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HOMOSEXUALITY AND BIOLOGY

An introduction to a muddled and sometimes contentious world of scientific research—
one whose findings, now as tentative as they are suggestive, may someday shed light on the sexual orientation of everyone

BY CHANDLER BURR

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The issue of homosexuality has arrived at the forefront of America's political consciousness. The nation is embroiled in debate over the acceptance of openly gay soldiers in the U.S. military. It confronts a growing number of cases in the courts over the legal rights of gay people with respect to marriage, adoption, insurance, and inheritance. It has seen referenda opposing gay rights reach the ballot in two states and become enacted in one of them—Colorado, where local ordinances banning discrimination against homosexuals were repealed. The issue of homosexuality has always been volatile, and it is sure to continue to inflame political passions.

It is timely and appropriate that at this juncture a scientific discipline, biology, has begun to ask the fundamental question What is homosexuality? And it has begun to provide glimmers of answers that may in turn not only enhance our self-knowledge as human beings but also have some influence, however indirect, on our politics.

What makes the science in this case so problematic, quite apart from the usual technical difficulties inherent in biological research—particularly neurobiological research, which accounts for much of the present investigation—is the ineffable nature of our psychosexual selves.

This encompasses a vast universe of stimulation and response, of aesthetic and erotic sensibilities. There are those who see an element of hubris in the quest to explain such things in biological terms. Others see not so much hubris as hype: certain well-publicized findings, they fear, could turn out to be milestones on the road to an intellectual dead end.
It is undeniably true that neurobiological research is often pursued in a context of great ignorance. The brain remains an organ of mystery even in general, not to mention with regard to specific functions. "We don't know" may be the most frequently used words in neurobiology, and they seem to be used with special frequency when the subject of sexual orientation comes up. Once, I mentioned to a researcher how often I heard these words on the lips of her colleagues, and she replied, "Good—then they're saying the right thing." In this context, and also considering that the subject matter is politically charged, professional rivalries are inevitable and occasionally bitter. Some of those involved in the research are motivated not only by scientific but also by personal concerns. Many of the scientists who have been studying homosexuality are gay, as am I.

Homosexuality's invitation to biology has been standing for years. Homosexuals have long maintained that sexual orientation, far from being a personal choice or lifestyle (as it is often called), is something neither chosen nor changeable; heterosexuals who have made their peace with homosexuals have often done so by accepting that premise. The very term "sexual orientation," which in the 1980s replaced "sexual preference," asserts the deeply rooted nature of sexual desire and love. It implies biology.

Researchers can look back on two histories: a century-long, highly problematic psychological investigation of homosexuality, and a short but extremely complex history of biological research that started out as an examination of ovulation in rats. Three distinct but interrelated biological fields are involved in the recent work on sexual orientation: neuroanatomy, psychoendocrinology, and genetics.

THE BACKGROUND

Biologists embarked upon research into homosexuality in response to an intellectual vacuum created by the failure of other sciences to solve the riddle of sexual orientation. "Other sciences" mostly means psychiatry. As Michael Bailey and Richard Pillard, the authors of one of the most important genetic inquiries into homosexuality, have observed, decades of psychiatric research into possible environmental causes of homosexuality—that is to say, social and cultural causes—show "small effect size and are causally ambiguous."

As a distinct concept, homosexuality is relatively recent. David Halperin points out in One Hundred Years of Homosexuality that the term itself first appeared in German (Homosexualität) in a pamphlet published in Leipzig in 1869; it entered the English language two decades later. That some human beings engage in sexual activity with others of the same sex has, of course, been noted since antiquity. Historically, however, the focus was on the acts themselves rather than on the actors. The historian John Boswell, of Yale, has noted that during the Middle Ages "same-sex sex" was regarded as a sin, but those who committed that sin were not defined as constituting a type of people different from others. Between the sixteenth and the eighteenth century same-sex sex became a crime as well as a sin, but again, those who committed such crimes were not categorized as a class of human being. This changed in the nineteenth century, when modern medicine and particularly the science of psychiatry came to view homosexuality as a form of mental illness. By the 1940s homosexuality was discussed as an aspect of psychopathic, paranoid, and schizoid personality disorders.

Having defined homosexuality as a pathology, psychiatrists and other doctors made bold to "treat" it. James Harrison, a psychologist who produced the 1992 documentary film Changing Our Minds, notes that the medical profession viewed homosexuality with such abhorrence that virtually any proposed treatment seemed defensible. Lesbians were forced to submit to hysterectomies and estrogen injections, although it became clear that neither of these had any effect on their sexual orientation. Gay men were subjected to similar abuses. Changing Our Minds incorporates a film clip from the late 1940s, now slightly muddy, of a young gay man undergoing a transorbital lobotomy. We see a small device like an ice pick inserted through the eye socket, above the eyeball and into the brain. The pick is moved back and forth, reducing the prefrontal lobe to a hemorrhaging pulp. Harrison's documentary also includes a grainy black-and-white clip from a 1950s educational film produced by the U.S. Navy. A gay man lies in a hospital bed. Doctors strap him down and attach electrodes to his head. "We're going to help you get better," says a male voice in the background. When the power is turned on, the body of the gay man jerks violently, and he begins to scream. Doctors also tried castration and various kinds of aversion therapy. None of these could be shown to change the sexual orientation of the people involved.

