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SCIENTIFIC AMERICAN PRESENTS

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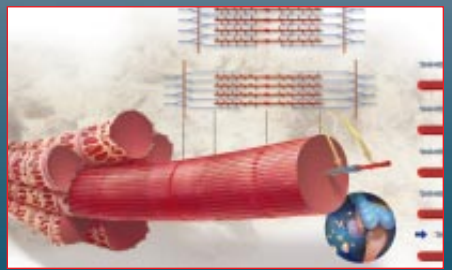

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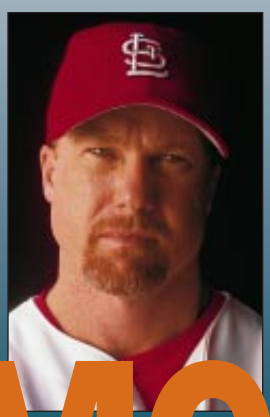
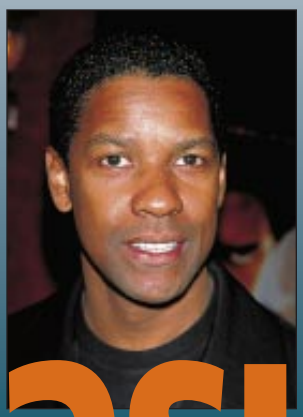



Measures of

Athletes, actors, entrepreneurs and high-ranking politicians shape our definitions of male gender. Mark McGwire, Denzel Washington, Bill Gates and Bill Clinton. Heroes of summer and screen, the self-made billionaire and the self-destructive philanderer. This typology of our transmillennial culture marks only one measure of what it means to carry a Y as well as an X chromosome. Whether muscleman or nebbish, the male of the species fulfills a destiny shaped not just by batting average and bank balance but by genes, hormones and psyche.

Biology and psychology both confirm and deny the prevailing stereotypes. Statistically, men do live up to expectations as tough guys: killing and being killed, drinking, sleeping around and generally ignoring what ails them. Testosterone, the hormone that defines the essence of maleness, may foster life-threatening recklessness—and may also raise the risk of heart disease and stroke. If only the strong survive, then men are the weaker sex. Dying like a man in the U.S. means to expire, on average, six to seven years earlier than the opposite sex.

Fortunately, men have taken a few lessons from how the other half lives. The influence of the women's movement—or in some cases a reaction to it—can be witnessed in the hundreds of college courses in men's studies and a burgeoning preoccupation with men's health issues. The campaign to combat prostate cancer is similar in scope to the fight against breast cancer. Intervention programs for domestic batterers and adolescent boys attempt to curtail the tough-guy swagger that can fracture families and lead to jail time.

It is assumed, of course, that radical change is possible and all to the good. Men's studies often focus on the protean nature of male identity and how the infinitely mutable male persona can evolve from the John Wayne archetype to the more sensitive Alan Alda image.

Meanwhile the scientific literature has begun to paint a different portrait—one that demonstrates that postmodernist interpretations of gender may have well-defined limits. Biology, in fact, dictates much of who we are. Neuroscientists have begun to explore how sex hormones may lead to different wiring in the brains of boys and girls, engendering not just differing styles of play but fundamentally distinct modes of

Man

Hormones and bluster produce the hero, the cad and the shorter-lived of the sexes. Insights into both male psychology and biology may temper untoward behavior and enhance longevity

cognition. The aggression and risk-taking behavior that may be promoted by male hormones stem from selection pressures on men to procure the most mates, evolutionary psychologists assert.

Molecular biologists have traced the locus of maleness—the DNA software that programs the development of the testes, which make testosterone and other male hormones—to a gene on the Y chromosome. The Y proves to be a shrunken version of the female-defining X chromosome. Contrary to the Bible, man derives from woman.

