

APHRODISIACS AND ANAPHRODISIACS: BETTER LOVING THROUGH CHEMISTRY

*(reproduction, behavior, pheromones, love potions,
biological control)*

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SUMMARY

Reproductive behavior in animals is modulated by an assortment of chemical signals. This paper focuses on substances that are externally emitted and are effective when a male and female are near or in contact with each other. Aphrodisiacs enhance an individual's propensity to mate, whereas anaphrodisiacs have the opposite affect. Both classes of chemicals occur intrinsically in insects and vertebrates. The existence either of intrinsic or of extrinsic aphrodisiacs and anaphrodisiacs in humans is suspected. Sexual modulators help us understand basic processes in animal reproduction. Furthermore, they may become important biological control agents. Genetics offers a valuable, but very under-exploited, approach in studies of intraspecific chemical communication.

INTRODUCTION

Many organisms interact with each other predominately through chemical signals (WHITTAKER AND FEENY 1971, WILSON 1970a). For example, bacteria (ADLER 1975, BERG 1975), insects (SCHOONHOVEN 1972, DETHIER 1970), fish (HARA 1971, TODD 1971) and mammals (ARNOLD and HILL 1972, EWER 1968) locate and select food sources at least in part on the basis of odors and tastes which emanate from them. As a counterploit, animals and plants use various combinations of alarm substances (SNYDER and SNYDER 1971, PFEIFFER 1974, BLUM 1969, MULLER-SCHWARZE 1971), repellent and distasteful factors (EISNER 1970, BATE-SMITH 1972), toxins and growth regulators (HARBORNE 1972, WILLIAMS 1970) and phytoalexins or antibodies (DEVERALL 1972) to defend against the everpresent threat posed by foraging microbes and animals. Comparable interactions occur even

among plant species wherein competition is mediated *via* allelopathic substances (RICE 1974, WENT 1970, WHITTAKER 1970).

Within a species, chemical signals are employed during different phases of reproduction (BONNER 1970, RAPER 1970, BIRCH 1974a, WILSON 1975). Much is known about long-range sex attractant systems in animals, especially insect sex pheromones (FARKAS and SHOREY 1974, SHOREY 1974, JACOBSEN 1972). For instance, a female gypsy moth (*Porthetria dispar*) emits dis-parlure (Figure 1) to lure male moths from as far as several kilometers downwind (WILSON and BOSSERT 1963). Sticky traps baited with synthetic pheromone are now employed to monitor wooded areas threatened by the gypsy moth (BEROZA and KNIPLING 1972). Since pheromone-containing devices might also serve to control infestations of major pest insects, emphasis is placed on developing a thorough understanding of the chemistry and biology (BEROZA 1971, SCHNEIDER *et al.* 1974, ROELOFS 1975). Similar studies with mammalian species are in progress (BIRCH 1974a).

Recently it has become apparent that close-range chemical signals are as important as long-range attractants in animal reproduction. When prospective mates encounter each other, regardless of the events that brought them close together, their sexual receptivity can be modulated by externally released substances. Such substances may be called aphrodisiacs and anaphrodisiacs. An aphrodisiac is defined as a substance either that "stimulates sexual desire or ability" (HOCKING 1955), or that "prepares the opposite sex for copulation after the pair has been brought together" (BUTLER 1970). On the other hand, an anaphrodisiac "allays or depresses sexual desire or ability in the opposite sex" (HOCKING 1955).

It is necessary to emphasize that an aphrodisiac or its antagonist, like any other communicative signal, can be effective in a very subtle manner. Complete, stereotypic sexual arousal or depression need not, and most likely will not, be exhibited in response to a chemical stimulus. As WILSON (1970b) states, "Communication is an alteration of the response probabilities which is adaptive in nature, meaning that the rules have been programmed by natural selection." Thus for a chemical signal to be an aphrodisiac or anaphrodisiac two criteria need to be fulfilled: (1) there must be a significant change in the probability of copulation (insemination) resulting from chemical cues emitted by one sexual partner acting on the other at close range or on contact; and (2) this change in sexual receptivity must be adaptive.

Before presenting material on animal aphrodisiacs and anaphrodisiacs, I wish to describe briefly some widely used love potions. I do this for two reasons. The first one is academic. Scientific studies of love potions predate those of animal secretions and, as a result, they have exerted a historical influence on the entire field. Moreover, it appears that both types of signals may have some of the same biological and chemical properties. The second reason is strictly emotional. People have been and continue to be preoccupied with sex and its

promote their sexual interests. In most instances the objective is to enhance sexual receptivity, performance, or fertility. Some potions are thought to work only on one sex, whereas others are designed for both. Most are aimed at making a woman more receptive to a man's sexual advances. Another common class of potions supposedly restores potency in aging men. The least common group is said to induce chastity in women and men.

Modern pharmacological and chemical evidence for the aphrodisiac or anaphrodisiac effects of love potions is scanty, and much of it is contradictory. The available information suggests that all herbal and animal preparations may fit into six categories:

1. Suggestive shapes, devoid of chemical factors.
2. Pallatives and tonics.
3. Narcotics.
4. Irritants.
5. Hormones.
6. Pheromones (unknown).

Often a potion is compounded from various sources to incorporate several of these properties. But of all six categories, it would seem that organic materials containing human hormones and pheromones or their analogs have the greatest potential to be really effective.

Herbal Philters

In western cultures a widely known and used aphrodisiac plant is the mandrake, *Mandragora officinarum*, a native of the Near East (TAYLOR 1965). Superstitions connected with the mandrake are described in HEISER'S (1969) delightful book on the nightshades, or Solanaceae. The root, which purportedly contains medicinal juices, is branched and spindle-shaped (Figure 2A). Using one's imagination, a particular root may resemble a human, a man, or a woman (Figure 2B,C). From Biblical times onward, according to the Doctrine of Signatures, the form of the root indicated the sex of person in which it would be effective.

The mandrake also was used as an anaesthetic and soporific agent in ancient times. These properties, as well as its reputed aphrodisiac ones, are thought to reside mainly in root extracts. Chemical analysis has shown the plant to contain several narcotic alkaloids, including hyoscyamine, scopolamine, and mandragorine (HEISER 1969).

The name mandrake is applied in other parts of the world to nonsolanaceous plants that have fleshy, humanoid roots and possible medicinal value. In the United States the local mandrake is the mayapple, *Podophyllum peltatum* (BAILEY 1929). This member of the Berberidaceae is easily located in shady de-

cidous forests because of its large, umbrella-like leaves (Figure 3A). *Podophyllum* roots (Figure 3B) now serve, not as an aphrodisiac, but rather as a tonic and antitumor agent, especially in the Appalachian region (KROCHMAL and KROCHMAL 1973, MEYER 1960).