Among those who looked into the matter was the sex researcher Alfred Kinsey, whose 1948 report Sexual Behavior in the Human Male showed homosexuality to be surprisingly common across lines of family, class, and educational and geographic background. In his book Being Homosexual, the psychoanalyst Richard Isay writes,

Kinsey and his co-workers for many years attempted to find patients who had been converted from homosexuality to heterosexuality during therapy, and were surprised that they could not find one whose sexual orientation had been changed. When they interviewed persons who claimed they had been homosexuals but were now functioning heterosexually, they found that all these men were simply suppressing homosexual behavior. . . and that they used homosexual fantasies to maintain potency when they attempted intercourse. One man claimed that, although he had once been actively homosexual, he had now "cut out all of that and don't even think of men—except when I masturbate."

Psychiatry not only consistently failed to show that homosexuality was a preference, a malleable thing, susceptible to reversal; it also consistently failed to show that homosexuality was a pathology. In 1956, in Chicago, a young psychologist named Evelyn Hooker presented a study to a meeting of the American Psychological Association. Hooker had during her training been routinely instructed in the theory of homosexuality as a pathology. A group of young gay men with whom she had become friendly seemed, however, to be quite healthy and well adjusted. One of them, a former student of hers, sat her down one day and, as she recalls in Changing Our Minds, said, "Now, Evelyn, it is your scientific duty to study men like me." She demurred. It was only when a fellow scientist remarked to her, "He's right—we know nothing about them," that Hooker sought and received a study grant from the National Institute of Mental Health. She chose a group of thirty gay men as the objects of her research and thirty straight men as controls; none of the sixty had ever sought or undergone psychiatric treatment. "It was the first time [homosexuals] had been studied outside a medical setting or prison," she says. "I was prepared, if I was so convinced, to say that these men were not as well adjusted as they seemed on the surface."

Hooker administered psychological tests to her sixty subjects, including the Rorschach ink-blot test, producing sixty psychological profiles. She removed all identifying marks, including those indicating sexual orientation, and, to eliminate her own biases, gave them for interpretation to three eminent psychologists. One of these was Bruno Klopfer, who believed that he would be able to distinguish homosexuals from heterosexuals by means of the Rorschach test. As it turned out, none of the three could tell the homosexuals and heterosexuals apart. In side-by-side comparisons of matched profiles, the heterosexuals and homosexuals were indistinguishable, demonstrating an equal distribution of pathology and mental health. Reviewing Hooker's results from a test in which the subject creates pictures with cutout figures, one of the interpreters, a psychologist named Edwin Shneidman, stumbled onto a particular subject's orientation only when he came across a cutout scene depicting two men in a bedroom. Shneidman remembers, "I said to Evelyn, 'Gee, I wish I could say that I see it all now, that this is the profile of a person with a homosexual orientation, but I can't see it at all.'"

Hooker's research throughout her long career was driven by the belief that for psychiatry to be minimally scientific, pathology must be defined in a way that is objective and empirically observable. Her study was the first of many showing that homosexuality could not be so defined as pathology. In 1973 the American Psychiatric Association removed homosexuality from its official Diagnostic and Statistical Manual, signifying the end of homosexuality's official status as a disease. Today's psychiatrists and psychologists, with very few exceptions, do not try to change sexual orientation, and those aspiring to work in the fields of psychiatry and psychology are now trained not to regard homosexuality as a disease.

ANATOMY LESSONS

With homosexuality moved from the realm of psychiatric pathology into the realm of normal variants on human sexual behavior, research efforts took a new turn. Psychiatry had succeeded in defining what homosexuality is not—not in explaining what it is. Questions of etiology, in this as in other psychiatric matters, thus became by default questions for neurobiology. Are homosexuals and heterosexuals biologically different? In thinking about this question, biologists have been greatly influenced by findings that involve what may be a related question: Just how, neurologically, do men differ from women?

In 1959, at the University of California at Los Angeles, the neuroendocrinologist Charles Barraclough found that if a female rat was injected shortly before or after birth with testosterone, a male sex hormone, the abnormal amount of this hormone would make the rat permanently sterile, unable to ovulate. "Ovulation" as used here is in part a technical term: it refers both to what a lay person would think of as ovulation—the movement of an egg from the ovary into the fallopian tube—and to the series of hormonal interactions that cause that event.

Rats have short estrous cycles. Every four days various glands in the rat's body start pumping estrogens, or female sex hormones, into the bloodstream, setting in motion a series of chemical events. Estrogen levels reach a certain concentration and stimulate part of the hypothalamus, the small portion of the brain that regulates (among other things) body temperature, hunger, thirst, and sexual drive. The hypothalamus in turn stimulates the pituitary gland; the pituitary then releases a burst of something called luteinizing hormone, which causes the ovary to release an egg. Barraclnugh discovered that in female rats even a single perinatal exposure to testosterone will prevent this entire process from ever occurring. If that discovery was intriguing, a subsequent one was even more so: the discovery that male rats can ovulate—at least in the sense of going through the hormonal preliminaries. In 1965 Geoffrey Harris, a neuroendocrinologist at Oxford University, castrated a group of newborn male rats, depriving them of the testosterone from their testes. He found that if estrogen was injected into the bodies of these rats after they reached adulthood, it stimulated the hypothalamus, which initiated the sequence of hormone releases described above. The male rats obviously had no ovaries or wombs, but they went through the biochemical motions of ovulation. If one grafted an ovary onto a male rat, he would ovulate perfectly.