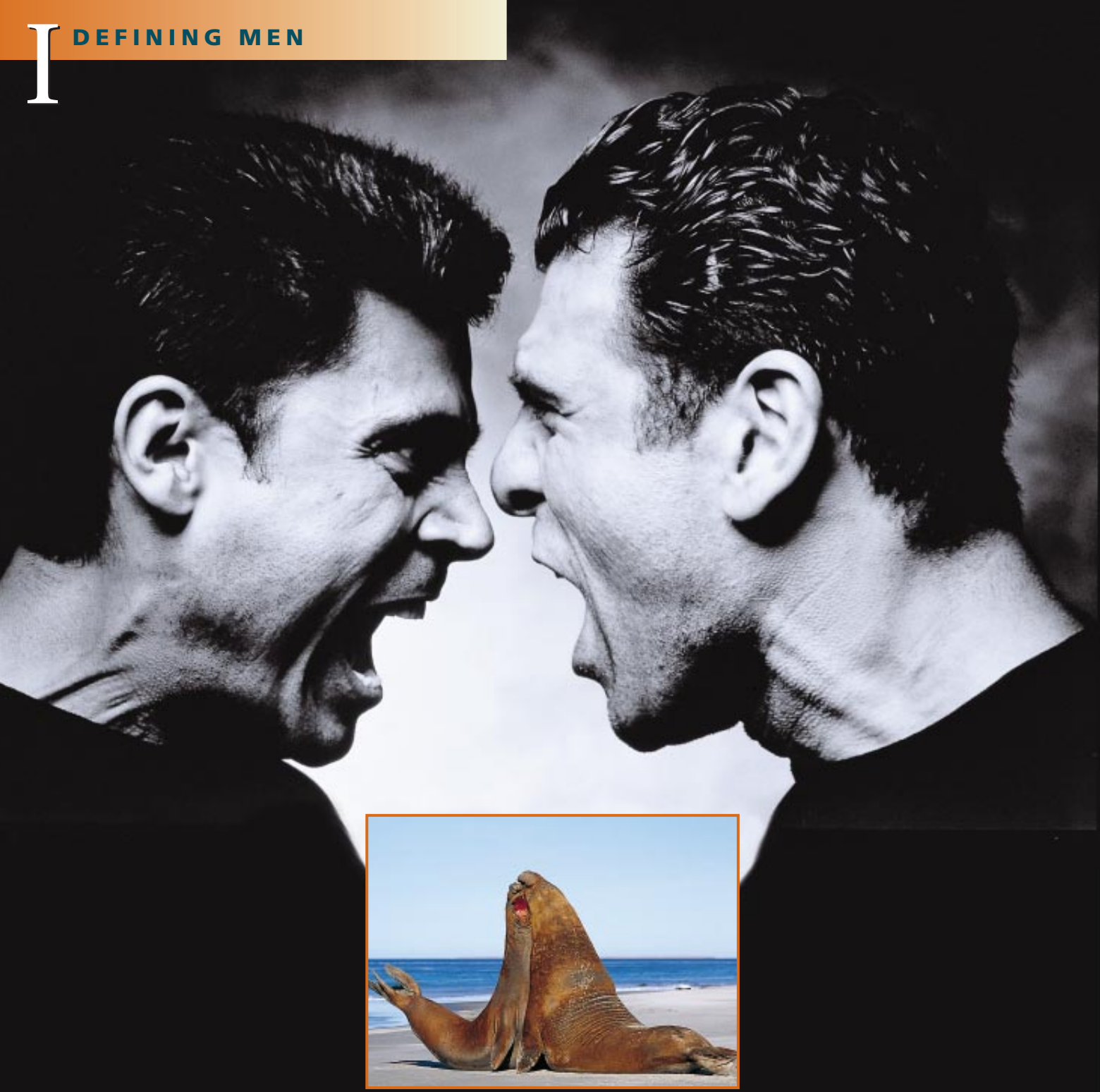
Into this fray step the social scientists, whose investigations into men's habits and health suggest that genes cannot explain everything and that prevailing notions of modern maleness are fraught with nuance. Their research has shown that certain culturally influenced behaviors—such as avoiding one drink too many or finding a supportive spouse—may influence a man's longevity more than his genetic heritage does. Even a predisposition to violence may depend on native culture: whether, for instance, you were brought up north or south of the Mason-Dixon Line. Sociological studies reveal diverging profiles for the modern father: men in two-parent families spend more time with children, but many of the divorced may not have seen a son's or daughter's face in at least a year.

In a perverse sense, the biological determinism that challenges social theorists may also lend them the last word. Some of the most caustic critics of science lambaste it for reducing humanity to a simple electrical and plumbing schematic of the body. Yet deciphering the underlying electrical potentials and fluid flows may finally allow men to be all that they can be, at least in the sexual department. The little blue pill called Viagra takes its power from Nobel-winning research into the molecular signals that lead to an erection. Viagra represents the lure of age-warping identity change: it is the promise that men can indulge themselves as boys. And more novelties may be on the way. Studies of the byzantine complexity of skeletal muscle have revealed a growth factor that may restore the lost tone of sagging flesh. The discovery may provide a remedy for age-related muscle loss or the next illegal performance enhancer for buffed bodybuilders.

