increased sexual activity with men. The ingredients of Athena 10:13 have not been revealed, but it is described as being a synthetic blend that resembles women's axillary secretions.

Many studies have been conducted on the behavioral and physiological effects of axillary odor without attempting to distinguish which chemical components are active. Several studies have indicated that people can differentiate the axillary odors of men and of women (Russell 1976; Doty et al. 1978; Schleidt et al. 1981; Schleidt and Hold 1982). However, one of these studies (Doty et al. 1978) concluded that the subjects achieved this merely by guessing that stronger odors were male, and this may also have been true in the other studies.

Axillary odors and menstrual synchrony

It has been reported that menstrual cycles synchronize among social groups of women, and that this synchrony is mediated by axillary odors. Ovulatory synchrony exists in several other social mammal species, including laboratory rats (McClintock 1978), hamsters (Handelmann et al. 1980), banded mongooses (*Mungos mungo*; Rood 1975), and dwarf mongooses (*Helogale parvula*; Rood 1980). It is also found in one New World primate, the golden lion tamarin (*Leontopithecus rosalia*) and in over a dozen Old World primates (French and Stribley 1987). Besides the possible case of humans, examples include ring-tailed lemurs (*Lemur catta*; Jolly 1967), vervet monkeys (*Cercopithecus aethiops*; Rowell and Richards 1979), hamadryas baboons (*Papio hamadryas*; Kummer 1986), gelada baboons (*Theropithecus gelada*; Dunbar 1980), and chimpanzees (Wallis 1985).

Pheromones have not been indicated as the cause of any primate ovulatory synchronizations except those of humans. However, in guinea pigs (*Cavia porcellus*; Jesel and Aron 1976), laboratory rats (McClintock 1978), and laboratory mice (McClintock 1983), it has been shown that it is possible to change the length of a female's cycle by exposing her to another female's urine. In rats, this has also been done by exposing the subject animal to air ventilated from the cage of another female (McClintock 1984).

McClintock (1971) reported synchronization of the cycles of roommates and close friends living in a women's university dormitory. Two later studies attempted to replicate this work: one found significant synchrony, not only among close associates but throughout an entire dormitory population (Little et al. 1989); the other found no evidence of synchrony at all (Wilson et al. 1991). Aron and Leonard Weller have reported signs of synchrony among lesbian couples living together (Weller and Weller 1992), family members living in urban households (Weller and Weller 1993a; Weller et al. 1999b), friends and roommates living on a kibbutz (Weller and Weller 1993b), friends in women's college dormitories (Weller et al. 1995), family members in rural Bedouin households (Weller and Weller 1997), and friends sharing offices (Weller et al. 1999a). They have also sought and failed to find cycle synchrony among roommates in women's college dormitories (Weller and Weller 1993a), officemates (Weller and Weller 1995a), and professional women's basketball teammates (Weller and Weller 1995b).

All studies done to date on human menstrual synchrony have been criticized for their methods (Arden and Dye 1998; Schank 2001). For example, almost none of these studies have used control groups; few have been conducted blind or double blind, and almost all have depended on the memory of the subjects as the main or only source of data. It therefore cannot be said with certainty whether human menstrual synchrony occurs among humans, although there are many indications that it does.

Three studies have reported success in experimentally altering women's menstrual cycles by exposing them to other women's axillary odors (Russell et al. 1980; Preti et al. 1986; Stern and McClintock 1998). Wilson (1992) criticized the experimental and analytic methods of the

former two studies, noting among other things that sample sizes were too small and duration too short to warrant their conclusions. Stern and McClintock (1998) found that if the women donating the odors were in the ovulatory phase of their cycles, then the recipients' cycles would accelerate significantly, while if the donors were pre-ovulatory, then the recipients' cycles would slow significantly. Similar findings have been reported in rats (McClintock 1984). One study has reported that the smell of axillary extracts can affect women's LH levels (Shinohara et al. 2001). If ovulatory synchrony occurs among humans, it is possible that it is mediated by axillary odors of some kind.