Further tests revealed a strange asymmetry. Whereas newborn male rats deprived of testosterone will, as Harris found, experience female-like ovulation, newborn female rats deprived of estrogen will continue to develop as females. In adulthood they will not seem somehow male. Although the rats' ovaries have been removed, their brains will still produce the stimulus to ovulate. Scientists realized that without testosterone the genetic blueprint for masculinity was essentially worthless. Indeed, they learned, for a male rat's brain to become truly organized as male, the rat must be exposed to testosterone within the first five days of life. After the fifth day the masculinizing window of opportunity is closed, and the genetic male will grow up with a "female" brain. In contrast, the brain of a female needs no estrogen for organization; left alone, it will become female.

Thus it came to be understood that what one might think of as the "default brain" for both sexes of the rat is feminine, and that testosterone is as necessary in the creation of a masculine brain as it is in the creation of masculine genitals. This concept, which is the basis of one approach to the neurobiological search for the origins of sexual orientation, is known as the "sexual differentiation of the brain."

Roger Gorski, a neurobiologist at the University of California at Los Angeles who has long been involved in research on sexual differentiation, looked back recently on the development of his field: "We spent much of our professional careers trying to understand this process of sexual differentiation, and what functions happen within it—male sex behavior, female sex behavior, control of ovulation, control of food intake, body weight, aggressive behavior, some aspects of maternal behavior. You know why male dogs lift their legs when they pee? Because the brain has changed. So this is really a fundamental concept, that the brain is inherently female and to develop as male it must be exposed to masculinizing hormones."

Several years after Harris's experiment other researchers at Oxford University succeeded in confirming anatomically what the principle of the sexual differentiation of the brain had strongly implied: that an observable difference exists between the brains of male rats and those of female rats. In 1971 the anatomists Geoffrey Raisman and Pauline Field published a paper that compared the synapses, or connections between brain cells, in the hypothalamuses of male and female rats. The prevailing view at the time was that all structures of male and female brains were alike. Raisman and Field found that female and male rat brains differed in the number of synaptic connections between brain cells in the hypothalamus: females had more. Rat brains, which varied by sex in terms of function,

also varied in terms of structural shape—were "sexually dimorphic." In 1977 a team of neurobiologists led by Roger Gorski located a second sexual dimorphism, again in the rat hypothalamus: a small nucleus, or cluster of cells, five times larger in volume in the male rat than in the female. Gorski found that with the naked eye he could sex rats' brains with almost 100 percent accuracy. Gorski's team named the nucleus, logically, the sexually dimorphic nucleus. Its function is not known.

The groundwork had been laid in rodents. The next step was to see if sexual dimorphism of some kind could be found in the brains of human beings. In 1982 the cell biologist Christine de Lacoste-Utamsine and the physical anthropologist Ralph Holloway published in Science an examination of a structure in the human brain called the corpus callosum. The corpus callosum, which is made up of nerve fibers known as axons, is a long, narrow structure that connects and transmits information between the brain's right and left hemispheres. It is one of the largest and most clearly identifiable portions of the brain, and has for years figured prominently in brain research. De Lacoste-Utamsing and Holloway found that the shape of a portion of the corpus callosum called the splenium differed so dramatically between the sexes, with the splenium being larger in women than in men, that impartial observers were able to sex brains easily by looking at this single feature. The De Lacoste-Utamsing and Holloway study is well known and frequently cited, despite the failure of many of the attempts to replicate it. Whether the dimorphism found by De Lacoste-Utamsing and Holloway truly exists remains a matter of considerable debate.

In 1985, three years after the publication of the De Lacoste-Utamsing and Holloway article, Dick Swaab, a researcher at the Netherlands Institute for Brain Research, in Amsterdam, reported that he, too, had found evidence of sexual dimorphism in human brains—in the form of a human homologue of the sexually dimorphic nucleus that Gorski had found in rats. Swaab announced an even more remarkable discovery five years later, in 1990. He had found, he wrote in an article in the journal Brain Research, that a cluster of cells in the human brain called the suprachiasmatic nucleus was dimorphic—but dimorphic according to sexual orientation rather than sex. Swaab said that the suprachiasmatic nucleus was nearly twice as large in homosexual men as it was in heterosexual men.

If true, this was something wholly new: an anatomical difference between homosexuals and heterosexuals.

Simon Levay is a young neurobiologist who at the time of Swaab's second discovery was conducting research at the Salk Institute, in La Jolla, California. LeVay would soon become the author of what is surely the most publicized neurobiological article on homosexuality that has appeared to date. I spoke with him one day recently in his West Hollywood apartment. LeVay is a wiry, muscular man, remarkably intense. Perhaps the most striking thing about him is the way he talks. In a crisp British accent he zeroes in on each point and then moves on with an air of impatience.

"You shouldn't draw such a distinction between biological and psychological mechanisms," he chided me at one point during our conversation. "What people are really getting at is the difference between innately determined mechanisms and culturally determined mechanisms, but people screw that up and say that's the difference between biology and psychology. It isn't. It's two different approaches for looking at the same thing: the mind. Biologists look at it from the bottom up, from the level of synapses and molecules, and psychologists are looking at it from the top down, at behavior and such."

LeVay had been intrigued by Swaab's research, but he was troubled by the fact that the portion of the brain examined by Swaab seemed to have nothing to do with the regulation of sexual behavior, at least not in animals. The suprachiasmatic nucleus governs the body's daily rhythms; dimorphism there according to sexual orientation might be provocative, certainly, but it would seem to constitute an effect, not a cause. Why not check out the hypothalamus, a region that is intimately involved with sexual behavior?