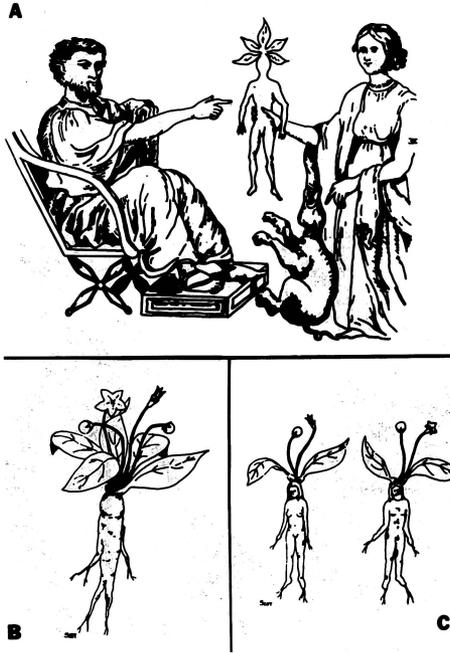


FIGURE 2. (A) Dioscorides receiving the mandrake (after GUNTHER 1968). The dog has gone mad after hearing the painful cries of the uprooted plant. (B) Actual mandrake plant. (C) Female and male renderings of the mandrake (B, C after HEISER 1969).

Ginseng may today be the most widely used aphrodisiac plant. Like the mandrake, its branched root resembles a human form (Figure 3C,D). Two types of ginseng are available. American ginseng, *Panax quinquefolius*, is raised commercially in Appalachia and the Ozarks for shipment almost exclusively to the Orient. On the other hand, roots of Asian *Panax* species are used in the United States (KROCHMAL and KROCHMAL 1973). As its generic name suggests, ginseng was thought by the Chinese to be a panacea as well as a love potion. Recently in the United States there has been a major resurgence in its consumption as a tonic, cathartic and aphrodisiac. Chemical evidence supports the stimulatory effects of ginseng. Several saponins, molecules in which sugars are attached to steroids such as panaxsapogenin (Figure 1), have been isolated from ginseng root extracts (KARRER

1958, NAKANISHI *et al.* 1974).

Indoasian cultures have produced numerous herbal aphrodisiacs for aging males. In ancient China old men would daily consume doses of powders blended from several different plants to restore their sex drive and potency. If the treatment was continued for several weeks or months, supernormal sexual prowess was to be achievable. Ingredients seem to have been selected either for their palliative properties or for their suggestive form. For example, the Bald Chicken Potion, which dates back to the Sui Dynasty (600 AD), contains a fungus that looks like an erect penis, a milkwort that mythically increases semen flow, and parts of other plants that may have a high protein content (VAN GULIK 1961).

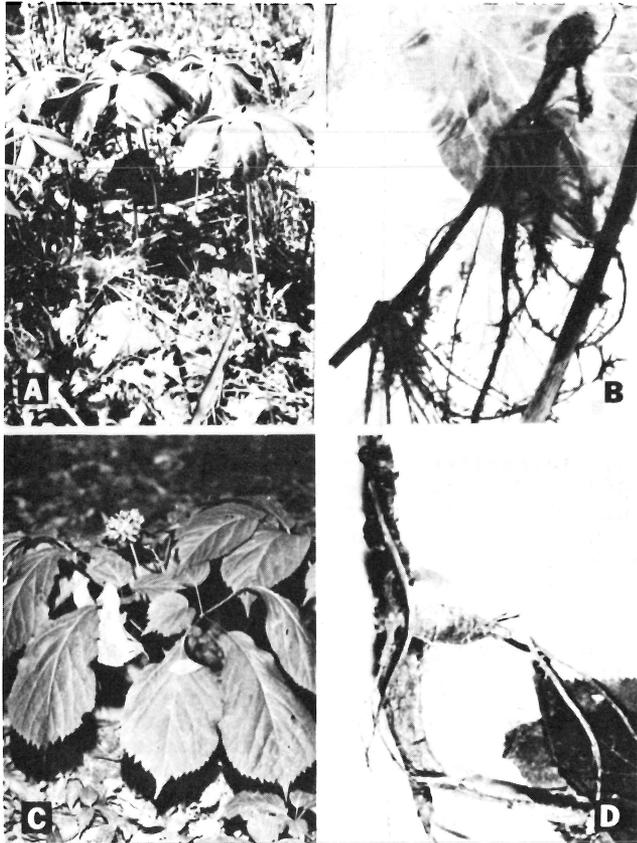


FIGURE 3. (A) Mayapple, *Podophyllum peltatum*, a local mandrake. (B) Root of the mayapple. (C) American ginseng, *Panax quinquefolius*. (D) Root of American ginseng.

Animal Philters

The idea that love potions made from animals are more efficacious than those made from plants was promulgated in Europe and Asia during the Middle Ages. It led to a profound change in folk medicine. Whereas animal parts were only occasionally used in ancient times, after the fourteenth century there was a trend to substitute them for herbal materials (VAN GULIK 1961, BRASH 1973). Animal organs and tissues associated with sexuality or vitality became prized aphrodisiacs. Instead of phallic shaped mushrooms, deer antlers and rhinoceros horns were pulverized and consumed as aphrodisiacs. Blood, hearts, milk, semen, honey, gonads, bones, and feces also were recommended in various cultures (BRASH 1973). Odiferous glandular products of several mammals often were employed by Asian men as aphrodisiacs. In particular, musky secretions from beavers, musk deer (Figure 4A) and civet cats (Figure 4B) were eaten as well as rubbed on the body to enhance their love-making (VAN GULIK 1961, READ 1941).

There may be a real biological basis for the simulatory effects of musky animal philters. Most musks are complex mixtures of many volatile and non-volatile compounds. For example, the secretion of male musk deer contains about forty-six different substances. Although muscone (Figure 1) traditionally is mentioned as the major active component, recent evidence (Table 1) indicates that androstane derivatives comprise almost one half of the ether-soluble exudate (DO *et al.* 1975). Hence, whereas we tend to think of deer musk exclusively as an animal perfume, in reality it appears to be both an odorant and a hormone concentrate. One suspects the various stimulatory effects of musk taken internally by humans (DO *et al.* 1975) are due largely, if not exclusively, to the androgenic substances in it. Since plants contain androgenic and estrogenic steroids (HEFTMANN 1953, CLAYTON 1970) there may be a common pharmacological and biochemical basis for certain animal and plant love potions.



FIGURE 4. (A) Musk deer, *Moschus moschiferus*, in which male preputial glands contain muscone and other substances. (B) Civet cat, *Civettictis civetta*, in which anal glands of both sexes contain civetone.

TABLE 1. Ether-soluble compounds in musk from the musk deer, *Moschus moschiferus**

Name	Number	Abundance in Musk (%w/w)
C ₁₄ -C ₄₀ Cholesterol Esters	≥ 22	12.5
C ₂₀ -C ₃₄ Waxes	≥ 10	7.1
Muscone	1	23.6
Cholesterol	1	8.0
Cholest-4-en-3-one	1	0.3
Androstane Derivatives	11	48.4

*Data are taken from DO, KITATSUJI and YOSHII 1975.

The most notorious and widespread class of animal philters utilizes as its active component a powerful irritant, cantharidin (Figure 1). Commonly known as Spanish Fly in the West and Pan Mao in the Orient, the substance is obtained from bodies of blister beetles (CARREL and EISNER 1974). From ancient times onward cantharidin has been administered in various forms, called Cantharides, to humans and to domestic animals for aphrodisiac purposes (POLSON and TATTERSALL 1959). In nineteenth-century America it was also thought to be a remedy for baldness, pregnancy, and almost any illness, including venereal disease and arthritis (SOLLMAN 1948). However, clinical evidence contradicts most of the curative properties once attributed to cantharidin. Cantharides now are rarely used in medicine because of their deleterious effects on most human organs, especially the urogenital system. Yet they still are employed as an aphrodisiac by horse breeders.

