The Natural History of a Lost Sense

by

Siri Lefren Steiner

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Signature of Author: ....
Graduate Program in Science Writing
May 28, 2005

Certified by: ....
Thomas Levenson
Associate Professor, Graduate Program in Science Writing
Thesis Advisor

Accepted by: ....
Robert Kanigel
Professor of Science Writing
Director, Graduate Program in Science Writing

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ABSTRACT

This thesis is an investigation of the vomeronasal organ, which senses pheromones. It traces the use of the organ in land-dwelling vertebrates, and suggests evidence that the organ is vestigial in humans and Old World monkeys. Possible explanations for the loss of the vomeronasal organ in these groups are described and evaluated. Notably, the development of tri-color vision may have replaced pheromones for sexual selection in these lineages. This may explain the human proclivity for visual information over pheromonal cues.

Thesis Supervisor: Thomas Levenson

Title: Associate Professor of Science Writing

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The orange-red brake lights glow like embers, suspended a few feet above the unlit highway. They snake up the road and spill over the horizon. When they fade, we ease up on the left foot pedal. Like a caterpillar, we roll forward together, segmented and uniform.

But what if we couldn't see those alternately glowing, ruby bits of plastic hung low above the pavement? How would we know where to go?

If we couldn't see, what other sense might we rely on to organize our lives?

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We watch other humans more than we taste or smell them. We hang on their expressions and we scrutinize their hairstyles. We see beauty in certain combinations of eyes, mouth and nose and in the way that paint is arranged on a canvas. We look at maps to orient ourselves. "Put it in writing," we say, when unsure or mistrustful, or "I won't believe it until I see it."

But what if we smelled the wax of red lipstick before we saw it? If another sense took over, beauty and television would become irrelevant. The text on this page would be meaningless. In sight's absence, what other sense might glue humans together? Though humans are numb to it, many other animals rely on a sixth sense to orient themselves: they send and receive pheromones. Though we see examples of pheromones all around us, they are difficult to describe. Like a scent, a pheromone is chemical. But unlike smelling, the body can register these heavy molecules without meta-awareness, and they often have profound physiological effects. From tiny yeast in the bread-bowl to giraffes on the African Savanna, pheromones organize other animal communities.

Take ants. Most of us have seen lines of them, marching from nowhere. Tidy and single file, they can wind under the kitchen door, hang a left at the linoleum, disappear behind the refrigerator, re-emerge at the base of the cabinet, march vertically at an inconceivable ninety degree angle, continue up the crevice where the walls meet, make a non-sense semi-circle, and then, with aggravating innocence, arrive at the drips that cling to the already crowded plastic honey-bear in the cupboard.

How do such tiny beings see the long, winding route from the nest to the honey? They don't. Unlike humans, ants don't rely on sight for most of their information. They use pheromones. Ants leave the nest and spread in different directions, scouting for food. Like Hansel and Gretel's breadcrumbs, the scouting ants leave a light trail of pheromones they can follow back to the nest. This trail evaporates rapidly, so ants don't dilly-dally. Once an ant finds food, he drags his behind all the way back to the nest, releasing a heavier trail back to the food. Other ants in his community are recruited. Without knowing exactly where it leads, they follow the chemical road. As they go, they lay down more pheromones, making the path even more obvious. More ants come to feast and carry bits back to the nest. Eventually, the food source is depleted and the ants stop laying track. Without re-enforcement, the trail evaporates and ants start scouting all over again.

For many insects, pheromones help organize communities. "Honeybees put pheromones in their honey in order to communicate," said John Ascher, a bee expert at the Museum of Natural History in New York. "They don't just use it for food. It's amazing how quickly it can spread messages." These powerful chemicals keep the hive running smoothly. Honeybee hives, for instance, only have one reproducing female—the queen. The rest are workers, who are not able to reach sexual maturity because the queen releases pheromones that make them labor with the drones. They work and die to keep the queen comfortable and fertile, but if the pheromones didn't exist, they would also mature, develop eggs, and get lazy.

Moths rely on pheromones for love. Males have feathery antennae for detecting the female perfume. The females don't fly, but can call the males to them from nearly five kilometers away. Some clever moth-hungry spiders mimic these strong pheromones. Like an addict who risks his life for a fix, the male moth flies to the spider, eventually falling directly into her web.

Sound and light don't travel as well in water as they do on land. Fish, therefore, use pheromones to communicate. The Caribbean Bluehead Wrass Fish lives in a harem. The largest Wrass in the group is male, and he exudes chemicals that prevent the other fish from developing male gonads. He lords over his females until he gets old or killed, and then the pheromones go away. Now the largest female in the harem becomes male, makes new pheromones of "his" own, and mates with his former electric-blue comrades.