Laura Allen, a postdoctoral assistant in Gorski's laboratory, had identified four small groups of neurons in the anterior portion of the hypothalamus, naming them the interstitial nuclei of the anterior hypothalamus (INAH) 1, 2, 3, and 4. Allen's research had shown that INAH 2 and INAH 3 were sexually dimorphic in human beings—significantly larger in men than in women. Was it possible that these nuclei were dimorphic according to sexual orientation as well? That was the focus of LeVay's research, and he presented his conclusions in a short paper titled "A Difference in Hypothalamic Structure Between Heterosexual and Homosexual Men." It was published in Science in August of 1991. In the introduction LeVay defined sexual orientation as "the direction of sexual feelings or behavior toward members of one's own or the opposite sex" and hypothesized that Allen's INAH nuclei were involved in the generation of "male-typical sexual behavior." He went on,

I tested the idea that one or both of these nuclei exhibit a size dimorphism, not with sex, but with sexual orientation. Specifically, I hypothesized that INAH 2 or INAH 3 is large in individuals sexually oriented toward women (heterosexual men and homosexual women) and small in individuals sexually oriented toward men (heterosexual women and homosexual men). LeVay dissected brain tissue obtained from routine autopsies of forty-one people who had died at hospitals in New York and California. There were nineteen homosexual men, all of whom had died of AIDS; sixteen presumed heterosexual men, six of whom had been intravenous drug abusers and had died of AIDS; and six presumed heterosexual women. No brain tissue from lesbians was available. LeVay's conclusions included the following:

INAH 3 did exhibit dimorphism.... [T]he volume of this nucleus was more than twice as large in the heterosexual men ... as in the homosexual men.... There was a similar difference between the heterosexual men and the women.... These data support the hypothesis that INAH 3 is dimorphic not with sex but with sexual orientation, at least in men.

The results were sufficiently clear to LeVay to allow him to state, "The discovery that a nucleus differs in size between heterosexual and homosexual men illustrates that sexual orientation in humans is amenable to study at the biological level." The study, as LeVay himself readily admits, has several problems: a small sample group, great variation in individual nucleus size, and possibly skewed results because all the gay men had AIDS (although LeVay found "no significant difference in the volume of INAH 3 between the heterosexual men who died of AIDS and those who died of other causes"). As of this writing, LeVay's findings have yet to be replicated by other researchers. LeVay himself has extended his search for dimorphism according to sexual orientation to the corpus callosum, which he is studying by means of magnetic-resonance imaging. Until his original findings are confirmed, the notion that homosexuals and heterosexuals are in some way anatomically distinct must hold the status of tantalizing supposition.

It needs also to be remembered that, as noted earlier, the issue of dimorphism of any kind in the brain is hotly contested. The idea that the brains of heterosexuals and homosexuals may be different morphologically is derived from the idea that the brains of men and women are different morphologically—recall the corpus callosum study by De Lacoste-Utamsing and Holloway. But that study is itself problematic, efforts to replicate it having turned up inconsistent results. Anne Fausto-Sterling is a developmental geneticist at Brown University. She, along with William Byne, a neurobiologist and psychiatrist at Columbia University, has been among the chief critics of neurobiological investigations of homosexuality. Fausto-Sterling during an interview not long ago itemized some of the results from a long line of attempts to replicate sexual dimorphism: "1985: no sex differences in shape, width, or area. 1988: three independent observers unable to distinguish male from female. 1989: women had smaller callosal areas but larger percent of area in splenium, more-slender CCs, and more-bulbous splenium." A new corpus callosum study by Laura Allen, conducted in 1991, did find sexual dimorphism—and the debate continues. Part of the difficulty is methodological, involving whose brains are being compared, and how. Dead people or living people? Old or young or mixed? Healthy or sick? By means of brain sections or magnetic-resonance imaging? LeVay calls studies of the corpus callosum "the longest-running soap opera in neurobiology." And, of course, he himself is now part of the cast.

Even if LeVay's hypothalamus study stands up to scrutiny, it will not justify drawing extravagant conclusions. Establishing a distinction is not the same thing as finding a cause. Anatomy is not etiology, but it may offer a starting point for a journey backward in search of the ultimate origins of sexual orientation. That journey takes us into the realm of hormones and genetics.

THE PUZZLES OF CHEMISTRY

In a large room at the UCAL department of anatomy, Roger Gorski and I recently stood facing a dozen black-topped lab tables, each below a ceiling-mounted video monitor. We were about to watch a tape of rats having sex. Gorski, an eternally cheerful, almost elfin man of fifty-seven, was energetically describing the tape. "There are six couples," he explained, though at the moment I saw only one uninterested-looking white rat. "That's an unaltered female," he said. "They're going to put in another female that has been injected with testosterone." Sure enough, someone's hand reached down into the screen and a second rat landed in the cage. The rats at first edged around each other, but in just a few seconds on the dozen monitors I saw the testosterone-injected female begin to sniff the other female rat and then mount her aggressively. At the lab tables a handful of medical students went on with their work, paying no attention. After a few moments the tape cut to two males, one perinatally castrated and injected with estrogen, one unaltered. After some initial maneuvering the castrated male responded to the advances of the unaltered male by bending his back and offering himself in what was to me indistinguishable from female-rat lordosis—behavior indicating receptivity to sex, pictures of which Gorski had shown me in his office. The altered rat submitted as the other male mounted him. The tape continued with similar scenes. It was quite dramatic.