Besides menstrual synchrony, another body of evidence of human pheromones is the acceleration of menstrual cycles in the presence of men. In female guinea pigs (Jesel and Aron 1976), laboratory mice (McClintock 1983), and sheep, (*Ovis aries*; Signoret 1991), exposing females to the smell of males induces ovulation or accelerates the ovulatory cycle. Three studies have found that women who see men socially at least three or four nights a week have significantly shorter menstrual cycles than women who do not (McClintock 1971; Cutler et al. 1980; Veith et al. 1983), even if the contact in these encounters is nonsexual. One small study (seven experimental subjects) has reported that male axillary odors accelerated women's menstrual cycles (Cutler et al. 1986), but this experiment has apparently not been repeated.

Vaginal aliphatic acids

Female rhesus macaques (*Macaca mulatta*), an Old World monkey, produce six aliphatic acids (acetic, propanoic, methylpropanoic, butanoic, isovaleric, 2-methylpentanoic; Fig. 1) in their vaginal fluids in substantially greater amounts when they are estrous than when they are not (Michael et al. 1971). This combination of aliphatic acids has been termed the "copulins". Michael and Zumpe (1982) reported that topical application of copulins to the vaginal mucosae of non-estrous female rhesus macaques elicited mating behaviors from males, similar to those that are elicited by estrous females.

Michael et al. (1975) reported that acetic acid is found in human vaginal fluids, and that the other five copulins are found en bloc in about one-third of women tested, but not in the other two-thirds. Among the women who had all six copulins, the quantities of these chemicals were found to increase during the fertile pre-ovulatory week of the menstrual cycle and to drop sharply after ovulation. An independent study has confirmed that about a third of women produce copulins, but failed to find a monthly cycle of copulin production (Huggins and Preti 1981). Possibly only one human behavioral experiment using copulins has been published, and it made no significant findings (Cowley and Brooksbank 1991). Richard Michael filed a French patent for use of copulins in the perfume industry, but they have apparently never been marketed (Michael 1972).

The fact that human ovulation is concealed is an important piece of indirect evidence against the existence of any pheromone that advertises the fertile part of the ovulatory cycle. Pawlowski (1999) surveyed 19 studies that have looked for measurable increases in aspects of women's sexual behavior, including intercourse, during phases of the ovulatory cycle. At least 15 of these studies found increases during the fertile pre-ovulatory week, but 12 studies found increases during the infertile post-ovulatory week, and 6 during the infertile pre-menstrual week. If there is any tendency for humans to increase sexual activity when a woman is fertile, the tendency is very slight.

Since human ovulation is effectively concealed, copulins cannot serve the same purpose in our species that they appear to serve in rhesus macaques, namely as an estrous advertisement. One possible explanation of the data is that copulins may exist for physiological reasons that are independent of sexual communication. In some primate lineages, including that of the rhesus macaque, males may have evolved the ability to detect them, while in others such as humans males have not.

Vomodors: chemicals that stimulate the vomeronasal organ

The VNOs serve as receptors of a sex-attractant pheromone in red-sided garter snakes (*Thamnophis sitalis*; Gartska and Crews 1986). In laboratory mice, removal of the VNOs: (a) prevents the ovulatory suppression usually seen in all-female groups (called the Lee-Boot effect; Reynolds and Keverne 1979), (b) prevents delayed puberty in all-female groups (Lepri et al. 1985), (c) decreases some aspects of male sexual response to females (Wysocki et al. 1983; Wysocki and Lepri 1991), and (d) decreases male intrasexual aggression (Bean 1982; Maruniak et al. 1986). Removing the VNOs also disrupts pheromone systems in guinea pigs (Beauchamp et al. 1985), hamsters (Fernandez-Fewell and Meredith 1995), and prairie voles (*Microtus ochrogaster*; Wysocki and Lepri 1991). However, the VNOs are not the only pheromone receptors used by mammals. Female pigs still respond to androstenone even if their VNOs are blocked (Dorries et al. 1997), and the smell of a ram induces ovulation in ewes even if the ewes' VNOs are removed (Signoret 1991).