As we move up the evolutionary tree, a special organ designed to detect these powerful chemicals appears. It is called the vomeronasal organ, or VNO. The VNO responds to chemicals in the environment by transmitting nerve signals directly to the brain. Most animals that evolved from fish use the VNO to detect pheromones, but in humans it breaks down. For us, the VNO is the neurological equivalent of the appendix. It simply doesn't work anymore. The human VNO is small and mucousy and so difficult to see that scientists have just recently discovered that everybody has one. It lies dead between our mouth and our nose and it looks like two tiny, parallel tubes of flesh. Upon close inspection of human cadavers, researchers have found that it lacks the nerves it needs to function in our bodies. But this vestige made our ancestors fight and mate, simply because a nearby molecule drifted inside and sent nerve impulses to the brain. Most of our living relatives still use this organ, and scientists have begun to study how VNO stimulation can change animal behavior. From single-celled animals that came together according to chemicals in the ether to eyebrow-raising, art-appreciating humans, we can tell a new story about our evolution by examining this teeny, spongy footprint to our sensual past.

The organ appears in most land-dwellers that evolved from fish. The overlap between land animals and the VNO may give us some clues about the organ's special purpose. Ellen Dawley, who researches vomeronasal evolution in salamanders, explained: "Some people think the vomeronasal organ may have been a land adaptation, because it senses molecules that are too heavy to float in the air." This traditional view is that the organ evolved to help land animals receive pheromone molecules that are too cumbersome for the nose. Heavy molecules, whether licked from urine or sniffed from an airborne water droplet, had a harder time reaching the receiver when they were not suspended in a thick fluid medium. So a special organ evolved to make the process more efficient for animals that were surrounded by air rather than water. "But," Dawley cautioned, "there are some reasons to think that the VNO might not be a land adaptation after all."

Heather Eisthen is a researcher at Michigan State University who was the first to object to the presumption that the VNO was built for land. Back when this idea was new, Eisthen investigated the theory by digging into the skulls of aquatic and terrestrial salamanders. She found a functional vomeronasal organ in some fully aquatic salamanders, but none at all in mudpuppies, which spend time on land. Her findings contradicted the new story that the VNO had originated as a land adaptation. She convinced many other scientists to abandon the volatility notion, but now she worries that she may have "thrown the baby out with the bathwater." Today, Eisthen feels that she might have overreacted because her aquatic salamanders don't seem to detect pheromones with their VNO, while her terrestrial species do. "It's kind of frustrating," she tells me, "Ok, it's really frustrating. Some people have thrown up their hands and said that maybe they [The VNO and the nose in aquatic salamanders] do the same thing." She thinks that her aquatic species might have formed a vomeronasal system for some unrelated purpose—much like the randomly vibrating jawbone in fish that eventually led to the first eardrum. The original reason, whatever it was, may have become obsolete and given way to the sense organ that we recognize today in land species. Or, perhaps the raw material for the organ arose in aquatic animals for no reason at all. The VNO may have been born as useless as it is today in humans. From the ancient womb in the amphibian skull to the grave in our modern bodies, the vomeronasal organ may have finally come full circle.

Millions of years after fish climbed to land, the structure and function of the vomeronasal organ is less murky. Pheromones and the VNO clearly go hand in hand for most modern land animals. Ellen Dawley's land-dwelling salamanders, for example, show a great deal of vomeronasal sophistication. "Salamander VNOs can change annually as the organism needs it," Dawley explained. The red-backed species she studies mate in the fall, but their vomeronasal cells proliferate in preparation as early as May. When fall comes, "the male puts his chin on the female's nose to release pheromones and convince her that she is ready to be fertilized." Some of the males scrape the skin on the female with their teeth in order to deliver pheromones directly into her bloodstream. This makes mating efficient, keeping the squat little salamanders less vulnerable to predators.

Even more than amphibians, reptiles may be the most vomeronasal of the animal kingdom. The snake's tongue flicks in and out, grabbing heavy chemicals. When the tongue flicks back in, it's forked end fits perfectly into the tiny ducts at the roof of its mouth. Short, mucousy tunnels lead directly to the VNO. The tongue jams the molecules into the organ, causing physiological and behavioral changes in the whole animal.

Lizards are essentially snakes that don't burrow and have legs. Some species of whiptail lizards are all female. There is not a drop of sperm to share among this whole species, and offspring are simply clones of their mother. Though they do not technically need a partner to reproduce, old habits die hard. They rely on the rub and the scent of another female to increase their egg load. When they breed, one female mimics typical male behavior in related species. The "male" mounts the female and grips her neck in "his" teeth. The lizards have hormone cycles that coincide with sexual behavior. In the days up to ovulation, a whiptail will assume the female role because her estrogen levels are rising. After she ovulates, her estrogen peaks and falls sharply. In her next sexual encounter, she will play the male for a lizard with an opposite cycle. Though fluids are never exchanged, a magic combination of movement and pheromones induces ovulation and increases egg loads.

The organ is also alive in the majority of mammals. Of this class, mice are the most studied and most reliant on the VNO. With their underdeveloped blood-drop eyes, mice need pheromones to decide who to mount and when to fight. After Harvard researchers blocked the VNO in a group of male mice, "they mounted both males and females, trying to copulate indiscriminately," said Adish Dani, a researcher who worked on the project. Even when their potential foe or mate was standing before them, they couldn't trust their eyes. "And infants," he added, "without use of a VNO, couldn't even find their mother's nipple to get milk." Without pheromones, mice had no idea who they were dealing with. Though their sex behavior kicked into overdrive, the VNOless males strangely lost all aggressive behavior. They no longer fought and they no longer killed foreign offspring, a common practice of male mice when in the presence of unrelated youngsters.