The reasons that men live shorter, more brutish existences than women may be rooted deep within biology and evolutionary history. Ultimately, wholesale transformation of character may be beyond the reach of any pill or injection. But an understanding of why men do what they do, combined with the power of these new technologies, may help narrow the longevity gap between men and women and lead to better lives for all.

—The Editors

left to right: PETER RODGER *Outline;* GREGORY PACE *Sygma;* BLAKE LITTLE *Sygma;* RICHARD ELLIS *Sygma*



HEAD TO HEAD: Men and other animals such as elephant seals often fight over status. Competition for mates helps to explain such risky tactics.

Darwinism and the Roots of

Machismo

Men's evolutionary heritage probably has made them risk takers. But some of the harmful consequences can be moderated

by Martin Daly and Margo Wilson

How long people live varies among times and places, but women almost always live longer. According to current estimates by the United Nations, Japan leads the world in life expectancy at birth: 76.9 years for males and 82.9 for females. In the U.S. the corresponding figures are 73.4 and 80.1 years, and in Russia, 58.0 versus 71.5. Of more than 200 countries, men outlive women only in the Maldives and Nepal, where birth rates are exceptionally high and may contribute to mortality among women. The typical female advantage was probably as evident in our preagricultural ancestors as it is in modern society.

Why do men die younger? There is no single answer. Demographers distinguish external causes of death (homicides, suicides and accidents) from internal causes (disease). In modern countries, males die at higher rates than females from both internal and external causes, at all ages, and differences between the sexes in external mortality in adolescence and young adulthood are especially striking [*see illustration on page 11*]. What limited evidence is available indicates that the same is true in foraging societies, which are more like those in which humans evolved.

External mortality in young men is largely a consequence of their behavior. They drive more recklessly than women or older men, for example, and they are relatively unconcerned about the hazards of taking street drugs and about invisible threats such as environmental contaminants and sexually transmitted diseases [see "Teenage American Males: Growing up with Risks," on page 86]. They are also more inclined to choose immediate rewards over larger but later ones and more often experience a close brush with danger as a rewarding thrill. They are more likely than other demographic groups to escalate an altercation to a dangerous level, to kill and to be killed.

Why are young men more risk-loving than other people? The ubiquity of these tendencies across cultures implies that they cannot be simply a consequence of modern society. The question must instead be addressed like others that concern life history and differences between the sexes, such as why men tend to be a little taller than women and to experience puberty a little later. What needs explaining is how and why these aspects of human nature evolved.

Sexual Selection and Sex Differences

A major source of differences between females and males is sexual selection, the component of Darwinian natural selection that consists of nonrandom differences in mating success. Over evolutionary time, sexual selection engenders distinct attributes in females and males whenever the mating tactics that leave the most descendants are different for the two sexes.