The epithelial cells of women's VNOs, but not those of men, show an electrochemical response to androstadienone, an abundant axillary steroid with a urinous odor (Monti-Bloch and Grosser 1991). PET scanning has shown that exposure to airborne androstadienone, with its smell masked with cloves, increases limbic system activity in women doing a repetitive chore (Jacob et al. 2001b), and it has also been found to alter skin temperature and conductance in both sexes (Jacob et al. 2001a). Three behavioral studies, done by two indepen-

dent groups, have reported that airborne androstadienone reduces women's feelings of tension and negative emotions (Grosser et al. 2000; Jacob and McClintock 2000, Jacob et al. 2002). One of these studies also found that androstadienone significantly reduces negative emotions in men (Jacob et al. 2002), while another reported the opposite (Jacob and McClintock 2000).

The epithelial cells of men's VNOs, but not those of women, show an electrochemical response to airborne estratetraenol [estra-1,3,5(10),16-tetraen-3-ol; Fig. 1], an odorless steroid found in the urine of pregnant women (Monti-Bloch and Grosser 1991). An MRI scanning study found that exposure to estratetraenol caused increased activity in some parts of men's brains (Sobel et al. 1999), and it has also been found to alter skin temperature and conductance in both sexes (Jacob et al. 2001a). A behavioral study found that airborne estratetraenol worsens men's moods (Jacob and McClintock 2000). This same study reported that exposure to airborne estratetraenol also enhances the moods of women. This suggests that even if the VNOs are partially responsible for reception of this steroid in humans, other tissues must also be involved.

PDD (pregna-4,20-dien-3,6-dione; Fig. 1), a synthetic steroid, has also been found to stimulate men's VNO epithelium, and inhalation of this steroid lowers men's LH and testosterone levels (Monti-Bloch et al. 1998). Four other chemicals have been reported to stimulate the VNO epithelium in a sex-specific manner and to affect the autonomic nervous system, but the identity of these chemicals has not been revealed (Monti-Bloch et al. 1994).

In no case have experiments on putative human vomodors used a control group of subjects who lack VNOs, though removal of the VNOs is a common incidental result of nasal surgery. It is, therefore, not clearly established whether the effects of these chemicals on the brain are due to the observed stimulation of the VNOs, or due to stimulation of other sensory tissues.

The company, Human Pheromone Sciences, holds patents on many putative vomodors, and scientists employed by this company have published most of the research done on these chemicals. The company claims that it has "produced and has patents for more than 1,000" vomodors (Kodis et al. 1998, p 159). It markets androstadienone and estratetraenol as mood-enhancing fragrance products for women and men, respectively. It has also proposed developing PDD as a commercial product for treatment of sex criminals (Kodis et al. 1998).

Summary of the evidence

The main indications that humans use pheromones, roughly in order of importance, are as follows.

1. Airborne androstadienone, a steroid produced by the axillary scent glands, alters limbic system function and causes a positive affective reaction in women, even when its odor is effectively masked from conscious recognition. This is supported by studies done by two independent research teams (Grosser et al. 2000; Jacob and McClintock 2000; Jacob et al. 2001b, 2002).
2. It is apparently possible to alter the rate of a woman's menstrual cycle by exposing her to the axillary odors of other women (or, perhaps, men). The chemical components of axillary sweat responsible for these effects are unidentified. This is only given strong support by one study (Stern and McClintock 1998), which was relatively small (experimental N=20).
3. Humans have large, sexually dimorphic axillary scent glands, which become active only at puberty, and which have structural and functional similarities to the pheromone-producing scent glands of some other mammals. There is, however, good evidence that these glands are used for a function that is technically non-pheromonal: to produce odors that communicate information about the individual's immune system. This does not preclude the possibility that these glands are used for more than one purpose, but it weakens the argument that the existence of the glands themselves constitutes evidence of human pheromone use.
4. Human axillary glands, and especially those of men, produce androstenone, which is known to serve as a sexual releaser pheromone in pigs. However, the results of a large number of experiments have established no clear pattern of behavioral effects of androstenone on humans.
5. It has been reported that an undisclosed mixture containing components of human axillary sweat acts as a sex attractant. This report (McCoy and Pitino 2002) is based on a single, fairly small study (experimental N=19).
6. Women produce certain aliphatic acids in the vaginal fluids in greater quantities during the fertile part of their ovulatory cycles, and the same acids serve as estrous sexual attractants in rhesus macaques. However, there is no evidence that these acids serve as sexual attractants in humans. Furthermore, since humans have an effective system of concealed ovulation, it seems extremely unlikely that women use estrous sexual attractants of any kind.