Large mammals also use the vomeronasal organ. Have you ever seen a dog's lips curl back or watched a horse bare its teeth in an awkward grimace? These gestures represent the same basic goal—getting pheromones to reach the VNO as effectively as possible. It's called the flehmen response, and it is not unique to horses and dogs. Elephants, with their huge trunks and giant olfactory systems, have a foot-long VNO that helps the male figure out which day, over the course of the entire year, the female will be fertile. The male sticks his trunk near the female's genitals and she urinates just enough so he can get a whiff of her hormones. Then he touches the tip of his trunk to the roof of his mouth in order to make the pheromones contact his VNO. The male will sniff the urine daily until concentrations get large enough to bind to the receptors in the VNO. Her pheromones are strong on the only day of the year that she may get pregnant, so he goes for it. Not only do pheromones stimulate intercourse, they dictate when it ends. As the act nears completion, his receptors get overloaded and stop binding the pheromone. The male finishes and dismounts.

You can watch other animals in the zoo use pheromones as well. "A giraffe will go up to a pool of urine and suck it up to the VNO with a pumping action, like a pipette." Dr. Dawley explained. She wants to make her point clear: you can't confine pheromone use to a single lifestyle, habitat, size, or mating ritual. The VNO is almost universal among fish ancestors, from frogs to horses, and humans are among a very few odd species that are left out of the pheromone game. But there is one giant caveat. Old World

Monkeys, who are the closest living relatives of humans, also don't use the VNO. And thanks to some recent developments, we might actually be able to explain why.

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Bobo was a male ancestor of Old World monkeys. One day, sometime between 35 and 23 million years ago, Bobo caught a whiff of something irresistible. Without even thinking about it, his hunched, primate body found the soft, warm source of the scent and he automatically mounted. He unwittingly gave his mate a seed that would change history. When his sperm bound to her egg, a small, greedy piece of the X chromosome became overzealous. The male baby wound up with this extra piece, which happened to code for color vision. With a spare copy of this gene, Bobo's descendents could see three colors—red, blue and green. This was the start of a sexual revolution. Males and females shared a new sense, and, like everything else sensual, it was bound to become an important part of sex.

Bobo's baby eventually had sons of his own, and they also had sons who preferred the sight of red buttocks to the smell of the most pungent perfume.

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Have we traded swelling for smelling?

Old World primates—the baboon with his extravagant cape of hair, the mandrill with his blue scrotum, the macaque with her turgid, pink, perineal skin—have a looks-obsessed culture. They have a high degree of sexual dimorphism (males and females look very different from each other) that humans can only hope to achieve with suggestive lipstick, push-up bras, phallic ties and trendy, gender-specific haircuts.

New World monkeys, on the other hand, often look androgynous. They make up for their vanilla countenance with bizarre urine cupping rituals, specialized glands that release powerful scents, and highly developed olfactory systems—including a functioning vomeronasal organ. Scent marking governs the most important things in these societies: sex and property. Male *Lemur catta*, for example, engage in stink fights during mating season. Various species of galago wash each other in urine. Each tamarin and marmoset has a unique scent fingerprint that indicates the species, age, sex and dominance status.

Why do New World monkeys have bizarre sniffing rituals, while Old World monkeys simply look bizarre? Some primatologists think these traits have to do with what they call the "trade-off theory." New World male monkeys only see in two colors. But soon after New World and Old World monkeys became separated by the Atlantic Ocean around thirty million years ago, an Old World male had a mutation that added red-color vision in both sexes. Tri-color vision in Old World primates spread and encouraged greater visual eroticism, which led to wild sexual displays. Visual displays slowly replaced the airborne pheromones worshipped by lovers in all other species.

But for tradeoff to make sense, we have to assume that the little vomeronasal lump of flesh in the Old World primate cranium is not very important. To test this assumption, it helps to analyze how the VNO works in animals with a functioning vomeronasal organ. Like smell and taste, pheromone detection can be broken into three basic steps: A pheromone comes into contact with a receptor in the organ; the receptor is stimulated, causing a gradient (essentially an electrical signal) in a nearby ion channel; this signal causes an impulse in a nerve that travels to the brain and causes a physiological response. "It often stimulates a part of the brain that releases hormones in the body," explained Adish Dani, the Harvard researcher who studies VNO receptors.

The channels that lead from the VNO to the brain are called TRPC-2 (pronounced "trip see two"). In every animal that uses the VNO, the TRPC-2 ion channel is essential; but in humans, the genes that code for these channels don't work. They are called pseudo genes because most of the sequence is still intact—so they obviously descended from the functional version--but a nonsense mutation has muddled a tiny part of the gene sequence. Without a readable sequence, the gene cannot translate into real life. VNO ion channels, therefore, do not exist in humans. Since ion channels are the connection between the receptors and the brain, it is impossible to get any response from pheromones in a VNO without them, even if you had some functional receptors. Like a rusted-out model-T, the TRPC-2 sequence has become useless to us. But we can still study it to learn something about our past.