Such research in animals has led to hypotheses that hormones are, in some way, a cause of homosexuality in human beings. No one, of course, suggests that the sexuality of rats and that of human beings are strictly comparable; some critics of neurobiological research on homosexuality question the utility of animal models entirely. Nonetheless, it was investigations involving animals that got researchers thinking.

Of the scientists who have concentrated on hormonal or psychoendocrinological studies of homosexuality, Günter Dörner, of Germany, is one of the best known. In the 1970s Dorner classified homosexuality as a "central nervous pseudohermaphroditism," meaning that he considered male homosexuals to have brains with the mating centers of women but, of course, the bodies of men. For decades endocrinologists had speculated that because male sex hormones are known to be responsible in human beings for masculine body characteristics and in animals for certain aspects of male sexual behavior, it follows that adult homosexual men should have lower levels of testosterone, or else higher levels of estrogen, in the bloodstream than adult heterosexual men, and that homosexual and heterosexual women should display the opposite pattern. This is known as the "adult hormonal theory" of sexual orientation, and Dorner claimed that some initial studies bore it out.

In 1984 Heino Meyer-Bahlburg, a neurobiologist at Columbia University, analyzed the results of twenty-seven studies undertaken to test the theory. According to Meyer-Bahlburg, a score of the studies in fact showed no difference between the testosterone or estrogen levels of homosexual and heterosexual men. Three studies did show that homosexuals had significantly lower levels of testosterone, but Meyer-Bahlburg believed that two of them were methodologically unsound and that the third was tainted by psychotropic drug use on the part of its subjects. Two studies actually reported higher levels of testosterone in homosexual men than in heterosexual men, and one unhelpfully showed the levels to be higher in bisexuals than in either heterosexuals or homosexuals.

As it came to be widely accepted that adult hormone levels were not a factor in sexual orientation, scientists shifted their attention to prenatal hormone exposure. Many of the glands in a human being's hormone system are busily functioning even before birth—tiny hormone factories that produce the chemicals that help to mold the person who will eventually emerge. Perhaps, it was thought, different levels of prenatal hormones produce different sexual orientations. For obvious reasons, the sometimes brutal hormonal experiments done on monkeys and rats cannot be done on human beings, but nature at times provides a narrow window onto the mysteries of prenatal hormonal effects in ourselves.

Congenital adrenal hyperplasia (CAM) has been called by Meyer-Bahlburg a "model endocrine syndrome" for examining the effects of abnormal amounts of prenatal sex hormones. CAH, which can affect both males and females, is caused by a simple problem: an enzyme defect makes it impossible for a fetus's adrenal gland to produce cortisol, an important hormone. In a normal fetus, as the adrenal gland produces cortisol, the brain stands by patiently, waiting for the signals that the cortisol level is appropriately high and production can be shut off. But in CAH fetuses, which lack the enzyme to create cortisol, the brain doesn't get those signals, and so it orders the adrenal gland to continue production. The adrenal gland continues pumping out what it thinks is cortisol, but it is unknowingly producing masculinizing androgens. It dumps these into the fetus's system, thereby overexposing it to male hormones.

The consequences are most dramatic in females. Once, in his office, Roger Gorski dug into a desk drawer and grabbed a few photographs. "What sex is it?" he asked. I squinted at close-ups of a child's genitals and saw a penis, plain as day. "It's a boy,', I said confidently. Gorski's eyebrows shot up. "Where are the testicles?" he asked. I looked closer. Oops.

This was a CAH baby. In this case, Gorski told me, the doctors had decided at the time of birth that the child was a boy with undescended testicles, a relatively common and minor condition. But in fact I was looking at a genetic female.

With surgery a CAH female's external genitals can be made to look feminine, as her internal apparatus already fully is, and she will be raised as a girl. But hormones may have already had their effect in an area that plastic surgery cannot touch: the brain. Or at least so proponents of the prenatal-hormone theory of sexual orientation would argue. The sexual orientation of CAH females tends to bear them out. A 1984 study by the Johns Hopkins University sex researcher John Money found that 37 percent of CAH women identified themselves as lesbian or bisexual; the current estimate of the proportion of lesbians in the general female population is from two to four percent.

One possible clue as to whether the prenatal-hormone theory of sexual orientation is a profitable line of inquiry involves something called luteinizing-hormone (LH) feedback. The brain releases several hormones, including LH, which initiate the development of an egg in a woman's ovary. As the egg develops, the ovary releases increasing amounts of estrogen, stimulating the brain to produce more LH, which in turn promotes the production of still more estrogen. The process is called positive feedback. In men, estrogen usually acts to suppress the production of luteinizing hormone—it results in negative feedback. These differences in LH feedback in human beings, together with the discovery that male rats hormonally altered after birth will display both positive LH feedback and same-sex sexual behavior, led some researchers to a hypothesis. They speculated that gay men, their brains presumably not organized prenatally by testicular hormones, just as women's are not, would show a positive LH feedback, like that of a heterosexual female, rather than the negative feedback of the typical heterosexual male. If such feedback were to be found consistently in homosexual men—by means of chemical analysis of the blood after injection with estrogen—could this not be taken as evidence that some decisive prenatal hormonal event, with important bearing on subsequent sexual orientation, had indeed occurred?