Only the first of these pieces of evidence can be taken as unambiguously supportive of the existence of human pheromones, and probably none of this evidence can be regarded as conclusive. The "discovery" of human pheromones has been announced to the media by scientists at least four times: copulins in 1975, androstenone in 1977, axillary sweat in 1986, and vomodors in 1991. Even today, however, it would be premature to make any such announcement until large, well-designed studies have corroborated at least one of the pieces of evidence listed above.

Acknowledgements I would like to gratefully acknowledge the following individuals, who spoke to me about their research and gave perspective to this review: David Berliner, Michael Kirk-

Smith, Martha McClintock, Richard Michael, George Preti, Lisa Rapaport, Charles Wysocki, and Doria Zumpe. Thanks also go to Andrew Brittain, Sue Davie, David Horgen, and Julian Talbot for their help and ideas.

References

Albone ES, Shirley SG (1984) Mammalian semiochemistry: the investigation of chemical signals between mammals. Wiley, New York

Arden M, Dye L (1998) The assessment of menstrual synchrony. J Comp Psychol 112:323–324

Bean NJ (1982) Modulation of agonistic behavior by the dual olfactory system in male mice. Physiol Behav 29:433–437

Beauchamp GK, Doty RL, Moulton DG, Mugford RA (1976) The pheromone concept in mammalian chemical communication: a brief critique. In: Doty RL (ed) Mammalian olfaction, reproductive processes and behaviours. Academic, New York, pp 143–160

Beauchamp GK, Wysocki CJ, Wellington JL (1985) Extinction of response to urine odor as a consequence of vomeronasal organ removal in male guinea pigs. Behav Neurosci 99:950–955

Beer AE, Semprini AE, Zhu XY, Quebbeman JF (1985) Pregnancy outcome in human couples with recurrent spontaneous abortions: HLA antigen profiles, HLA antigen sharing, female serum MLR blocking factors, and paternal leukocyte immunization. Exp Clin Immunogenet 2:137–153

Benton D (1982) The influence of androstenol—a putative human pheromone—on mood throughout the menstrual cycle. Bio Psychol 15:249–256

Benton D, Wastell V (1986) Effects of androstenol on human sexual arousal. Bio Psychol 22:141–147

Berliner DL, Jennings-White C, Lavker RM (1991) The human skin: fragrances and pheromones. J Steroid Biochem Mol Biol 39:671–679

Bhatnagar KP, Smith TD (2001) The human vomeronasal organ. III. Postnatal development from infancy to the ninth decade. J Anat 199:289–302

Black S, Biron C (1982) Androstenol as a human pheromone: no effect on perceived attractiveness. Behav Neural Biol 34:326–330

Brody B (1975) The sexual significance of the axillae. Psychiatry 38:278–280

Cooper WE, Burghardt GM (1990) Vomerolfaction and vomodor. J Chem Ecol 16:103–105

Cowley JJ, Brooksbank BWL (1991) Human exposure to putative pheromones and changes in aspects of social behaviour. J Steroid Biochem Mol Biol 39:647–659

Cowley JJ, Johnson AL, Brooksbank BWL (1977) The effect of two odorous compounds on performance in an assessment-of-people test. Psychoneuroendocrinology 2:159–172

Cutler WB, Garcia CR, Krieger AM (1980) Sporadic sexual behavior and menstrual cycle length in women. Horm Behav 14:163–172

Cutler WB, Preti G, Krieger A (1986) Human axillary secretions influence women's menstrual cycles: the role of donor extract from men. Horm Behav 20:463–473

Cutler WB, Friedmann E, McCoy NL (1998) Pheromonal influences on the sociosexual behavior of men. Arch Sex Behav 27:1–13

Dorries KM, Regan EA, Halpern BP (1997) Sensitivity and behavioral responses to the pheromone androstenone are not mediated by the vomeronasal organ in pigs. Brain Behav Evol 49:53–62