In 2003, Emily Liman and Hideki Innan at the University of Southern California analyzed the TRPC-2 sequence in fifteen primate species. Each Old World genome had the TRPC-2 psuedogene, just like humans. New World Monkey genomes, on the other hand, all had functional TRPC-2 gene sequences, and therefore functional ion channels in the VNO. Liman and Innan suggested that before Old World monkeys and New World monkeys diverged, they still used the organ. But just after the lineages split, some other sense took the place of pheromones in Old World Monkeys, making the organ superfluous. They said that tri-color vision, which is unique to Old World Monkeys, allowed the organ to drift into obsolescence. Drift is a common phenomenon in biology. When a certain trait becomes less important for survival or reproduction, random mutations can easily be passed on to new generations because they are not weeded out by natural selection. Pretty soon, if a trait is no longer needed, it can be lost to a population in a "use it or lose it" scenario. With tricolor vision and sexy, blushing genitals, pheromones were no longer essential for mating. And so, in this account, the VNO simply drifted out of use.

As color vision replaced pheromones, there may have been an overall transition toward visual communication. This change is obvious in Old World Monkeys innuendo. The lewd male mandrill, for example, would not be out of place at a seedy bar on a Saturday night. He initiates sex by following a female and inspecting her swollen buttocks with a large grin. He parts his lips so they are parallel over his teeth, edges turned abruptly up at the canines. As he stares at her rear, he shakes his head from side to side and smacks his lips. Females also use their face to ask for sex. They initiate lovemaking with intense eye contact. This kind of flirting has also been found in every human group studied, and, universally for women, involves first making eye contact, and then quickly glancing down before reestablishing it. But New World monkeys, on the other hand, are less subtle. They often sniff each other's genitals like dogs. Bald Ukakai's catch female urine in their palms to smell and taste it.

The relative delicacy of visual mating rituals seems strange in evolutionary terms. Pheromones are more honest than visual flirtation because individuals have less control over them—you either do or do not smell like a female spider monkey in heat. But smiles, winks and nods can come at any time of the month. Why should courtship evolve to be less dependent on fertility, and therefore less productive? Charles Marshall, a Harvard paleontologist, speculated, "If animals have more time to mate productively, it makes sense that the vomeronasal organ would be less important." On the other hand, if your mate only ovulates a few hours a year, you don't want to mess around with a pretty smile. If you are an elephant, sniffing urine prevents you from wasting sperm all year long. But if you are an Old World monkey and you ovulate each month, you might have the luxury of a sugary romance.

The mystery of visual romance might also benefit pregnant females. In many monkey groups, for example, a male will kill the babies of any female he has not mated. But, if she is sexy enough, a pregnant female can stop him with seduction. Old World females get irresistible swollen buttocks not only when they are fertile, but also when it would be advantageous to attract a new male. The male responds to the swellings, though it is no real indication of fertility. Richard Wrangham, curator of the Peabody museum at Harvard, said, "Female sexual swellings are pornographic." Even fake rubber swellings can attract males in captivity. Like silicone implants in women, the males want to mate with a swollen female, even though her lure is purely aesthetic. The sexual experience sticks in the male memory and he will not kill her babies.

This defense is sophisticated enough to deal with to new threats as they arise. When a male baboon rises in rank or enters a new community, for example, he will kill babies right and left, singling out the offspring of those mothers he has not yet mated. When researchers introduced dangerous new male baboons at the Max-Planck research institute, pregnant females immediately developed sexual swellings, though their pregnancies and estrous cycles did not change. The swelling encouraged the new males to mate with them, which in turn saved their babies. Such complex deception would not be possible with pheromones that allow your sexual partner to see right through you.

Vision is directional, private and can be planned. It is possible to learn expressions and gestures that can benefit the actor. But it is hard to imagine learning to make a particular scent. If smell is most important in determining status, you are stuck in your place. "I like this idea, vision can be learned, but smells can't be learned," said Dr. Wrangham, sitting in his office, in front of a windowsill that cradled a saber-toothed skull. "With chimps, they will say, "look at me!" by chewing a leaf. Then they will display some behavior in order to communicate." It takes a very long time for male chimps to move up the social ladder. It requires hanging around older, dominant chimps for a while; eventually "asserting dominance with a smile, but a smile no longer paired with a submissive gesture," said Wrangham.

The loss of the VNO, then, might benefit the wily males as well as the pregnant females. In a visual society, you can learn to make gestures to trick others—obtaining mates and resources that are otherwise out of your league. "Sight can give more private information than smell. I can't send a scent to you and not the person next to you." explained David Haig of the Harvard Natural History Museum. "If I'm trying to get into a liaison with you a scent near a dominant male would put me in danger. But I could secretly wink at you." If we assume that behavior can be learned, then a visual society would provide new incentive for a brain that is elegant, crafty, and diplomatic.