This line of inquiry has given rise to an active field of study that as yet has little to show for itself. The uncertainties are of two kinds. The first one involves the following question: Do LH feedback patterns of the sort being sought in fact exist in human beings? The second comes down to this: Even if LH feedback patterns of the sort being sought do exist, will they really tell us anything about events that occurred before birth? Unfortunately, neuroscientists lack unequivocal answers to both questions, despite considerable efforts. Different studies have yielded conflicting data. No one has yet come up with what one neurobiologist facetiously terms a "gay blood test." In an article published in 1990 in the Journal of Child and Adolescent Psychopharmacology, Heino Meyer-Bahlberg surveyed the work done so far on hormonal research in general and concluded: "The evidence available to date is inconsistent, most studies are methodologically unsatisfactory, and alternative interpretations of the results cannot be ruled out." On the other hand, Meyer-Bahlberg went on, "not all potential avenues to a psychoendocrine explanation of homosexuality have been exhausted."

Among the unexhausted avenues is one being explored by Richard Pillard.

A PSYCHIATRIST AT THE BOSTON UNIVERSITY SCHOOL of Medicine, Richard Pillard is a tall, pleasant man in his fifties with a neatly trimmed moustache and a relaxed manner. Even when talking seriously, he remains goodnatured. When we spoke one afternoon in his Boston townhouse, he joked that he is uniquely equipped to investigate whether homosexuality has a biological basis: he, his brother, and his sister are gay, and Pillard believes that his father may have been gay. One of Pillard's three daughters from a marriage early in life is bisexual. This family history seems to invite a biological explanation, and it made Pillard start thinking about the origins of sexual orientation.

Pillard says that it had long puzzled him why transsexuals—men or women who wish to live in bodies of the opposite sex—are so different from gay people: "You'd think they'd be on the far end of the spectrum, the 'gayest of the gay.'" And yet transsexuals are not in fact gay. Whereas gay men, quite comfortably and unalterably, see themselves as men, male transsexuals see themselves as women trapped in men's bodies. Pillard and a colleague, James Weinrich, a psychobiologist at the University of California at San Diego, began to theorize that gay men are men who in the womb went through only a partial form of sexual and psychosexual differentiation. More precisely, Pillard and Weinrich theorized that although gay men do undergo masculinization—they are, after all, fully male physically—they go incompletely if at all through another part of the process: defeminization.

As fetuses, Pillard points out, human beings of both sexes start out with complete female and male "anlages," or precursors of the basic interior sexual equipment—vagina, uterus, and fallopian tubes for women, and vas deferens, seminal vesicles, and ejaculatory ducts for men. These packages are called the Mullerian (female) and Wolffian (male) ducts, and are tubes of tissue located in the lower abdomen. How do the sexual organs develop? It happens differently in men and women. At the moment of conception an embryo is given its chromosomal sex, which determines whether it will develop testes or ovaries. In female human beings (as in female rats) the female structures will simply develop, without any help from hormones; the Wolffian duct will shrivel up. The process of becoming male, however, is more complex. Where women need none, men need two kinds of hormones: androgens from the testes to prompt the Wolffian duct into development, and a second substance, called Mullerian inhibiting hormone, to suppress the Mullerian duct and defeminize the male fetus. Pillard speculates that Mullerian inhibiting hormone, or a substance analogous to it, may have brain-organizing effects. Its absence or failure to kick in sufficiently may prevent the brain from defeminizing, thereby creating what Pillard calls "psychosexual androgyny." In this view, gay men are basically masculine males with female aspects, including perhaps certain cognitive abilities and emotional sensibilities. Lesbian women could be understood as women who have some biologically induced masculine aspects.

An experimental basis is provided by research by the psychiatrist Richard Green, of the University of California at Los Angeles, which shows that children who manifest aspects of gender-atypical play are often gay. Green has concluded that an inclination toward gender-atypical play in prepubescent boys—for example, dressing in women's clothes, playing with dolls, or taking the role of the mother when playing house—indicates a homosexual orientation 75 percent of the time. If that is true, it is important, because it would be an example of a trait linked to sexual orientation which does not involve sexual behavior—suggesting how deeply rooted sexual orientation is. Discussing this line of research, Simon LeVay told me, "It's well known from animal work that sex-typical play behavior is under hormonal control. Robert Goy [at the University of Wisconsin at Madison] has done many studies over the years showing that you can reverse the sex-typical play behavior of infant monkeys by hormonal manipulations in prenatal life. [Play] is an example of a sex-reversed trait in gay people that's not directly related to sex. It's not sex, it's play. When you get to adulthood, these things become blurred. It's easier to tell a gay kid than a gay adult--kids are much of a muchness. Most gay men, even those who are very macho as adults, recall at least some gender-atypical behavior as children."

The Pillard-Weinrich theory also accords with what Green refers to as male "vulnerability" during the process of sexual differentiation. A considerably larger number of male embryos come into existence than female embryos, and yet males and females come into the world in about the same numbers. Therefore, phenomena linked to sex must reduce the number of males who survive to term. Many disorders are, in fact, more common in men than women, and some of these could result from problems originating in masculine differentiation. Although good statistics do not exist, it appears that there may be two gay men for every gay woman, which would be consistent with the vulnerability theory.

It is important to remember that although homosexuals and heterosexuals may be "sex-reversed" in some ways, in other ways they are not. For example, neither gay nor straight men tend to be confused on the subject of what sex they are: male. LeVay says, "It's not just that you look down and see you have a penis and you say, 'Oh, I'm a boy. Great.' I think there must be some internal representation of what sex you are, independent of these external signals like the appearance of your body. I think most gay men are aware of some degree of femininity in themselves, yet there is no reversal of gender identity." Gay men and straight men also seem to display an identical strong drive for multiple sexual partners; lesbians and straight women seem to be alike in favoring fewer sexual partners.