Doty RL, Orndorff MM, Leyden J, Kligman A (1978) Communication of gender from human axillary odors: relationship to perceived intensity and hedonicity. Behav Biol 23:373–380

Doty RL, Green PA, Ram C, Yankell SL (1982) Communication of gender from human breath odors: relationship between perceived intensity and pleasantness. Horm Behav 16:13–22

Dunbar RIM (1980) Demographic and life history variables of a population of gelada baboons (*Theropithecus gelada*). J Anim Ecol 49:485–506

Fernandez-Fewell GD, Meredith M (1995) Facilitation of mating behavior in male hamsters by LHRH and AcLHRH: interaction with the vomeronasal system. Physiol Behav 57:213–221

Filsinger EE, Braun JJ, Monte WC, Linder DE (1984) Human (*Homo sapiens*) response to the pig (*Sus scrofa*) sex pheromone 5-alpha-androst-16-en-3-one. J Comp Psychol 98:219–222

Filsinger EE, Braun JJ, Monte WC (1985) An examination of the effects of putative pheromones on human judgments. Ethol Sociobiol 6:227–236

Filsinger EE, Braun JJ, Monte WC (1990) Sex differences in response to the odor of alpha androstenone. Percept Mot Skills 70:216–218

French JA, Stribley JA (1987) Synchronization of ovarian cycles within and between social groups in golden lion tamarins (*Leontopithecus rosalia*). Am J Primatol 12:469–478

Garcia-Velasco J, Mondragon M (1991) The incidence of the vomeronasal organ in 1000 human subjects and its possible clinical significance. J Steroid Biochem Mol Biol 39:561–563

Gartska WR, Crews D (1986) Pheromones and reproduction in garter snakes. In: Duvall D (ed) Chemical signals in vertebrates 4. Plenum, New York, pp 243–260

Gorman ML, Ndwell DB, Smith RM (1974) An analysis of the contents of the anal scent pockets of *Herpestes auropunctatus* (Carnivora: Viverridae). J Zool 172:389–399

Gower DB, Ruparelia BA (1993) Olfaction in humans with special reference to odorous 16-androstenes: their occurrence, perception and possible social, psychological and sexual impact. J Endocrinol 137:167–187

Gower DB, Nixon A, Mallet AI (1988) The significance of odorous steroids in axillary odour. In: Van Toller S, Dodd GH (eds) Perfumery: the psychology and biology of fragrance. Chapman & Hall, London, pp 47–76

Gower DB, Holland KT, Mallet AI, Rennie PJ, Watkins WJ (1994) Comparison of 16-androstene steroid concentrations in sterile apocrine sweat and axillary secretions: interconversions of 16-androstenes by the axillary microflora and a mechanism for axillary odour production in man? J Steroid Biochem Mol Biol 48:409–418

Grosser BI, Monti-Bloch L, Jennings-White C, Berliner DL (2000) Behavioral and electrophysiological effects of androstadienone, a human pheromone. Psychoneuroendocrinology 25:289–299

Gustavson AR, Dawson ME, Bonett DG (1987) Androstenol, a putative human pheromone, affects human (*Homo sapiens*) male choice performance. J Comp Psychol 101:210–212

Handelmann G, Ravizza R, Ray WJ (1980) Social dominance determines estrous entrainment among female hamsters. Horm Behav 14:107–115

Howard JC (1977) H-2 and mating preferences. Nature 266:406–408

Hudson R, Distel H (1984) Nipple-search pheromone in rabbits: dependence on season and reproductive state. J Comp Physiol A 157:599–605

Huggins GR, Preti G (1981) Vaginal odors and secretions. Clin Obstet Gynecol 24:355–377

Immerman RS, Mackey WC (1997) A biocultural analysis of circumcision. Soc Biol 44:265–275

Jackman PJH, Noble WC (1983) Normal axillary skin microflora in various populations. Clin Exp Dermatol 8:259–268

Jacob S, McClintock MK (2000) Psychological state and mood effects of steroidal chemosignals in women and men. Horm Behav 37:57–78

Jacob S, Hayreh DJS, McClintock M (2001a) Context-dependent effects of steroid chemosignals on human physiology and mood. Physiol Behav 74:15–27