Visual culture may also encourage larger groups. Unlike scents, colors and gestures can't waft through the trees. Visually oriented individuals have to move close together to mate and communicate. Colorful Old World primates, therefore, tend to live in larger groups than their perfumed New World relatives. "Maybe for individuals living in groups," David Haig suggested, "visual cues are more specific and useful than pheromones," This invokes an old adage: If you have a blue scrotum and nobody sees it, is it really blue?

As groups get larger, group dynamics get more complex, creating even more incentive for social smarts. Larger groups will favor larger brains packed with charm and intellect. "There is some general association between group size and brain size," Wrangham said, back in his office. There isn't a dramatic difference between Old World and New World, but there is a gradation. From prosimians, to New World monkeys to Old World monkeys to great apes you get a gradual progression from small to large groups and small to large brains. "But it does get a little tricky," cautioned Wrangham, "For example, in chimps the group size always changes." Chimps are the primates with the next best thing to human intelligence. They use crushed leaves to sop up water and make tools out of twigs. And chimps, like humans, have 'fission-fusion' societies. They live in large communities but break off into groups of six or seven to forage and go about their daily business. Researchers can make a group size estimate that will fit their curve. Did they count the chimps that spent time together in one day? In one year? "I think they said that a human group is about 150 people, but where do they get that number?" he asked. And what about the orangutan? They have brains that are proportional to their bodies. But they live alone. According to the group size/brain size correlation, they should have pea brains.

Unlike the gregarious chimps and maquaques, orangutans live in Asia where fruit does not come in concentrated enough patches to support whole groups at a time. Orangs wander around the forest alone, looking for food. They come together briefly to mate. Though they are solitary, they do not have a reduced brain, but they do have reduced visual culture. "They don't have any sexual swelling, they hide their fertility," explained Cheryl Knott, a bio-anthropologist who studies orangs in the wild. "When females get pregnant, though, they'll get a little swelling. But it's kind of more like in humans, it's basically like their vulva swelling a bit." She laughed a little, "If you can imagine human females swelling…it isn't attractive." Female orangs are less showy and the courtship ritual is not elaborate. Brute force takes the place of romance for many male orangutans and rape is common. Subtle gestures are generally rare in this isolated species: "I'm sure there is something going on with the expressions," continued Knott, "but it's not like gibbons or macaques or things like that where you have a lot of facial expression." It does seem odd that these marginally social creatures have relatively large brains, but who's to say the over-sized noggin is not a hand-me-down from a more gregarious ancestor? Other than the recluse orangutan, the relation between brain size and group size is undeniable.

The association between visual communication, larger societies, and a larger brain starts to sound so human. Vision allows subtle communication, which sophisticates the culture. Chimps, for example, hold hands, hug and even kiss their friends, but lemurs have no real gestures or facial expressions at all. It is tempting to think that visual culture and larger groups might have caused the evolution of the human brain. Laura Alport, of the University of Texas, explored this possibility by examining primate skulls. She looked at the neocortex--which is the part of the brain responsible for abstract thinking--in monkeys, apes and man. She wondered if more complex group dynamics might favor greater intelligence. She predicted a growth in the neocortex among the most competitive groups, because competition for resources or females is at the heart of most group dynamics. The more intense such pressures are, she figured, the more developed the brain should be. Alport's results surprised her. Larger brains were not associated with greater competition. But then she realized that her conception of competition was problematic. She'd defined competition as the number of confrontations that involved brute force. After evaluating her results, she realized that these animals could use their brains to compete without getting physical. In spite of poor physique or low status, social primates can use their smarts to manipulate others and get what they want. Brute force, therefore, should actually be less common in big-brained societies. Her results consistently supported this idea. She concluded that, "visually oriented communication and social intelligence may have co-evolved."

It just seems right; the evidence is flashy and obvious. "Old World primates are unique in having routine color vision, high visual acuity, large neocortices, great social complexity, and more visual communication," Alport wrote. She cited examples such as "color of the genitalia, eye movements, and flashing of canines." But, she admitted, it is difficult to actually show a neat connection. Our understanding of how each part of the primate brain works is quite limited and it is difficult to assess intelligence by simply examining brain size and anatomy. It's not just the size that matters; it's how you use it.

The human brain is complex, and its evolution will never be fully explained by a tidy story. But if you've ever walked a dog past a urine-soaked fire hydrant, you've probably asked some form of this ponderous question: *Have humans traded scent for sensibility?*

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A woman stands on the beach wearing nothing but bikini bottoms. She is barely covering her breasts with a straw hat. The wind blows her long, blonde hair from her face. She looks hungry as she stares at the camera. Below the snapshot is "scientific" testimony: "It has been well documented that pheromones can trigger powerful sexual responses in women. Unfortunately, evolution has robbed men of the ability to naturally produce sufficient quantities of these pheromones to have a discernable effect on the opposite sex." But the ad proposes a solution: Men can replace the missing pheromones for only $49.95 an ounce, and "Achieve incredible results with women, virtually overnight!!!"

Evolution is a deformed thief. It has robbed us of tails, fur, and now—this?! In the mid-nineties, a rash of studies tried to prove that humans responded to pheromones, followed by attempts to synthesize them. The mysterious chemicals captivated the public. 20/20, Dateline-NBC, and Hardcopy all featured stories about these magical love potions. But if humans don't have a functioning vomeronasal organ, what was all they hype about?