The evidence from hormonal research may circumstantially implicate biology in sexual orientation, but it is far from conclusive. William Byne raises a warning flag: "If the prenatal-hormone hypothesis were correct, then one might expect to see in a large proportion of homosexuals evidence of prenatal endocrine disturbance, such as genital or gonadal abnormalities. But we simply don't find this." Moreover, the hormonal research does not answer the question of ultimate cause. If hormones help to influence sexual orientation, what is influencing the hormones?

THE GENETIC QUEST

In 1963 Kulbir Gill, a visiting scientist from India working at Yale University, was conducting research into genetic causes of female sterility. His experiments involved exposing the fruit fly Drosophila melanogaster, that workhorse of genetic research, to X-rays, and observing the behavior of the resulting offspring. Gill noticed that a certain group of mutant male flies were courting other males, following each other and vibrating their wings to make characteristic courtship "songs." Gill published his findings in a short note in the publication Drosophila Information Service and then returned to the question of female sterility.

A decade later Jeffrey Hall, a biologist at Brandeis University, followed up on Gill's odd discovery. Every discovered Drosophila gene mutation is given a name, and Gill had called his mutation "fruity." Hall, considering this name to be denigrating, redubbed it, still somewhat tongue-in-cheek, "fruitless." Hall explains that the fruitless mutation produces two distinct behaviors. First, fruitless-bearing male flies, unlike nonmutant male flies, actively court other males as well as females, although for reasons that remain poorly understood, they are unable actually to achieve intercourse with members of either sex. Second, fruitless-bearing males elicit and are receptive to courtship from other males, which nonmutant males reject.

Fruit flies can live for two or three months, and this "bisexual" fly strain has existed behaviorally unchanged through hundreds of generations. Some gene mutations are lethal to flies; fruitless is not one of these, nor does it cause illness. It is, Hall says, a nonpathological genetic mutation that causes a consistent, complex behavior. And fruitless displays an anatomical sexual dimorphism, bringing LeVay's study to mind. In the abdomen of male Drosophila flies there is a muscle, the so-called muscle of Lawrence, whose function is unknown; female fruit flies don't have it, and neither do fruitless males. Although fruitless flies don't mate, the perpetuation of the fruitless trait is made possible by the fact that it is recessive--a full pair of the mutations is needed for fruitless behavior to be expressed. When males that carry a single fruitless gene mate with a fruitless-carrying female, a percentage of their offspring will carry the full pair and display typical fruitless behavior. If a genetic component of homosexuality in human beings exists, it could possibly operate by means of a comparable mechanism.

Angela Pattatucci, a geneticist at the National Institutes of Health, gave me a demonstration a few months ago in her lab. She took a small glass container of tiny Drosophila flies, popped off the top, and plugged an ether-soaked cotton ball into the mouth. Within a few seconds the flies were lying stunned on the glass floor. Using a plastic stick Pattatucci separated out a few of the flies into a larger glass jar. I looked at a group of males and females through a microscope, their bodies vibrating, red eyes bulging. Pattatucci showed me how to differentiate the genitalia at the end of the abdomen--smooth and light-colored for females, furry and dark for males. Pattatucci said that researchers are relatively close to finding the actual fruitless gene. It is already known that fruitless is located physically on the right arm of the third chromosome. After establishing the precise location (or locations) of the mutation, researchers can determine the sequence of biochemical information in fruitless's genetic code—the order of thousands of units of the basic genetic components adenine, thymine, guanine, and cytosine. Once the combination is known, the search can begin for a similar combination—a fruitless analogue—in human beings.

In the jar the males, separated out, eventually came back to awareness. "Watch that one," Pattatucci said, pointing to a fly that had come up behind another fly, vibrating his wings in courtship. He then climbed on top of the male he was courting. I watched the two flies, one atop the other, the one on the bottom wandering around as if a bit bored. As noted, for a fruitless fly that is as far as things can go.

I once asked Jeffrey Hall if courtship alone could be satisfying for a fly. "Could be," he said. "Maybe it's delicious, maybe he's frustrated. But this becomes ludicrous. How do you know when a fruit fly is frustrated?" It is an important point: the danger of anthropomorphizing insect behavior is great, and I found myself doing it almost by reflex when watching Pattatucci's flies. How can we equate fly behavior with a vast something that in human beings generates aesthetic and intellectual perceptions—with something that encompasses emotional need and love and the pain of love? So Hall is careful to describe fruitless as "a mutation that leads to a mimic of bisexuality." He is skeptical that finding a fruitless analogue will lead to a full explanation of human homosexuality. DNA analogues for all sorts of fruit-fly genes do exist in human beings, and the process of looking for them is relatively straightforward. But, as Hall points out, "it is very unlikely that the genetics of homosexuality will ever devolve to a single factor in humans with such major effects as it has in Drosophila."

When biologists are interested in establishing whether genetics is involved in the appearance of certain characteristics or conditions, one obvious place to look is among people who are closely related to one another. In "A Genetic Study of Male Sexual Orientation," a study that has now achieved almost as much renown as LeVay's, the Northwestern University psychologist Michael Bailey and Boston University's Richard Pillard compared fifty-six "monozygotic" twins (identical twins, from the same zygote, or fertilized egg), fifty-four "dizygotic" (fraternal) twins, and fifty-seven genetically unrelated adopted brothers. Identical twins are important in sexual-orientation research because, of course, they have identical genomes, including the sex-chromosome pair. If homosexuality is largely genetic in origin, then the more closely related that people are, the greater should be the concordance of their sexual orientation.