Jacob S, Kinnunen L, Metz J, Cooper M, McClintock MK (2001b) Sustained human chemosignal unconsciously alters brain function. Neuroreport 12:2391–2394

Jacob S, Garcia S, Hayreh D, McClintock M (2002) Psychological effects of musky compounds: comparison of androstadienone with androstenol and muscone. Horm Behav 42:274–283
Jesel L, Aron C (1976) The role of pheromones in the regulation of estrous cycle duration in the guinea pig. Neuroendocrinology 20:97–109
Jolly A (1967) Breeding synchrony in wild *Lemur catta*. In: Altmann SA (ed) Social communication among primates. Chicago University Press, Chicago, pp 3–14
Jordan WC, Bruford MW (1998) New perspectives on mate choice and the MHC. Heredity 81:239–245
Karlson P, Luscher M (1959) 'Pheromones': a new term for a class of biologically active substances. Nature 183:55–56
Kirk-Smith M, Booth DA (1980) Effects of androstenone on choice of location in others' presence. In: van der Starre H (ed) Olfaction and taste 7. IRL, London, pp 397–400
Kodis M, Moran D, Houy D (1998) Love scents. Dutton, New York
Kouro-Mehr H, Pintchovski S, Melnyk J, Chen YJ, Friedman C, Trask B, Shizuya H (2001) Chem Senses 26:1167–1174
Kummer H (1986) Social organization of hamadryas baboons. Chicago University Press, Chicago
Labows JN Jr (1988) Odor detection, generation and etiology in the axilla. In: Felgen C, Laden K (eds) Antiperspirants and deodorants. Dekker, New York
Lepri JJ, Wysocki CJ, Vandenbergh JG (1985) Mouse vomeronasal organ: effects on pheromone production and maternal behavior. Physiol Behav 35:809–814
Little BB, Guzick DS, Malina RM, Rocha Ferreira MD (1989) Environmental influences cause menstrual synchrony, not pheromones. Am J Hum Biol 1:53–57
Maiworm RE, Langthaler WU (1992) Influence of androstenol and androsterone on the evaluation of men of varying attractiveness levels. In: Doty RL, Muller-Schwarze D (eds) Chemical signals in vertebrates. VI. Plenum, New York, pp 575–579
Maruniak JA, Wysocki CJ, Taylor JA (1986) Mediation of male mouse urine marking and aggression by the vomeronasal organ. Physiol Behav 37:655–657
McClintock MK (1971) Menstrual synchrony and suppression. Nature 229:244–245
McClintock MK (1978) Estrous synchrony and its mediation by airborne chemical communication (*Rattus norvegicus*). Horm Behav 10:264–276
McClintock MK (1983) Pheromonal regulation of the ovarian cycle: enhancement, suppression, and synchrony. In: Vandenbergh JG (ed) Pheromones and reproduction in mammals. Academic, New York, pp 113–149
McClintock MK (1984) Estrous synchrony: modulation of ovarian cycle length by female pheromones. Physiol Behav 32:701–705
McCoy NL, Pitino L (2002) Pheromonal influences on sociosexual behavior in young women. Physiol Behav 75:367–375
McCullough PA, Owen JW, Pollak EI (1981) Does androstenol affect emotion? Ethol Sociobiol 2:85–88
Melrose DR, Patterson RLS, Reed HCB (1968) Improvements relating to artificial insemination of pigs. British patent no. 35201
Meredith M (1994) Chronic recording of vomeronasal pump activation in awake behaving hamsters. Physiol Behav 56:345–354
Michael RP (1972) Fragrance blends based on the fatty acids and their employment in pharmaceutical products. French patent no. 2124399
Michael RP, Zumpe D (1982) Influence of olfactory signals on the reproductive behaviour of social groups of rhesus monkeys (*Macaca mulatta*). J Endocrinol 95:189–205
Michael RP, Keverne EB, Bonsall RW (1971) Pheromones: isolation of male sex attractants from a female primate. Science 172:964–966
Michael RP, Bonsall RW, Kutner M (1975) Volatile fatty acids, "copulins", in human vaginal secretions. Psychoneuroendocrinology 1:153–163