The love potion frenzy was unreasonable, sensational, and largely fantasy. But it wasn't quite crazy. Even without a working VNO, humans still might use this primitive sense in subtle, unconscious ways. Pheromones, if defined as a chemical signal from one individual in a species to another, might work small miracles through our regular olfactory bulb. The trick is to sort the fact from fiction.

As a senior-year college student at Wellesley, Martha McClintock was the first to show that pheromones might work in humans. She noticed that females in her dorm room had synchronized menstrual cycles. One woman would start a few days late, the other early; they met halfway and wound up with the same period. She wondered if pheromones might be responsible for this unconscious synchronization, and did a formal study that was published in *Nature* in 1971. She found that if she dabbed a woman's upper lip with a Q-tip saturated in the sweat of another menstruating woman, she was indeed able to induce the subject's period. She was the first to identify this phenomenon in humans, and she has become famous for her conclusive, reproducible studies that show human responses to unconscious chemical signals.

In 2002, McClintock started using a new word, *vasana*, for the mysterious social chemo signals that she demonstrated. "It's a Sanskrit word," she told me, "so I didn't invent it. It means to leave an unconscious impression on the mind and it comes from the verb to perfume." She avoids the word *pheromone* in her research with humans, because nobody seems to agree on a definition. Some people, like Charles Wysocki of the Monell Chemical Institute in Philadelphia, think a pheromone is like a smell, but heavier—too heavy to be "sniffed." Others, like McClintock, think that is ridiculous. "Volatile just means going from a solid to gaseous state," she explained. "Obviously, if you've ever seen dust in the air, you know that non-volatile compounds can be airborne, even if they are heavy." Some define a pheromone as a chemical that acts through the VNO, but most scientists no longer subscribe to that strict definition. "People used to equate odors with the main olfactory system and pheromones with the VNO, that's not true," said

McClintock. “They are both chemical transducers, they both transduce chemical information, just like the eye transduces light.” Scientists have also tried to distinguish pheromones from smell by saying that pheromones are not consciously registered. But McClintock has problems with this definition as well, “Pheromones have scents—of course they do. Anyone who’s lived near a pig farm knows that. Have you ever smelled pigs? What you are smelling is boar taint.” A tiny drop of boar taint, or androstenol, has been shown to work through the regular olfactory bulb, not the vomeronasal system. But it will cause a sow to assume a mating position with the grace and efficiency of a classic pheromone.

The best definition is probably this one: *A pheromone is a chemical released by one organism in a species that causes a change in the physiology or behavior of another organism in that species.* But even this definition has problems. Snakes, for example, scoop pheromones from mice in order to locate and eat them. “It’s not that mice are releasing snake attracting pheromones,” explained McClintock. But, since snakes operate almost solely using their VNO, the scent of their prey is often described as a pheromone. So, the question of what constitutes a pheromone may never be settled. “It seemed the easiest way out of that was to come up with a label for something that was not an odor, that still effected emotion,” she said, explaining her use for *vasana*, “something that we know affects the brain, but you don’t have to go to the extreme claim that it’s a pheromone.”

Carole Ober, McClintock’s colleague at the University of Chicago, has also found surprising effects of human vasana. She studied Hutterites: an isolated religious cultural group that is at risk of inbreeding because of their small population. In the 1870’s, four hundred of these European Anabaptists migrated to the United States, where they remained in an isolated community. All Hutterites today can trace their ancestry to the four hundred original founders. Hutterites do not marry outsiders, and therefore have a limited selection of mates, all with genomes similar to their own. Ober analyzed a specific part of the Hutterite genome in order to look for patterns in mate selection. She looked at the HLA (Human Leukocyte Antigen) region, which is the part of the genome that codes for many immune system functions. When it comes to the HLA, it is better to have varied alleles. In other words, you have a better immune system if you get different immunity traits from each parent. Hutterite parents with very similar HLA genes have babies with lower average birthrates and more commonly miscarry.

Although the Hutterites had a higher incidence of mate-similar HLA patterns than non-Hutterite couples, Ober found that the matching was far lower than would be expected by random chance. It seemed that the Hutterite couples were naturally pairing up to produce offspring with the greatest immunity. She suspected that humans, like mice, could sniff out a good mate. When people feel "chemistry," they may be subconsciously noticing how different a potential mate's scent is from their own.

In 2002, Ober conducted another study to investigate sexual chemistry. She asked women to sniff and rate the "familiarity, intensity, pleasantness, and spiciness" of T-shirts that different men had worn for a week. She then sequences the HLA region of each subject's genome. The subjects positively rated the mystery men according to a consistent pattern. They all preferred shirts from men with HLA genes most different from their own. It seemed that humans were able to "sniff out" the best match for themselves. Ober concluded, "Women have an exquisitely sensitive olfactory system that allows them to make choices based on small difference in HLA alleles."