Like many folk medicines, one wonders why cantharidin was used as an aphrodisiac. Was it because of its ability to red- den, inflame, and blister human skin and mucous membranes? Even though this seems somewhat logical, another explanation is equally tenable. People long ago thought protracted, intense copulatory behavior was a sign that an animal possessed a super- sexual substance in its body. By steeping the animal in wine, the aphrodisiac could be removed and made available directly for human consumption (VAN GULIK 1961). Perhaps this reasoning was applied to blister beetles. Many meloid species aggregate in dense clusters on plants (Figure 5A) and pairs mate continuously for hours while in full view (Figure 5C). When alarmed, a couple may fall to the ground and run to cover, one beetle pulling and

dragging another attached behind it. Other circumstantial evidence supports this idea: cantharides were made by soaking whole beetles or parts of them in alcoholic beverages (READ 1941).

Although pure cantharidin itself does not seem to be an aphrodisiac, possibly the crude form may be effective. Three lines of information provide circumstantial evidence for this idea. Firstly, although clinical studies with Spanish Fly have never been conducted, one documented case describes symptoms analogous to male sexual arousal in French Legionnaires who accidentally ate frog legs poisoned with cantharidin (BLYTH 1885). Secondly, the use of Spanish Fly is so long-standing and widespread that one suspects it may be the outcome of many somewhat successful experiments in folk medicine which happened independently on several continents. Finally, the Indian plant *Butea frondosa* contains palasonin (Figure 1), a close relative of cantharidin (BOCHIS and FISHER 1968), and its leaves are used as an aphrodisiac (DASTUR 1962). Perhaps Spanish Fly and other crude preparations of meloid beetles are sexually stimulating because they contain either an altered form of cantharidin or additional substances that synergize with it.

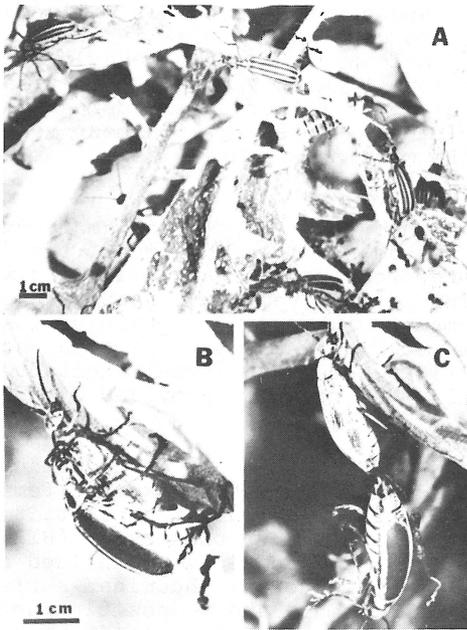


FIGURE 5. (A) Aggregation of blister beetles, *Epicauta lemnicata*, on a tomato plant. (B) Male *Epicauta pestifera* riding on back of female during courtship. Sexually unreceptive females permit mounting but refuse to extrude their genitalia for copulation. (C) Copulating pair of *Epicauta pestifera*. Male remained suspended in air for more than 2 hr.

INSECT APHRODISIACS

The best evidence for the natural occurrence of aphrodisiacs comes from insects. During terminal phases of courtship, it is not uncommon for one sex to emit chemical signals that release precopulatory behavior in the other. The responses provoked by aphrodisiacs are understandably quite different between the sexes: female insects generally become motionless and assume a mating posture, whereas males move around the female and attempt to copulate with her. Several examples with which I have some direct experience are here presented. For a more comprehensive review of the literature, I recommend papers by BIRCH (1974b) and BUTLER (1970).

At high concentrations, volatile sex attractants can act as powerful aphrodisiacs, releasing complete, stereotypic sexual behavior in adult male insects. This is easily demonstrated with American cockroach, *Periplaneta americana*. An adult virgin female lures a male from several meters away. The male walks rapidly to a female and inspects her briefly with his antennae and mouthparts. Shortly thereafter he faces away from her, raises his wings, and pivots around her while pumping the abdomen in an attempt to clasp her genitalia (BARTH 1970). The entire repertoire of male precopulatory behavior can be elicited by the female odor alone. Males approach, court, and attempt to copulate with a piece of filter paper impregnated with virgin females' odor. In other insects, like most vertebrates, aphrodisiac effects are much more context-dependent than in the American cockroach (BIRCH 1974b).

Identification of the *Periplaneta americana* sex attractant and aphrodisiac has been a long, difficult task fraught with controversy. After fourteen years of vigorous work, its characterization remains incomplete. Some natural product chemists think it is a complex mixture and certain of its components may be unstable when purified (L. Hendry personal communication). Tentative identification of one sexual excitant molecule, periplanone (Figure 1), was recently provided by PERSOONS *et al.* (1976).

Male cockroaches also produce aphrodisiacs for females of their species (BARTH 1968). But unlike the female odorants, male secretions are effective mainly on contact and might involve the sense of taste rather than smell (BIRCH 1974b). A female mounts the male and feeds in a ritualized fashion on exudates discharged onto his dorsal abdominal surface. The net effect is to subdue the female and to position her correctly for copulation. ROTH and DATEO (1966) coined the term seducin for the male *Nauphoeta cinerea* aphrodisiac.

Other male insects, particularly butterflies and moths (Lepidoptera), emit aphrodisiac odors that arrest flight in females (BIRCH 1974b). In some species a courting male appears to coat the female's antennae with his pheromone. In light of the problems inherent in olfactory communication (WILSON and BOSSERT 1963), this seems to be an adaptation for generating a long-last-

ing signal with a small amount of secretion. By juxtaposing the odor source and its chemoreceptor, the transmission distance and volume of air in which the signal concentration needs to be greater than threshold levels (the active space) are kept at a minimum.

Perhaps the best-understood lepidoperan aphrodisiac occurs in the queen butterfly, *Danaus gilippus berenice* (Nymphalidae: Danaiinae). Both sexes have large wings (Figure 6A) and are showy fliers. During aerial courtship males induce females to alight and permit copulation (Figure 6C) through a process called hair-pencilling (BROWER *et al.* 1965). In this behavior a male extrudes two brush-like structures, or hairpencils (Figure 6B), from the tip of the abdomen while flying just above and in front of the female. Microscopic cuticular particles impregnated with the pheromone fall off the hairpencils (Figure 6D), and some of them stick on the female's antennae (Figure 6F,G). Studies in the field and in a large flight cage (Figure 6E) with wild and laboratory-reared butterflies demonstrated that hairpencils are necessary for mating (PLISKE and EISNER 1969). Two major components were identified in hairpencil extracts: a volatile, plant-like pyrrolizidinone (Figure 1) and an oily, long-chain alcohol (MEINWALD *et al.* 1969). Behavioral and neurophysiological experiments revealed that the ketone is the olfactory aphrodisiac, whereas the alcohol acts both as a fixative for the ketone and as a glue which retains dust particles on the female's antennae (PLISKE and EISNER 1969, SCHNEIDER and STEIBT 1969).

INSECT ANAPHRODISIACS

Not only do insects turn on sexual behavior in females, they can also turn off sexual activity in their mates. After copulation or, more accurately, insemination is complete, females of some species remain sexually unreceptive for the remainder of their adult lives. In other instances celibacy is temporary, lasting until oviposition occurs. The latter situation gives rise to a wave or on-off sequence of sexual behavior.