Milinski M, Wedekind C (2001) Evidence for MHC-correlated perfume preferences in humans. Behav Ecol 12:140–149
Moeller JF, Meredith M (1998) Increase in gonadotropin-releasing hormone (GnRH) levels in CSF after stimulation of the nervus terminalis in Atlantic stingray, *Dasyatis sabina*. Brain Res 806:104–107
Montagna W (1964) Histology and histochemistry of human skin. XXIV. Further observations on the axillary organ. J Invest Dermatol 42:119–129
Monti-Bloch L, Grosser BI (1991) Effect of putative pheromones on the electrical activity of the human vomeronasal organ and olfactory epithelium. J Steroid Biochem Mol Biol 39:573–582
Monti-Bloch L, Jennings-White C, Dolberg DS, Berliner DL (1994) The human vomeronasal system. Psychoneuroendocrinology 19:673–686
Monti-Bloch L, Diaz-Sanchez V, Jennings-White C, Berliner DL (1998) Modulation of serum testosterone and autonomic function through stimulation of the male human vomeronasal organ (VMO) with pregna-4,20-diene-3,6-dione. J Steroid Biochem Mol Biol 65:237–242
Moran DT, Jafek BW, Rowley JC III (1991) The vomeronasal (Jacobson's) organ in man: ultrastructure and frequency of occurrence. J Steroid Biochem Mol Biol 39:545–552
Ober C, Elias S, O'Brien E, Kostyu DD, Hauck WW, Bombard A (1988) HLA sharing and fertility in Hutterite couples: evidence for prenatal selection against compatible fetuses. Am J Reprod Immunol Microbiol 18:111–115
Ober C, Weitkamp LR, Cox N, Dytch H, Elias S (1997) HLA and mate choice in humans. Am J Hum Genet 61:497–504
Pawlowski B (1999) Loss of oestrus and concealed ovulation in human evolution: the case against the sexual-selection hypothesis. Curr Anthropol 40:257–275
Penn D, Potts W (1998) How do major histocompatibility complex genes influence odor and mating preferences? Adv Immunol 69:411–436
Porter RH, Weinberg J (1999) Unique salience of maternal breast odors for newborn infants. Neurosci Biobehav Rev 23:439–449
Preti G, Cutler WB, Garcia CT (1986) Human axillary secretions influence women's menstrual cycles: the role of donor extract of females. Horm Behav 20:474–482
Reynolds J, Keverne EB (1979) The accessory olfactory system and its role in the pheromonally mediated suppression of oestrus in grouped mice. J Reprod Fertil 57:31–35
Reznikoff-Etievant MF, Bonneau JC, Alcalay D, Cavelier B, Toure C, Lobet R, Netter A (1991) HLA antigen-sharing in couple with repeated spontaneous abortions and the birthweight of babies in successful pregnancies. Am J Reprod Immunol 25:25–27
Rood JP (1975) Population dynamics and food habits of the banded mongoose. East Afr Wildl J 13:89–111
Rood JP (1980) Mating relationships and breeding suppression in the dwarf mongoose. Anim Behav 28:143–150
Rowell TE, Richards SM (1979) Reproductive strategies of some African monkeys. J Mammal 60:58–69
Russell MJ (1976) Human olfactory communication. Nature 260:520–522
Russell MJ, Switz GM, Thompson K (1980) Olfactory influences on the human menstrual cycle. Pharmacol Biochem Behav 13:737–738
Schank JC (2001) Menstrual cycle synchrony: problems and new directions for research. J Comp Psychol 115:3–15
Schleidt M, Hold B (1982) Human odour and identity. In: Breipohl W (ed) Olfaction and endocrine regulation. Information Retrieval, Oxford, pp 181–194
Schleidt M, Hold B, Attili G (1981) A cross-cultural study on the attitude towards personal odors. J Chem Ecol 7:19–31
Shinohara K, Morofushi M, Funabashi T, Kimura F (2001) Axillary pheromones modulate pulsatile LH secretion in humans. Neuroreport 12:893–895
Signoret JP (1991) Sexual pheromones in the domestic sheep: importance and limits in the regulation of reproductive physiology. J Steroid Biochem Mol Biol 39:639–645