For humans, smells are still sexy. In rural Austria, girls traditionally kept a slice of apple under their armpits as they danced. After the dance, each girl would present her apple slice to her favorite suitor—and he would happily eat his prize. And it's probably no coincidence that underdeveloped human genitals travel with an underdeveloped human nose. In 1856, a Spanish physician noticed a correlation between gonad atrophy and missing olfactory bulbs upon post-mortem examinations. Since then, this disorder has been labeled Kallman's syndrome--a rare condition where patients are anosmic (cannot smell) and are not able to release sex hormones or enter into puberty. Perhaps we rely on chemical cues from the rest of our species to tell us to become sexual.

Chemical cues may also be important for other kinds of subconscious communication. There has been some recent evidence that people can smell each other's moods. In 2002, researchers at the Ludwig-Boltzmann Institute set out to find if people, like dogs, could smell fear. Women subjects wore absorbent pads under their arms while they watched a movie. A neutral film was shown one day and a scary film was shown the next. Later, a fresh batch of subjects was able to determine which pads were worn during the "fear" videos, simply by smelling them.

Charles Wysocki and his colleague George Preti at the Monell Chemical Institute recently found evidence that men's sweat had calming effect on female hospital patients. The women were dabbed with male underarm sweat daily. Though they could not consciously smell the difference in samples, the group that was dabbed with a sweat solution experienced reduced tension. The control group that was dabbed with only the alcohol base did not. According to Wysocki, "humans are sharing much more chemosensory information among each other than we yet understand."

The positive, reproducible, and famous results of the McClintock, Ober and Wysocki studies ignited a pheromone frenzy. New studies popped up, looking for marketable love potions. But there is an important distinction between the kinds of chemicals cues that had actually been demonstrated and the pheromones that these new studies were looking for. The former studies had found evidence for pheromones that had physiological, rather than behavioral effects. Unlike the pheromones that make ants move toward honey, human pheromones are subtle, and so far have not been found to alter our behavior in any direct way. They may alter our menstrual period, affect our mood, or make us notice a tall handsome stranger who has the right "chemistry." But pheromones alone won't make us fight with an otherwise likable friend, direct us to a good restaurant in a foreign neighborhood, or entice us into sex with someone who is physically repulsive. These new studies were hoping to find something that would make people behave a certain way, to override information from their other senses. They were looking for Cupid's arrow. Ironically, the ads that marketed supposed love pheromones appealed to the consumer's visual sensibility. Muscle-bound men and buxom women littered the ads, suggesting that anyone with the right pheromone can score a good-looking lover. The erotic images were persuasive enough to make otherwise rational human beings buy dubious love potions over the internet—one internet-savvy pheromone company called HPS (Human Pheromone Sciences) made over ten million dollars in 1998 alone. The success of such ad images is further proof that the bottom line for humans, like Old World monkeys, is physical beauty. Millions of years of evolution have made vision our dominant sense, so why should it be trumped by something found in a bottle?

In the eighties, copulins were the rage. "Copulins" are aliphatic acids isolated in female rhesus macaques, which are Old World monkeys. In 1982, copulins were applied to the vaginas of non-estrous female macaques, inducing mating behavior in males. Some copulins had previously been found in human vaginal fluid. In these women, the concentration of copulins was found to increase in the fertile, preovulatory phase of the estrous cycle. The French researcher Richard Michael believed that since humans naturally exhibited traces of these chemicals, and since they induced mating in monkeys, they must induce men to feel sexual as well. He filed a French patent, but the copulins were never marketed. The biggest argument against their theoretical effectiveness is that humans, unlike rhesus macaques, do not advertise their cycle. Studies on the frequency of sexual encounters during various phases of human ovulatory cycles have shown that it is probably irrelevant for sexual attractiveness in humans. If a woman's cycle does not work to advertise for sex, how would copulins, which trick the male into thinking a woman is in estrous, help a woman get laid?

Later, androstenone took the spotlight. Androstenol is a steroid that is found in human axillary sweat, which is produced by the testes, ovaries and adrenal glands. Since young and middle aged men produce more androstenone than do women, older men and prepubescent boys, it seemed logical that this steroid might act as a sex pheromone, advertising virility. This idea was further supported by the observation that boars produce saliva with high concentrations of androstenone (the stinky chemical that McClintock alluded to earlier), which causes fertile sows to make their bodies rigid to invite males to mate with them. The response is so instant and automatic that farmers can use the marketed version of this pheromone to determine which of their sows are fertile.

Recently, McClintock has shown that a related scent, called androstadienone, helps to modulate mood. Regular exposure can stave off slowly deteriorating moods that generally follow long-term exposure to clove oil. But, in her report, she emphasized that the chemical is a simply mood enhancer and does not affect human behavior. Androstadienone, she wrote, does not "cause sudden, stereotyped behavior in the receiver."

In spite of this caveat, pheromone manufacturers have enthusiastically pumped out synthetic androstenone--promising that "no woman would be able to resist the man who wears their perfume," even though behavioral effects were only seen in pigs. Some companies even marketed this pheromone to women who wanted to attract men. In Diane Ackerman's book, The Natural History of the Senses, she imagines hordes of Manhattanite females splashing this porcine beacon on their décolletage. "Let me propose a naughty recipe," she writes, "Turn loose a herd of sows on Park Avenue. Mix well with crowds of women wearing Pheromone eau de cologne. Dial 911 for emergency."