Sexual unreceptivity can be induced in female insects by chemical, mechanical, or a combination of mating factors. In many instances, such as *Photurus* fireflies (NELSON *et al.* 1975), we do not yet understand the behavioral switching process. A major reason for this state of ignorance about anaphrodisiacs in comparison to our knowledge about sex attractants is that behavioral changes induced by the former group of substances are relatively slow and internalized. Therefore, it is difficult to determine rigorously cause-and-effect relationships for anaphrodisiac systems. I will discuss a few cases in which anaphrodisiacs definitely exist. The reviews of LEOPOLD (1976) and ENGLE-MANN (1970) contain additional details about these and other examples.

Many female flies (Diptera) are inseminated only once in a lifetime because specific seminal products render them sexually refractory (BAUMANN 1974). The mechanism of mating refusal involves a hormonal or, to be more precise, a neurohumoral pathway in houseflies, *Musca domestica* (LEOPOLD *et al.* 1971 a,b) and

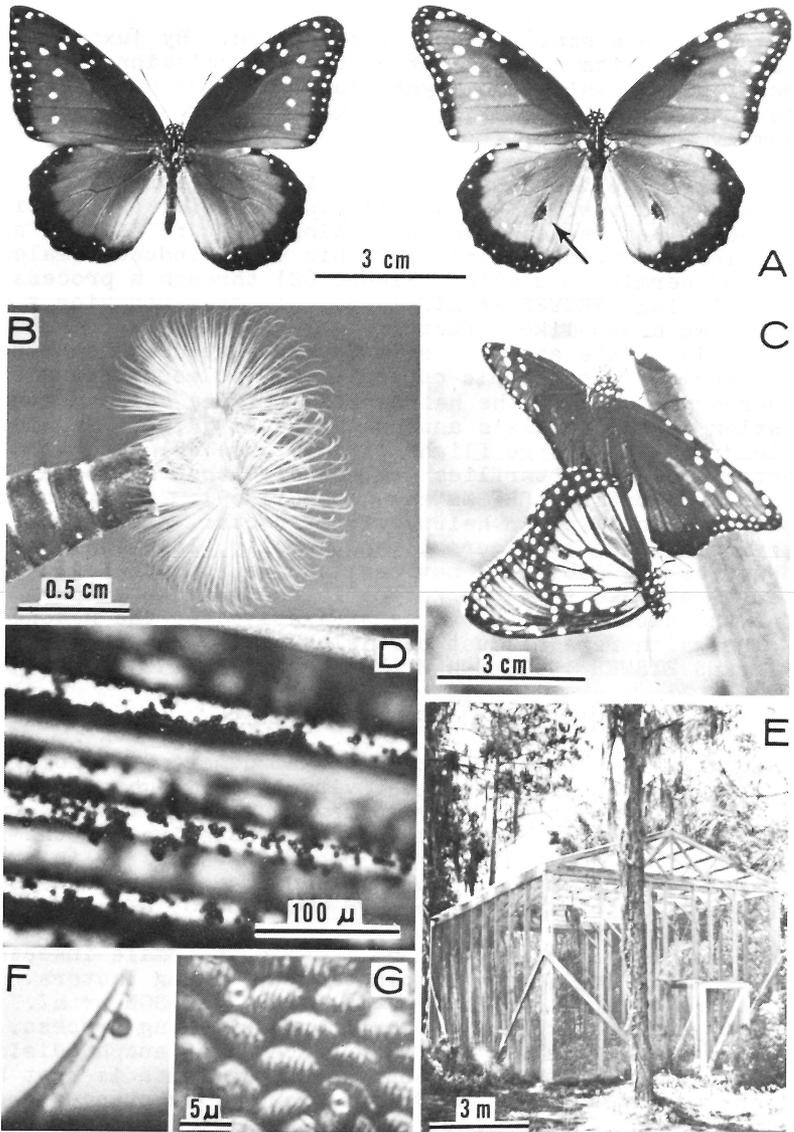


FIGURE 6. (A) The queen butterfly, *Danaus gilippus berenice*. Female is on left, male with wing patches (arrow) is on right. (B) Extruded hair-pencils of male queen butterfly. (C) Copulating pair of queen butterflies. (D) Close-up of hair-pencils showing sticky, cuticular particles laden with aphrodisiac pheromone. (E) Flight cage at Archbold Biological Station, Florida, site of pheromone testing. (F) and (G) Aphrodisiac pheromone-containing particles on antenna of courted female queen. (Courtesy of T. EISNER)

yellow fever mosquitoes, *Aedes aegypti* (GWADZ 1972). This was demonstrated by standard hormone replacement therapy tests. Implantation of accessory glands and injection of accessory gland extracts both invoke celibacy in virgin females. Absorption of male secretions from the reproductive system into the hemolymph was confirmed by radiolabel and other biochemical tests.

The target for seminal anaphrodisiacs seems to be the female's central nervous system. Decapitated, decerebrated, cervically ligated houseflies remain receptive after insemination (LEOPOLD *et al.* 1971 b). In *Aedes* mosquitoes the last abdominal ganglion, not the brain, is the control center for sexual receptivity (GWADZ 1972).

All seminal anaphrodisiacs studied chemically to date seem to be proteins (LEOPOLD 1976). In *Aedes* mosquitoes the active component, called matrone by CRAIG (1967), is a dimer of two polypeptides with molecular weights of 30,000 and 60,000 (FUCHS *et al.* 1970). The larger protein subunit is structurally similar to the sex peptide of male *Drosophila*, which by itself stimulates fecundity in females (HISS and FUCHS 1972). The peptide that induces monocoital behavior in female houseflies appears to be much smaller than matrone; its molecular weight is estimated to be about 750 (NELSON *et al.* 1969).

Nonproteinaceous, isoprenoid molecules also could be seminal anaphrodisiacs. Although no known examples definitely confirm this idea, three lines of evidence demonstrate that it is both logical and likely. Firstly, terpenoid hormones affect insect behavior. Juvenile hormone (Figure 1) is involved, not only in growth and metamorphosis, but also in the development of sexual receptivity (TRUMAN and RIDDIFORD 1974). Secondly, some isoprenoid molecules easily penetrate insect cuticle and enter the hemolymph. This has been demonstrated on many occasions with juvenile hormone analogs (BOWERS 1971, WILLIAMS 1970). Thirdly, male insects sequester terpenes in their reproductive tract and transfer them to females during insemination. We have demonstrated this for cantharidin in blister beetles, and we suspect it may be a common, but unexamined, situation in other taxa.

Cantharidin (Figure 1) is biosynthesized by blister beetles from farnesol (PETER 1973), a substance with juvenile hormone activity (BOWERS 1971). Adult females are unable to make this defensive substance (SCHLATTER *et al.* 1968, CARREL and EISNER 1974), but they appear to be armed by their mates (CARREL *et al.* 1973). Males accumulate cantharidin in their accessory reproductive glands at the surprising rate of about 300 $\mu\text{g}/\text{day}$ (Figure 7). During insemination it is transferred deep into the female's spermatophoral receptacle. Later, some of it is absorbed into her hemolymph (CARREL *et al.* 1973). After copulation, which usually lasts several hours, most females are sexually refractory for several days (SELANDER and MATHIEU 1969, CARREL unpublished observations). Receptivity returns when females deposit eggs coated with cantharidin in amounts comparable to the male's earlier donation. High titers of cantharidin or perhaps another seminal product circulating in a female blister beetle may inhibit mating receptivity. Studies currently are aimed at solving

this behavioral and endocrinological problem as well as others associated with the biogenesis of cantharidin. It would be ironic if cantharidin, a putative aphrodisiac for humans, actually turned out to be an anaphrodisiac in insects that produce it.