Smith AB III, Belcher AM, Epple G, Jurs PC, Lavine B (1985) Computerized pattern recognition: a new technique for the analysis of chemical communication. Science 228:175

Sobel N, Prabhakaran V, Hartley CA, Desmond JE, Glover GH, Sullivan EV, Gabrieli JDE (1999) Blind smell: brain activation induced by an undetected airborne chemical. Brain 122:209–217

Stensaas LJ, Lakver RM, Monti-Bloch L, Grosser BI, Berliner DL (1991) Ultrastructure of the human vomeronasal organ. J Steroid Biochem Mol Biol 39:553–560

Stern K, McClintock MK (1998) Regulation of ovulation by human pheromones. Nature 392:177–179

Veith JL, Buck M, Getzlaf S, Van Dalfesen P, Slade S (1983) Exposure to men influences the occurrence of ovulation in women. Psychol Behav 31:313

Wallis J (1985) Synchrony of estrous swelling in captive group-living chimpanzees (*Pan troglodytes*). Int J Primatol 6:335–350

Wedekind C, Furi S (1997) Body odour preferences in men and women: do they aim for specific MHC combinations or simply heterozygosity? Proc R Soc Lond Biol 264:1471–1479

Wedekind C, Seebeck T, Bettens F, Paepke AJ (1995) MHC-dependent mate preferences in humans. Proc R Soc Lond Biol 260:245–249

Weetman AP (1999) The immunology of pregnancy. Thyroid 9:643–646

Weller A, Weller L (1992) Menstrual synchrony in female couples. Psychoneuroendocrinology 17:171–177

Weller A, Weller L (1993a) Menstrual synchrony between mothers and daughters and between roommates. Physiol Behav 53:943–949

Weller L, Weller A (1993b) Multiple influences on menstrual synchrony: kibbutz roommates, their best friends, and their mothers. Am J Hum Biol 5:173–179

Weller A, Weller L (1995a) The impact of social interaction factors on menstrual synchrony in the workplace. Psychoneuroendocrinology 20:21–31

Weller A, Weller L (1995b) Examination of menstrual synchrony among women basketball players. Psychoneuroendocrinology 20:613–622

Weller A, Weller L (1997) Menstrual synchrony under optimal conditions: Bedouin families. J Comp Psychol 111:143–151

Weller L, Weller A, Avinir O (1995) Menstrual synchrony: only in roommates who are close friends? Physiol Behav 58:883–889

Weller L, Weller A, Koresh KH, ben Shoshan R (1999a) Menstrual synchrony in a sample of working women. Psychoneuroendocrinology 24:449–459

Weller L, Weller A, Roizman S (1999b) Human menstrual synchrony in families and among close friends: examining the importance of mutual exposure. J Comp Psychol 113:261–268

Wilson HC (1992) A critical review of menstrual synchrony research. Psychoneuroendocrinology 17:565–591

Wilson HC, Kiefhaber SH, Gravel V (1991) Two studies of menstrual synchrony: negative results. Psychoneuroendocrinology 16:353–360

Wirsig CR, Leonard CM (1985) Terminal nerve damage affects hamster mating behavior. Chem Senses 10:423

Witt M, Georgiewa B, Knecht M, Hummel T (2002) On the chemosensory nature of the vomeronasal epithelium in adult humans. Histochem Cell Biol 117:493–509

Wohrmann-Repenning A (2000) The human vomeronasal organ and pheromonal communication: facts and fantasy. Z Saugetierkd 65:380–382

Wysocki CJ, Lepri JJ (1991) Consequences of removing the vomeronasal organ. J Steroid Biochem Mol Biol 39:661–669

Wysocki CJ, Meredith M (1987) The vomeronasal system. In: Finger TE, Silver WL (eds) Neurobiology of taste and smell. Wiley, New York, pp 125–150

Wysocki CJ, Preti G (1998) Pheromonal influences. Arch Sex Behav 27:627–629

Wysocki CJ, Preti G (2000) Human body odors and their perception. Jpn J Taste Smell Res 7:19–42

Wysocki CJ, Katz Y, Bernhard R (1983) The male vomeronasal organ mediates female-induced testosterone surges. Biol Reprod 28:917–922