In humans, the most likely candidates for pheromone production are the apocirne glands. The fact that they vary with sex and develop at puberty suggests that they are involved in sexual communication. Human apocrine glands are concentrated around the genitals, nipples and cheeks. The steroids in axillary sweat are too small to be consciously noted, but axillary bacteria convert these compounds into more noticeable scents—urinous, musky, and even burnt overtones.

Pheromones have been imagined in almost every orifice and fluid that our body can come up with. A smelly compound called 1-pyrroline, which is the most odorous molecule in semen, was found in male pubic sweat. Since a full twenty percent of the population cannot smell 1-pyrroline, researchers concluded that the smell receptors for the chemical had some physiological adaptive significance for certain groups. Later, in 1999, it was shown that women's nipples produce smells that lead a newborn infant to them for nursing. In 1991, an anatomy professor named David Berlinger suggested that pheromones are even found in the cells that slough from the skin. Soon after this announcement, Berlinger helped start a company called Pherin Pharmaceuticals.

Pherin Pharmaceuticals was founded on the assumption that the human vomeronasal organ still works. They have patented nineteen compounds called "vomeropherins"—chemicals that supposedly produce physiological changes in our bodies by acting through our VNO. Their website advertises with the tagline: "Pherin therapeutics…from the VNO to the CNS [central nervous system]." But there should be one more acronym in the capital-letter heavy ad. Instead, the ad should read, "Pherin therapeutics…from the VNO to the TRPC-2 channels that can't reach the CNS!" In spite of such technical difficulties, Pherin supposedly made a pheromone that cured the irritability, depression and mood swings that define premenstrual syndrome. The so-called PH80 nasal spray can allegedly soothe symptoms for two to four hours. Pherin now plans to develop sprays to treat anxiety disorders, manage body weight, decrease depression and sleep disorders, improve cognitive performance, treat prostate cancer and enhance the libido—all through the out-of-order vomeronasal organ. The vice president of the company, Louis Monti-Bloch, has conducted a number of wild-card studies that counter the prevailing notion that the VNO doesn't work. In the late nineties, he claimed to show nerve pathways that were excited by pheromones routed from the VNO. He supposedly found electrical stimulation in human vomeronasal receptors in the presence of certain volatile chemicals. His baffling results were never confirmed or reproduced by other scientists.

All of Pherin's business is based on an organ that no longer works in humans, but the company has been afloat for fourteen years. Pherin's Harvard research associates ignore the lack of ion channels between the VNO and the brain, and consumers follow suit. But with a product that clearly doesn't work, how do companies like Pherin stay in business, and why do people buy their products? Are the advertisements clever enough to make gullible customers buy useless products? Or are we susceptible to the ads because we are eager to believe, on some primal level, that pheromones still work for us? When we buy pheromones in a bottle, is it because we miss primitive sex and animal life?

For now we have to forage in a civil human environment. For humans, food and sex are not found in the forest or on the savannah, instead they are scavenged from other humans. Unlike monkeys that scout fruit, hunt insects, and seem to mate at random, we must learn to trick or please the people around us in order to survive and reproduce. We fret in front of the mirror and replay ridiculous conversations in our head. We worry about the dandruff on our collar and the fact that we are boring dates. We sit in cars on loaded freeways, hoping to impress our boss by arriving before our co-workers. In our overwhelming civilization, we must compete for human affection to survive. Unlike the solitary orangutan, our success is defined solely by our place within the most complex group of creatures on earth.

Though we are lusty organisms with our own agendas, humans have invented a new emotion that squares our exceptionally intertwined lives. Shame, which even our social chimp cousins don't have, results from our unprecedented dependence on each other. Shame teaches us to chew with our mouths closed and to make love behind closed doors. Shame civilizes us, but sometimes we regret being tamed. Countless fables and legends reveal our longstanding grudge against this domesticating emotion. In Jean-Jacques Rousseau's vision of the noble savage, for example, he idealized "the ignorance of vice" in an uncivilized person. In a perfect world, humans, like animals, do not deny or apologize for their natural inclinations. And according to our most popular human fable, the biblical fall from grace, shame is a punishment from God. Adam and Eve's mistake marks the instant when man became aware of his own nakedness and God replaced his innocence with an awkward, regrettable morality. The first bite represents the rising and overwhelming self-consciousness that came with our seedy civilization. If visual culture made humans cluster together to form smart and clumsy societies, then the rise of color vision and the fall of vomeronasal organ made us painfully self-aware. Perhaps it was the crimson of the apple, and not aroma alone, that tempted Adam to bite the fruit of the knowledge of good and evil. If only we, like our blissfully ignorant new world cousins, could not see red. Would we still be animals?

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As we sit in traffic, we are frustrated. Sometimes we want to swerve off the road and turn back, but the cars in front and behind are too dense; we are stuck on this path. It is impossible to see where our ruby highways will take us—but like ants that obediently follow their antennae—we assume that we will reach some final destination if we just press on.

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