A second type of male anaphrodisiac involves marking females with repellent secretions. Instead of switching off a female's sexual behavior *via* a neuroendocrine pathway, this approach leaves her receptive but unattractive to additional males. Examples of deterrent anaphrodisiacs occur in *Tenebrio* beetles (HAPP 1969) and perhaps in *Heliconius* butterflies (GILBERT 1976). GILBERT (1976) suggests the abdominal "stink club" odor of male *Heliconius* might have evolved primarily as a male identification pheromone to protect teneral, newly emergent males from being harassed by other males. If there was a tendency to label females *in copula* with the repulsive odorant, then they would become the olfactory equivalent of a male. Thus an adaptation could have been co-opted to serve an additional, anaphrodisiac function.

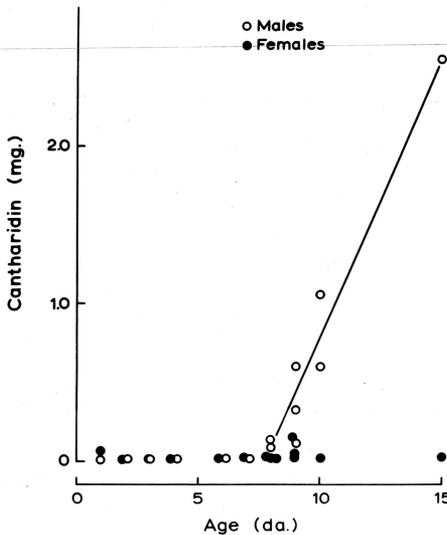


FIGURE 7. Cantharidin content of reproductive tracts of virgin male and female blister beetles, *Epicauta* sp. Males accumulate cantharidin starting about 1 week after eclosion in the laboratory; females do not.

VERTEBRATE APHRODISIACS

In comparison to arthropods, knowledge about close-range chemical communication in vertebrates is rudimentary. Most available information comes from anecdotal behavioral observations

and from highly specialized studies. Both fail to provide either the breadth or the depth necessary for an unambiguous understanding of potential vertebrate aphrodisiacs. My purpose is to review cursorily the area, focusing on a few cases selected for various arbitrary reasons.

Aphrodisiacs, as well as sex attractants, probably are common in fishes and salamanders. Certain gravid female fish emit substances that elicit courtship displays and nest-building by conspecific males (BARDACH and VILLARS 1974, HARA 1970). TAVOLGA (1956) demonstrated that an isolated male goby, *Bathygobius soporator*, will respond with courtship when stimulated with water from a gravid female's aquarium. Because ovarian extracts provoke the same behavior, he concluded the ovaries are the source of the aphrodisiac. Newts, such as *Triturus* and *Notophthalmus*, practice mutual seduction using secretions emitted from cloacal, hedonic, and other exocrine glands (SALTHER and MECHAM 1974). Like many insects, sexually aroused male newts become excited, whereas stimulated females often become quiescent. To my knowledge none of these secretions from fish and salamanders has been characterized.

The existence of aphrodisiac secretions in frogs, reptiles, and birds is questionable. Vision, audition, and touch appear to be their dominant sensory modalities (MARLER and HAMILTON 1966). On the other hand, the use of chemical cues by all three groups, particularly reptiles, may be vastly underrated. Orientation and navigation by odor signals is well-documented in many amphibians (SALTHER and MECHAM 1974) and reptiles (KIESTER 1976). Experiments with homing by pigeons (PAPI *et al.* 1973) and food localization by several avian species (WENZEL 1971, GRUBB 1972) suggest birds also may exploit environmental odors. Therefore, the discovery that sexual arousal and seduction by chemical stimuli is an integral part of courtship in reptiles and birds would not be unexpected.

Mammals have the most complex chemical communication systems of all terrestrial vertebrates. Their bodies are covered with a diversity of exocrine glands (MYKYTOWYCZ 1970). Urine, feces, and saliva also serve as sources of glandular and non-glandular products. Mammalian chemosensory systems are well developed to receive a variety of odor and taste cues (BEIDLER 1971, PFAFFMANN 1969). The production and function of olfactory signals has received much attention (EISENBERG and KLEIMAN 1972, EPPLE 1974a, MYKYTOWYCZ 1970, RALLS 1971), but little is known about the significance of gustatory cues in sexual behavior.

Close-range chemical communication in mammal reproduction is difficult to assess for several reasons. One reason is the individualistic nature of the signal and the response it evokes. Unlike insects which usually identify each other at a population level, mammals are capable of personal recognition (WILSON 1970, RUSSELL 1976). A second reason is the spatiotemporal variability of signal and response. An individual's chemical signature varies according to its diet, hormonal state, age, and external microfauna (LE MAGNEN 1970, PRETI and HUGGINS 1975, MARPLES 1965). Whether a member of the opposite sex reacts to that sig-

nal depends on internal and external stimuli interacting with experiential factors. All sensations probably contribute in some fashion to the final facilitation of mating, but in many instances the removal of any one of them does not totally interfere with it (HAFEZ 1962). Moreover, conditioning, habituation, and other forms of learning allow mammals to modify their responses to a stimulus such as a sex pheromone (HAFEZ 1962, JOHNSTON 1975, ZAHORIK and JOHNSTON 1976).

Two classes of mammalian aphrodisiacs may readily be recognized. Using the terminology of WILSON and BOSSERT (1963), secretions that immediately evoke sexual behavior are called releasers, whereas those that cause a physiological change which later predisposes the receiver to respond sexually are called primers. The releaser/primer concept actually defines extremes of some sort of behavioral and physiological continuum, and in many instances it is not possible to assign mammalian sexual secretions to well-defined positions along it. More importantly, a single aphrodisiac secretion, be it one substance or a mixture of many, could have both primer and releaser effects, especially in highly social and gregarious species (EISENBERG and KLEIMAN 1972).

Primer pheromones emitted by both sexes of mice (*Mus musculus*) could be called primer aphrodisiacs because they produce endocrine changes that enhance sexual receptivity. Female mice in different reproductive categories respond in slightly different ways, which are named after their discoverers, to an unidentified odorant in male urine (BRONSON 1974, WILSON 1970a). Male scent induces precocial puberty, complete with ovulation and mating, in young females (the Vandenbergh Effect). In nonpregnant, noncycling adult females it induces and accelerates the estrous cycle (the Whitten Effect). Finally, in recently impregnated females the odor of a strange male's urine induces abortion and a rapid return to estrus (the Bruce Effect). Sex-related odors affect endocrine function in males as well as females. Exposure to the smell of a strange female leads to elevation of plasma testosterone levels within 30 to 60 minutes (MACRIDES *et al.* 1975). Elucidation of the precise effect on pituitary hormones in this mutual feedback system awaits isolation and identification of the active substances.