That is, in fact, what the study found. Bailey and Pillard reported a gay-gay concordance rate of 11 percent for the adoptive brothers, 22 percent for the dizygotic twins, and 52 percent for the monozygotic twins. The findings suggest that homosexuality is highly attributable to genetics—by some measures up to 70 percent attributable, according to Pillard. This figure is based on something geneticists call "heritability," a painstakingly calculated indicator of how much genes have to do with a given variation among people. If heritability is less than 100 percent, then the characteristic being studied is by definition "multifactorial." Eye color is 100 percent dependent on genetics. Height, on the other hand, though about 90 percent genetic, is also affected by nutrition, and thus is multifactorial.

If a large contribution to homosexuality comes from genes; where does the rest of it come from? The range of environmental and biological inputs a developing child receives is both enormous and enormously complex. "Whatever the other variables are," Pillard says, "they must be present early in life. I think this because the genderatypical behavior that so strongly prefigures an adult homosexual orientation can be observed early in development." And he goes on: "There certainly could be different paths to the same outcome. With individual cases, there are doubtless some that are mostly or all genes, and others that might be all environment. Our analysis [of twins] doesn't say anything about the individual." Jeffrey Hall can be so underwhelmed by the prospect of finding a human analogue of the fruitless mutation because, as he points out, if we do find it, we still will not have fully accounted for the etiology of homosexuality even in identical twins. "You will effectively know nothing from this genetic knowledge," Hall says. A behavior as simple as jumping, he notes, is quite complex genetically, having to do with all kinds of genes and other, unknown factors. He says, "We are not about to create a genetic surgical procedure which makes you Michael Jordan." LeVay made the same point in the course of our conversation: "It's one thing to say that genes are involved, as they almost certainly are. It's a whole other thing to actually identify those genes, because homosexuality may be polygenic, with each gene having a small effect. "

Whatever the uncertainties ahead, though, the important point is that the genetic work is already fairly compelling. A new Bailey and Pillard genetic study of lesbian twins, to be published soon in the Archives of General Psychiatry, echoes the researchers' original male-twin findings with strikingly similar results. "We're getting a lot of consistency where we should be getting it," Bailey says. The most interesting question is perhaps becoming not whether genetics plays a role in homosexuality but how. Why does nature preserve genes that influence sexual behavior and yet do not facilitate reproduction? Does less than 100 percent heritability mean that the Bailey and Pillard study is incompatible with a bipolar model of sexual orientation? In his study LeVay defined homosexuality in terms of the sex of a person's sexual-object choice: either men or women, either homosexual or heterosexual. Pillard and Bailey's multifactorial model suggests a shaded continuum of sexual orientations, and of origins and causes, more complex and subtle than a simple either-or model can accommodate, and closer to what may be the quirks and ambiguities of our real lives.

THE RAMIFICATIONS OF SCIENCE

What does it all mean? As we have seen, scientists must sift for their conclusions through ambiguous results from a disparate group of studies that are excruciatingly difficult to interpret. Yet even at this relatively early date, out of the web of complexities it is becoming ever clearer that biological factors play a role in determining human sexual orientation. Richard Green said to me, "I suspect that at least in your lifetime we will find a gene that contributes substantially to sexual orientation." Michael Bailey says, "I would—and have—bet my career on homosexuality's being biologically determined." The pace of neurobiological and genetic research is only increasing.

The search is not without its opponents. Some, recalling earlier psychiatric "treatments" for homosexuality, discern in the biological quest the seeds of genocide. They conjure up the specter of the surgical or chemical "rewiring" of gay people, or of abortions of fetal homosexuals who have been hunted down in the womb. "I think all of us working in this field," Pattatucci says, "have delusions of grandeur in thinking we can control the way this knowledge will be used." Certainly the potential for abuse is there, but that is true of much biomedical knowledge. It is no reason to forswear knowledge of ourselves, particularly when the potential benefits are great.

Some of the benefits could be indirect. Laura Allen points out, for example, that there are many now-mysterious diseases—autism, dyslexia, schizophrenia—that affect men and women differently, hiding inside parts of the human mind and body that we cannot penetrate. Neurobiological research into sexual differentiation may help us to understand and cure these diseases, as well as to unlock other mysteries—the mysteries of sexuality. And then there is the question with which we began—that of the acceptance of gay people in American society. The challenge posed by homosexuality is one of inclusion, and, as Evelyn Hooker would say, the facts must be allowed to speak. Five decades of psychiatric evidence demonstrates that homosexuality is immutable, and nonpathological, and a growing body of more recent evidence implicates biology in the development of sexual orientation.

Some would ask: How can one justify discriminating against people on the basis of such a characteristic? And many would answer: One cannot. Yet it would be wise to acknowledge that science can be a rickety platform on which to erect an edifice of rights. Science can enlighten, can instruct, can expose the mythologies we sometimes live by. It can make objective distinctions—as, for example, between sexual pathology on the one hand and sexual orientation on the other. But we cannot rely on science to supply full answers to fundamental questions involving human rights, human freedom, and human tolerance. The issue of gay people in American life did not arise in the laboratory. The principles needed to resolve it will not arise there either. *