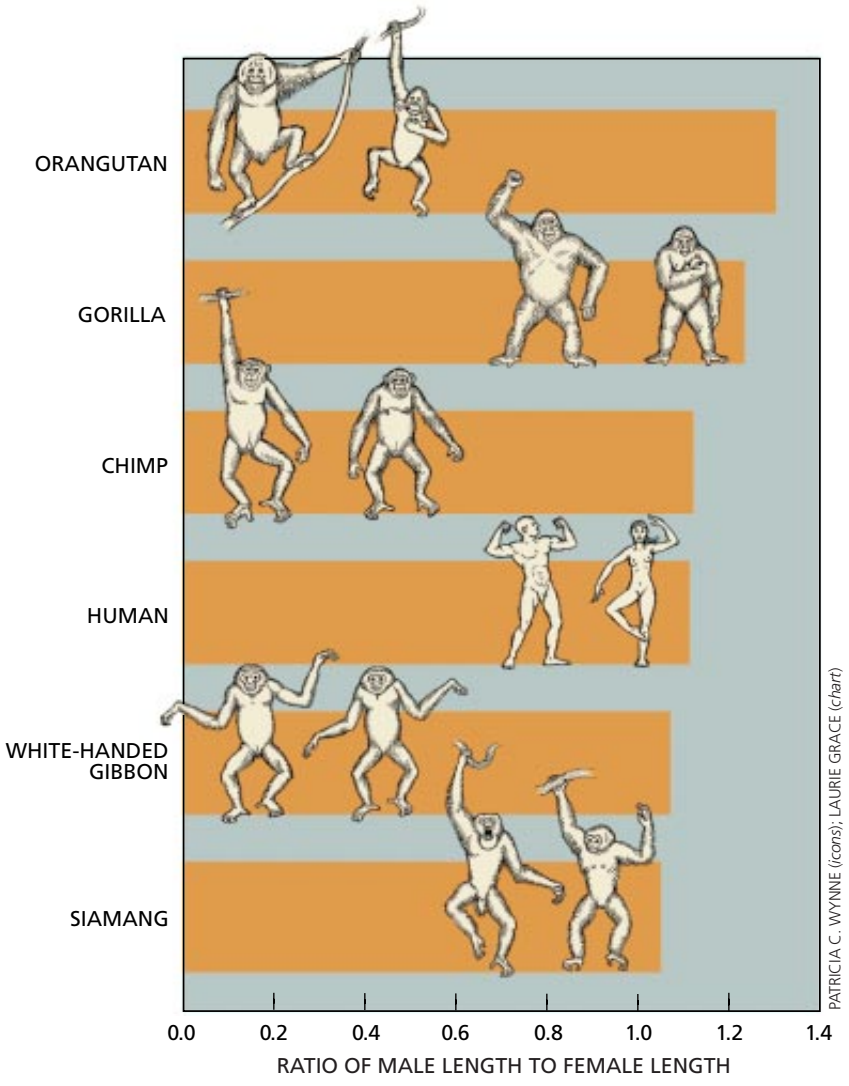
Consider, for example, a species in which females provide most of the time and energy needed to raise young. In such creatures, a male's reproductive posterity depends directly on the number of his mates, but a female has less to gain from polygamy because a single sperm donor can impregnate her many times. Thus, sexual selection tends to equip males with competitive traits that help them have as many sexual contacts as possible and tends to equip females with discriminatory traits that help to assure that especially healthy or otherwise superior males sire their young.

The northern elephant seal provides a famous example. Whereas a female can give birth to and raise only one pup a year, at best, a successful bull may sire dozens of pups. The males weigh four or five times as much as the females, even though growing bigger means maturing later, and they are much more violent, fighting to gain access to females. Males and females have evolved to look and act so differently because the reproductive prize for those who attain top rank is much higher for males than for females, and bigger prizes warrant bigger bets.

Even a male that survives to maturity is on average much less likely than a female to reproduce, because of competition from other males. This situation selects strongly for males that fight recklessly to attain the status of "beachmaster." In evolutionary terms, a long-lived, peaceful celibate has done no better than a male who dies after losing a battle: both will be nobody's ancestors. As many as 85 percent of male elephant seals die before they reach breeding age, and many die from wounds after this age. High male mortality from fighting is seen in other species with similar mating systems.

The situation is quite different in mammals that form enduring pairs and share the burden of parenting, such as foxes, beavers, some small African antelopes and a few species of monkeys. In these monogamous mammals, females and males are about the same size, about equally armed and armored, and about equally combative. Evolutionists attribute this similarity to the fact that the distribution of reproductive success among members of one sex is matched in the other sex, so that fe-

TELEGRAPH COLOUR LIBRARY FPG; FRED BRUEMMER *Peter Arnold, Inc. (inset)*



MALES are much bigger than females in polygynous orangutans and gorillas but are of similar size in monogamous siamangs. The human male-female difference is intermediate, which is consistent with our species' evolutionary history.

males and males have been selected to compete with their same-sex rivals with about equal intensity.

Different species practice polygamy to varying extents. Elephant seals represent an extreme: large numbers of fertile females nurse close together, so one bull can keep other males away from his "harem." When females are more spread out, successful male mammals are often polygamists on a smaller scale. A crude but useful index of the degree of polygamy is the ratio of the variability in reproductive success among males (measured by a statistic called the variance) divided by the same statistic computed for females.

For a truly monogamous species, this ratio equals one. If the reproductive success of females is more variable than that of males, the ratio is less than one, and the system is effectively polyandrous (one female mates with multiple males). If the ratio exceeds one, which is the more common case, the system is effectively polygynous (one male mates with multiple females). For the elephant seal, we estimate the ratio at 4.2.