Primer aphrodisiacs might also exist in other mammals. According to BRONSON (1974), pregnancy blockade and estrus induction commonly occur in female rodents in response to urinary odors from conspecific males. He also cites some evidence that male odors synchronize or enhance estrous cycles in cats, pigs, rabbits, and other domestic animals. There are speculative reports that synchronization of reproductive activity in primates might also be partly under pheromonal control (EPPLÉ 1974a,b).

Releaser aphrodisiacs in vertebrates are much better understood at all levels than are primers. In several instances the active substances have been isolated, characterized, and tested. Both males and females may emit odorous secretions that sexually arouse their sexual partners.

Sexual receptivity in female pigs is enhanced by boar odors. This is clearly evident during courtship, as described by SIGNORET (1970). A boar releases two odors in the presence of sows and gilts. Frothy, musky saliva is produced on his snout (Figure 8A) and a musky secretion from preputial glands may be discharged by rhythmic urination. A female approaches and sniffs the boar's snout (Figure 8B) and preputial region (Figure 8C). The boar then noses the female's flanks and sniffs or licks her ano-genital region (Figure 8D). If receptive to male cues, a female cocks her ears, assumes a typical lordosis stance, and allows a male (Figure 8E) or even another estrous female (Figure 8F) to mount her. Boar odors do not directly evoke the standing reaction in females, but they facilitate its occurrence: 50 to 60% of estrous gilts exhibit lordosis only if they smell the boar prior to being touched (SIGNORET 1970). Both male secretions contain testosterone derivatives which have musky smells. The preputial exudate has 5α -androst-16-ene-3-one (or boar taint), and the submaxillary gland secretes the former compound plus large amounts of 5α -androst-16-ene-3 α -ol (Figure 1) (PATTERSON 1968).

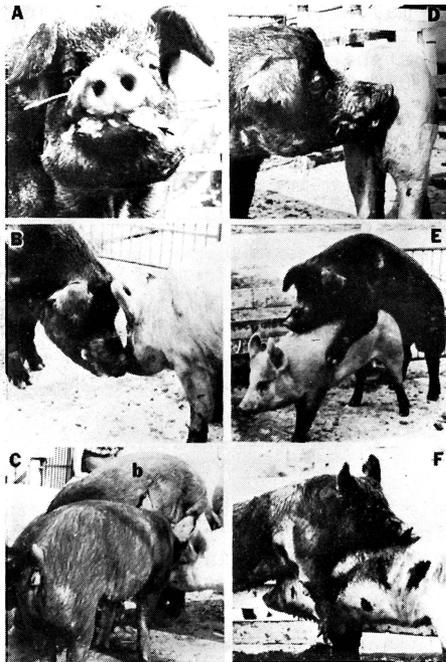


FIGURE 8. (A) Sexually aroused boar, *Sus scrofa*, with musky saliva on his snout (arrow). (B) Estrous gilt (on right) sniffing boar's snout. (C) Two estrous gilts sniffing and nosing boar's (b) prepuce. (D) Boar sniffing and nudging gilt's ano-genital region. (E) Boar mounting estrous gilt. (F) Estrous gilts mounting each other.

The two androgens in aerosol form have a limited use as an aid to detect estrus in pig artificial insemination (REED *et al.* 1974). Behavioral and physiological testing of these substances has not been thoroughly conducted.

Female mammals often produce chemicals that sexually arouse conspecific males. Although boars seem unable to discriminate between estrous and anestrus gilts (SIGNORET 1970), in other species males are greatly excited by females in heat. Males monitor the estrous state by sniffing or licking a female's ano-genital region (Figure 9A) and her urine (Figure 10). As depicted in Figure 10, male ungulates and carnivores manifest a definite facial expression, the Flehmen response, when stimulated by female urine (ALEXANDER *et al.* 1974, VERBERNE 1970). This behavior probably is designed to transfer chemicals in solution to chemoreceptor systems other than the olfactory one (EISENBERG and KLEIMAN 1972, EPPLE 1974a). The prime target might be the vomeronasal organ, or organ of Jacobson (Figure 11), an outpocketing of the nasal cavity, which opens in the nose or on the roof of the mouth (TUCKER 1971). In addition to direct inspection with nose and mouth, male primates also use their hands to sample the chemical aura of females (Figure 12). Ano-genital touching followed by hand sniffing and licking is a frequently observed element in primate courtship (EPPLE 1974a, HESS 1973, MICHAEL *et al.* 1973, TUTIN and MCGREW 1973).

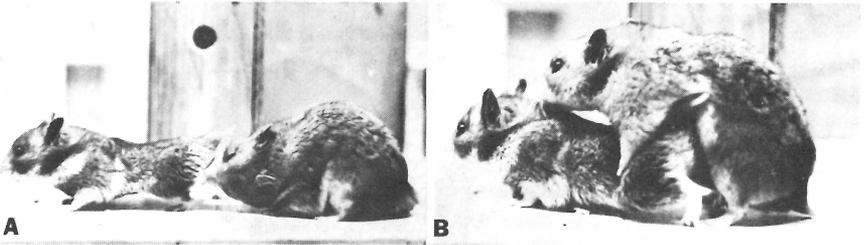


FIGURE 9. (A) Male golden hamster, *Mesocricetus auratus*, inspecting ano-genital region of a female. (B) Male golden hamster mounting a female. (A, B courtesy of R. E. JOHNSTON)

Male aphrodisiacs or sexual excitants have been described in detail for two mammalian species. In hamsters, *Mesocricetus auratus*, vaginal secretion elicits ano-genital inspection (Figure 9A) and an increase in the frequency of mounting (Figure 9B) of females by males (JOHNSTON 1974, 1975). It also stimulates a rapid rise in plasma testosterone levels (MACRIDES *et al.* 1974), which may explain many of the changes in male sexual motivation. Copious production of vaginal material coincides with peak sexual receptivity in female hamsters (ORSINI 1961), so internal and external reproductive changes seem to be appropriately synchronized

in both sexes. POWERS and WINANS (1975) demonstrated that the vomeronasal organ is needed by male hamsters to detect vaginal odors; without it all copulatory behavior ceases. Dimethyl disulfide recently was isolated from vaginal secretions of estrous hamster and was shown to attract males (SINGER *et al.* 1976), but whether it stimulates rapid testosterone release and copulatory behavior remains to be determined.

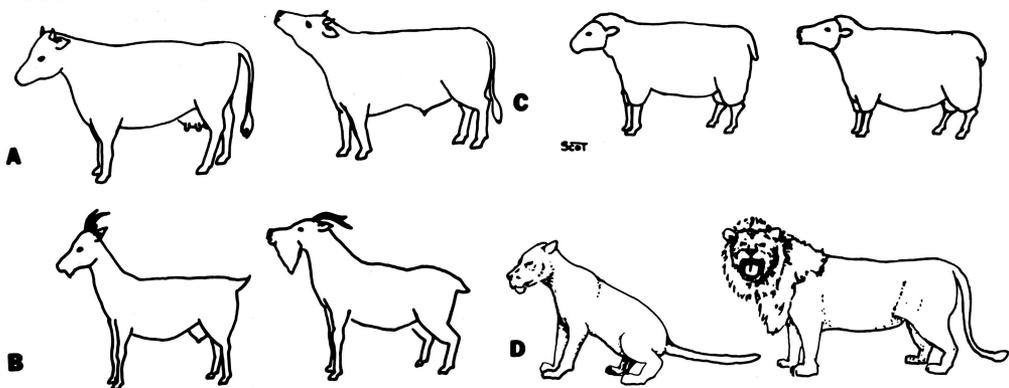


FIGURE 10. Flehmen response in male mammals (on right) elicited by urine of females (on left). Species represented are (A) cattle, *Bos taurus*, (B) goat, *Capra hircus*, (C) sheep, *Ovis aries*, and (D) lion, *Panthera leo*.

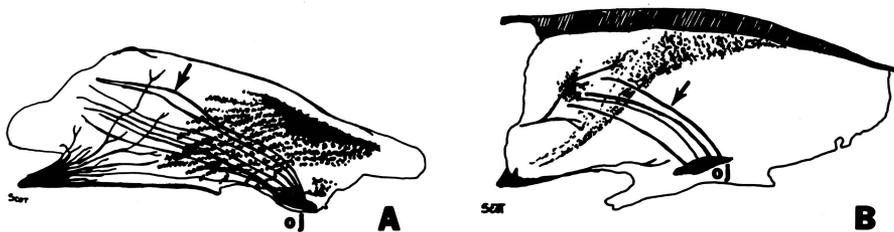


FIGURE 11. Section through nasal region of young pig (A) and rat (B) showing organ of Jacobson (oj) that opens onto roof of the mouth. Nerves (arrow) from organ of Jacobson lead posteriorly to the brain (after TUCKER 1971).

Assessment of the aphrodisiac properties of primate vaginal secretions is difficult. In large part this is due to the complexity and variability that is characteristic of their reproductive biology. The rhesus monkey, *Macaca mulatta*, serves as an excellent example. Only about 50% of pairs studied in captivity show evidence of maximum mounting activity and ejaculatory behavior at the expected time of ovulation near the middle of the

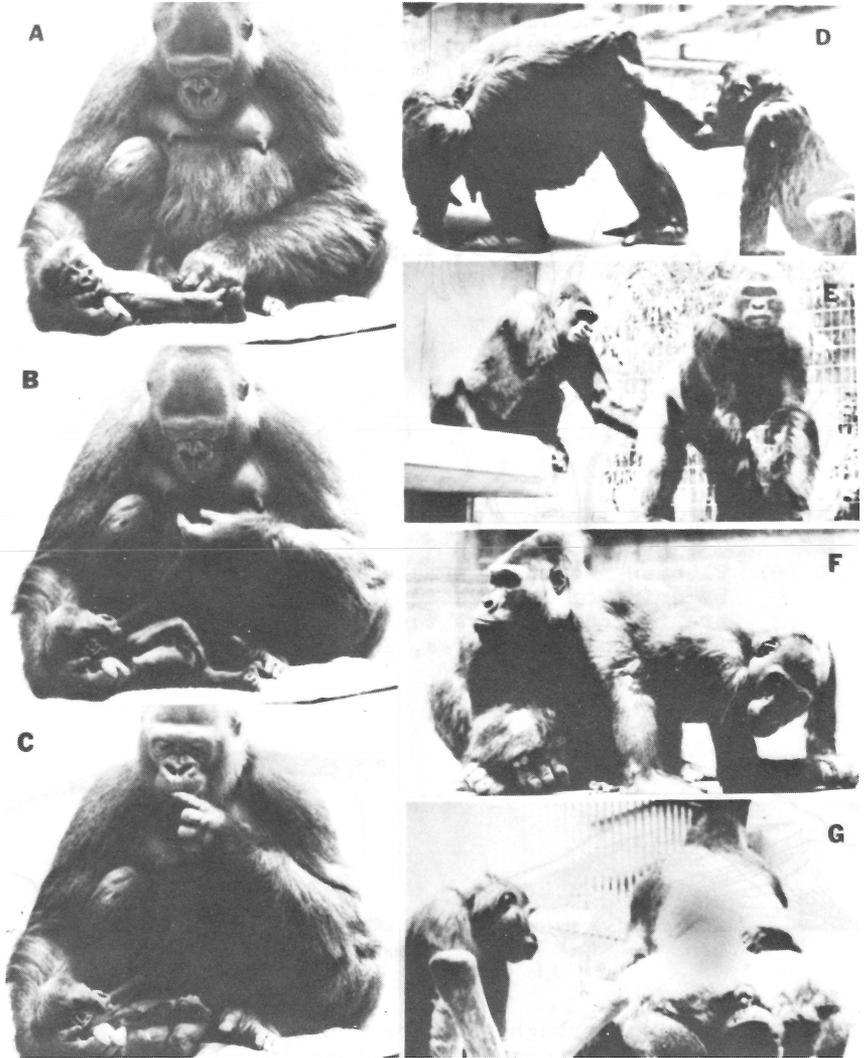


FIGURE 12. Close-range chemical communication in captive lowland gorillas, *Gorilla gorilla*. (A-C) Mother collecting, retrieving, and smelling or tasting genital secretions of her son. (D) Female infant touching genital region of her mother. (E) Young adult male touching genital region of dominant male. (F) Receptive female presenting ano-genital region to adult male. (G) Oral-genital contact between adult male and female, observed by young male. (Photos courtesy of J. P. HESS)

female's menstrual cycle and an equally well-defined decline during the luteal phase (MICHAEL 1972). Furthermore, there are several gestures and movements other than the sexual presentation posture that females individualistically employ to express their sexual excitement and to invite mounting by males (MICHAEL 1972).

To simplify and standardize the study of rhesus courtship, Michael and co-workers control both the hormonal and menstrual state of the female as well as the conditions under which reproductive events occur. Females are ovariectomized to eliminate the variable influences of endogenous hormones and then they receive known amounts of sex hormones as replacements. Subsequently, a male or a female in a pair may be trained to press a bar in order to gain access to its mate located in an adjoining compartment. Sexual receptivity is distinguished from sexual attractiveness by simple behavioral criteria. Highly receptive females show high levels of bar pressing and they rarely refuse the male's mounting attempts, so ejaculatory activity is high. On the other hand, highly attractive but unreceptive females rarely bar press and often reject males. Yet males bar press actively to gain access to females of the latter type and they persistently attempt to mount even in the absence of inviting signals. Blocking the noses of males abolishes their response to attractive females, indicating that attraction is communicated by olfactory signals (MICHAEL and KEVERNE 1968).

Vaginal secretions clearly are close-range attractants and aphrodisiacs in the rhesus monkey. As in the hamster, their production is under endocrine control. Ovariectomized rhesus females are unattractive to males. Treatment daily with small doses of estrogen (estradiol) restores attractiveness, but higher doses are needed to make females sexually receptive. Addition of progesterone to the treatment diminishes either attractiveness, receptivity, or both attributes. Untreated, ovariectomized females become sexually attractive when estrogen is implanted in their vaginas or when vaginal secretions from estrogen-pretreated females are applied to their sexual skin (MICHAEL 1972, MICHAEL *et al.* 1972). Attractiveness is due to the presence of several volatile, C₃-C₅ fatty acids (Figure 1) in vaginal exudates, not estrogen itself (MICHAEL *et al.* 1971). The fatty acids appear to be by-products of bacterial metabolism of vaginal secretions, suggesting that pheromone production in rhesus females is a symbiotic relationship regulated by ovarian hormones (MICHAEL *et al.* 1972).