If you rank a group of related mammalian species such as seals or primates by their effective polygamy index, several other features of their biology will fall roughly in order. Where the index is larger, males have more conspicuous weaponry, and relative to females they are bigger and reach reproductive maturity later. Furthermore, they have a shorter maximum life span, for reasons we will explain shortly. In species whose effective polygamy index is close to one, the sexes tend to be similar in all these attributes. The sex differences in various species are the predictable consequence of the relative intensity of sexual selection in males and in females.

It is clear where the human animal fits into this comparative scheme. The difference in male and female body size—less extreme than in the other great apes but greater than in exemplary monogamists—suggests that we evolved under conditions of slight effective polygyny: the most prolific fathers had more children than the most prolific mothers. Yet more males than females died childless, because if some men have more than one wife, others must have none. The slightly later puberty in boys than in girls is consistent with this suggestion, as is the tendency for men to deteriorate and die a little sooner.

Patterns of marriage and reproduction support the same conclusion. Before the emergence of agriculture, towns and complex economies a few thousand years ago, it was probably impossible for one man to keep many wives. In many foraging societies, however, the most successful hunters may have two or three wives, either simultaneously or successively, and some evidence indicates that they have more extramarital affairs than less successful men do.

For !Kung San living as foragers in the Kalahari Desert of Botswana a few decades ago, the effective polygamy index was about 1.4, and for Ache foragers in Paraguay it was about 1.6. It is clear that in these and other traditional societies, social status has always played a key part in a man's reproductive success and that a crucial factor determining that social status has been his competitive prowess. The polygamy index in modern nations probably still slightly exceeds 1, because men are more likely than women to have children with successive marriage partners. All these estimates neglect cases in which the declared father is not the real one: correcting for them would probably raise the estimates somewhat. In any event, we believe an evolutionary history of slight effective polygyny explains the tendency of men to be greater risk takers, a tendency that lowers their average life span.

Violence as Competitive Risk Taking

Men kill one another in competitive conflicts over both material goods and less tangible social resources far more than women do. The late U.S. criminologist Marvin E. Wolfgang dubbed the most common variety of homicide the "trivial altercation." Two men get into a dispute over a real or imagined insult,

perhaps a small debt or a minor social entitlement, usually in front of witnesses with whom they are acquainted. They are unable or unwilling to give way as the conflict escalates to a deadly level. Such cases are prevalent wherever the murder rate is high and constitute about half of all homicides in the U.S.

Calling the initiating disagreement "trivial" is, of course, a value judgment, and its implicit disparagement is unwarranted. Low-status men who become embroiled in barroom disputes are defending their honor as surely as were high-status duelists in times past. A reputation for refusing to succumb to threats may be the most valuable asset a low-status man possesses, and we do not know the average risks and benefits of the available options well enough to judge whether dangerous decisions in these situations are foolish.

In modern nations, killers are mostly of low status, but this was not always so. High-status men kill, too, but they can forgo personal violence when law and other societal institutions afford them other means of enforcing contracts and deterring competitors. In societies that lack such institutions, a credible threat of violence is essential for acquiring and keeping a high status. Napoleon A. Chagnon of the University of California at Santa Barbara has shown that among the Yanomamö in Amazonia, men who have killed have more wives and children than those who have not, and their society is surely not unique in this.

Still, low status, whatever its cause, often invites risk taking, for as Bob Dylan sang, "When you got nothin', you got nothin' to lose." Poor prospects for employment, marriage and reproduction may make risky tactics of social competition such as robbery and violent confrontation more attractive. If so, we would expect them to be more prevalent among the unemployed, the single and the childless. The available data are supportive: employed men and married men do kill male rivals at much lower rates than their unemployed and single counterparts do [*see illustration at top of next page*]. Nobody has yet determined whether fatherhood has additional effects.

The immense sex difference in murderous rivalry is apparently universal. But rates of such killing vary dramatically among times and places [see "Men, Honor and Murder," on page 16]. Despite a recent decline in homicides in the U.S., killings during altercations and robberies still happen at per capita rates many times higher than those in Scandinavia or Japan. Even U.S. rates, however, are dwarfed by those that have recently prevailed in societies that lack policing or central authority, such as various tribal communities in Amazonia and New Guinea.