Do humans have aphrodisiacs or sex pheromones of any kind? Opinions on the subject vary widely. Some deny their existence altogether. Others state that pheromonal functions are vestigial traits in humans (BRONSON 1968). Most authors, such as COMFORT (1974), SCHNEIDER (1971), and WIENER (1966), are much more optimistic about the likelihood of human pheromones, but their evidence is inconclusive.

Human vaginal secretions are a prime source of potential aphrodisiacs. The highest rates of human sexual intercourse may occur about the time of ovulation (UDRY and MORRIS 1968, O'CONNOR

et al. 1974). This corresponds to the period in the menstrual cycle when lactic, acetic, and other volatile fatty acids are most abundant in vaginal secretions (MICHAEL *et al.* 1974, PRETI and HUGGINS 1975). Human and rhesus vaginal secretions have a close chemical resemblance to each other, and material from both species collected in mid-cycle is sexually stimulating to male rhesus monkeys (MICHAEL 1972). Anecdotal reports, such as anthropological studies of primitive island cultures (DAVENPORT 1965), support the idea that human males also find vaginal odors erotically stimulating in coital situations.

Two recent articles question the stimulatory potential of human vaginal odors. One paper identifies about 20 odorous substances in vaginal exudates and confirms cyclical changes in some volatile acidic metabolites, but only 3 of 9 subjects consistently have the C₃-C₅ aliphatic acids that sexually arouse male rhesus monkeys (PRETI and HUGGINS 1975). Actually, this finding is not significantly different from the results of MICHAEL *et al.* (1974) with a larger (n=34) sample of women. One suspects that the homology between humans and rhesus monkeys is simply not as close as some would have it. It is conceivable that a highly complex and variable medley of human vaginal odors could be a reliable cue for conspecific communication, and the heterospecific reactivity is entirely incidental. The second article by Preti and his colleagues is more serious in that it addresses the problem of assaying the attractiveness of human vaginal secretions. Their method of magnitude estimation indicates that men and women only rarely rate vaginal odors as being attractive in a test tube situation. Cyclical changes in odor quality are detected by people, but human vaginal smells range only from very unpleasant at the beginning and end of the menstrual cycle to less unpleasant during the ovulatory phase (DOTY *et al.* 1975). A major criticism of this study is that it was performed out-of-context and the judges most likely were not sexually aroused (GLOBUS and COHEN 1976). DOTY *et al.* (1976) readily admit that this plus a host of other experiential factors might alter a person's judgement of an odor, and they suggest scientists should investigate vaginal odor perceptions in coital situations.

VERTEBRATE ANAPHRODISIACS

Sketchy information suggests most salamanders and newts mate many times (SALTHER and MECHAM 1974), but some snakes have mechanisms that restrict the frequency of copulation by females. In the common garter snake, *Thamnophis sirtalis*, and related species the male deposits a copulatory plug in the female's cloaca immediately after insemination (DEVINE 1975). The plug occludes the opening to her oviduct, which may serve to prevent sperm leakage and additional copulations by rival males for a few days (DEVINE 1975). The genetic and adaptive consequences of temporary chastity in garter snakes is discussed by GIBSON and FALLS (1975). The effect of copulatory plugs and associated seminal products may not be entirely mechanical. DEVINE (1975) and GIBSON and FALLS (1975) refer to reports that unsuccessful males ignore recently mated females. This suggests females might be labelled *in copula* with secretions that repel males, which would be comparable to the situation in some insects (GILBERT 1976).

Olfactory anaphrodisiacs probably are commonplace in mammals. Dominant males frequently mark their sexual partners by urinating on them or by rubbing ano-genital and other glandular products on their bodies (EISENBERG and KLEIMAN 1972). It is known, at least in rats, that urine from dominant males is aversive to subordinate males (JONES and NOWELL 1974). Scent marking of this type may be an adaptation to render mated females unattractive to other males, either by simply masking their odor or by making them repellent.

Semen conceivably has anaphrodisiac properties in higher primates, including humans. If one assumes vaginal odors are sexually arousing to males of this group, then it seems reasonable to expect that distortion of the odor following insemination would diminish a female's attractancy. Although this hypothesis seems not to have been considered, biochemical studies of semen lend at least inferential support for it. Mammalian semen contains a diverse assortment of organic substances (MANN 1964), and many of them or their metabolites are volatile. For example, using MANN's (1964) data, an average (3.5 ml) ejaculate of a human contains approximately 0.5 μ g estrogens, 3 mg cholesterol, 1 mg lactic acid, and 35 mg of other lipids and carbohydrates which can be metabolized in large part to various short-chain acids. Sperm deposited in the uterus have high rates of metabolism and they utilize uterine enzymes, which may peak in activity just prior to ovulation, to digest seminal components to lactic acid (WHITE 1972). Thus the addition of seminal plasma and living sperm to microbially infested vaginal fluids undoubtedly produces a significant, lasting alteration in vaginal odors. Much of the variation in vaginal chemistry and odor quality reported by PRETI and HUGGINS (1975) and DOTY *et al.* (1975) could be due to the uncontrolled coital activity of women who donated vaginal samples.

CONCLUSIONS AND PROSPECTS

Animals do use aphrodisiacs and anaphrodisiacs to coordinate various aspects of their reproductive behavior and physiology. In insects, amphibians, and rodents mutual signalling with chemical cues is commonplace. In other groups, particularly primates, it often is difficult to discern chemical communication of this sort. A distinction between releaser *vis-a-vis* primer effects of an aphrodisiac or anaphrodisiac may be difficult to make because stimulation of neuroendocrine systems can evoke a cascade of behavioral and physiological responses. Some convergence in the chemistry of aphrodisiacs is evident: volatile fatty acids, cyclic ketones, and steroids are used by insects and mammals alike (KULLENBERG and BERGSTROM 1975).

Many future breakthroughs in the area of close-range chemical communication are bound to involve genetics. Until now most genetical approaches have dealt with chemosensitivity (AMOORE *et al.* 1975, BRONSON 1974, TODD 1966), and sexual behavior (BEACH 1965, DIAMOND 1968, EHRMAN and PARSONS 1976). Genetic factors affecting production and release of substances that modify sexual attractancy or sexual receptivity have been largely ignored. In cases where the pheromones are derived from dietary plants

(SCHNEIDER *et al.* 1975) or external microorganisms (MICHAEL *et al.* 1972) the genetics of symbiotic relationships presents an intriguing research opportunity.

Aphrodisiacs and anaphrodisiacs have important implications for programs designed to regulate animal populations. Many species of mammals are threatened with extinction due to human-generated modification of their habitats. This is particularly true for primates. Attempts to breed endangered species in captivity often are difficult. Perhaps aphrodisiac sprays could be used to promote their sexual behavior. On the other hand, reproduction by pest species could be thwarted if such chemicals were improperly applied, at least from the pest's viewpoint. Since many insects have evolved resistance to conventional pesticides (DETHIER 1976), the commercial development of various insect pheromones is urgently needed (DJERASSI *et al.* 1974). Furthermore, some insect biocontrol measures already in use depend on natural anaphrodisiacs. The sterilized male technique for flies and mosquitoes (BORKOVEC 1975) is effective mainly because seminal anaphrodisiacs render once-mated females sexually unattractive or unreceptive.

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James Carrel



E.R. Sears & Provost O. Koeppe

An Informal Discussion



Alfred Novak & A. Eisenstark

Gisela Mosig



Esterházy String Quartet

The Banquet