Daring Tactics for Winning Big

Even for poor men with bleak prospects, violence may not be worth the risk. But when it is clear to all that some of the winners in social competition are winning big, dangerous tactics may become more attractive. This notion raises the intriguing possibility that the inequitable distribution of goods (or the perception of it) may play a greater role in promoting violence than poverty itself does.

Some findings support this idea. In comparisons between different countries and across the U.S., measures of income inequality are slightly better predictors of homicide rates than are average household and personal income. We have found the same to be true on a finer scale as well. In comparisons between neighborhoods in Chicago, income inequality is a better predictor of homicide rates than median household income is.

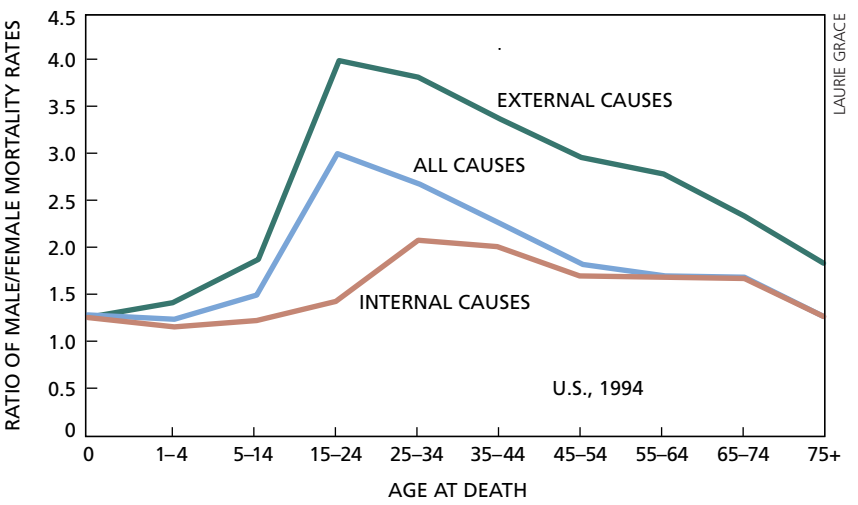
The best predictor of homicide rates in Chicago neighborhoods, however, is not an economic measure but a demographic one: the local life expectancy. Where life may be short anyway, men appear to be readier to resort to violence. In the worst of Chicago's 77 neighborhoods, male life expectancy at birth in 1990 was just 54 years, even with the contribution of homicide to mortality statistically removed. (Before homicide was removed, the figure was 51 years.) In the best neighborhood, life expectancy was 77 years [*see illustration on page 14*]. Whether awareness that death may come early actually affects a man's readiness to turn to violence, as we have proposed, is a question for future research.

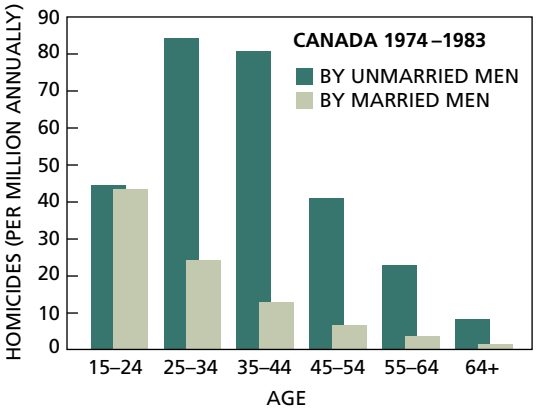
Although excess male mortality from external causes is striking, the lion's share of U.S. women's nearly six-year advantage in life span is the result of lower rates of death from internal causes, such as cancer and heart disease. But men's greater taste for risk is still highly relevant.

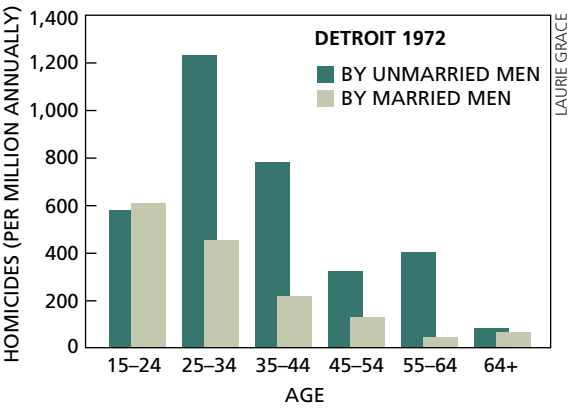
If reckless driving kills you, your death will be classified as external, but smoking is reckless, too, and the deaths that it causes are deemed internal. Some exposure to infectious disease is influenced by behavior, particularly sexual behavior, and what we eat and where we live also have predictable effects on the risk of coming into contact with infectious agents and toxins. Moreover, the likelihood of death often depends on how soon a condition is detected and treated, and several studies have found that men monitor their health less assiduously than women do [see "Longevity: The Ultimate Gender Gap," on page 106].

Still, even after all the reckless behav-

MALE DEATH RATES exceed female rates. The ratio is greater than one at all ages for both internal causes of death (disease) and external causes (accidents, homicides and suicides).







UNMARRIED MEN kill unrelated men at higher rates. Homicide rates throughout Canada and in Detroit differ dramatically, but both sets of data show that married men kill substantially less often than unmarried men do.

ior and lifestyle differences are allowed for, it remains true that on average men senesce, or deteriorate generally, somewhat earlier than women do. Surprisingly, even this trait can be linked to men's greater acceptance of risk, but the connection is a subtle one and works on an evolutionary timescale.

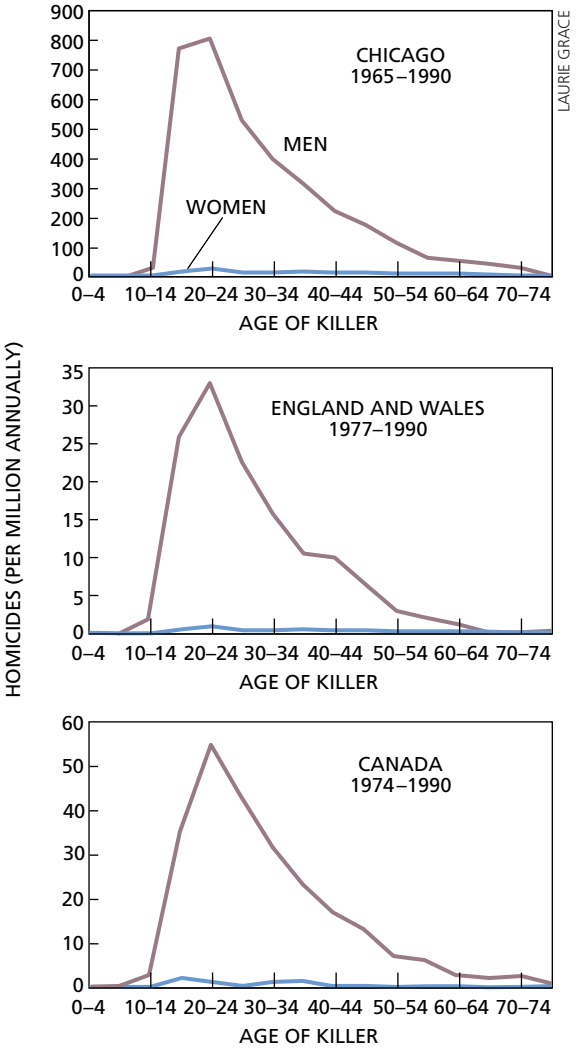
Accidents, enemies and infectious diseases ensure that of a group of people born in the same year, the proportion surviving decreases as the group ages. The result is that selection is weaker on traits that appear late in life: something that kills only old people can have little effect on the number of descendants they leave. Meanwhile selection for whatever may be required to reproduce early and successfully—such as competitive ability—is intense. Thus, mutations that engender physical and psychological advantages early in life tend to increase in number under selection and eventually become part of a species' adaptive design, even if they also have detrimental effects in old age.

One implication of this theory is that researchers are unlikely to find a single "silver bullet" that will halt or reverse senescence, which probably entails processes of deterioration that develop in synchrony because of past selection. Another implication is that over evolutionary time, the levels of mortality that prevail early in life affect later rates of senescence. If in the natural environment more individuals are killed before senescence in species A than in a similar species B, then selection will be weaker in later life in species A, simply because fewer individuals survive to be old. Mutations that are beneficial in the younger years but harmful later will consequently be more strongly selected for in species A. As a result, it is apt to senesce earlier and die younger, even when extrinsic sources of mortality are eliminated, as in a zoo. The same principle applies to comparisons between the sexes within species: the sex with the higher nonsenescent mortality rates early in life will evolve to senesce earlier.

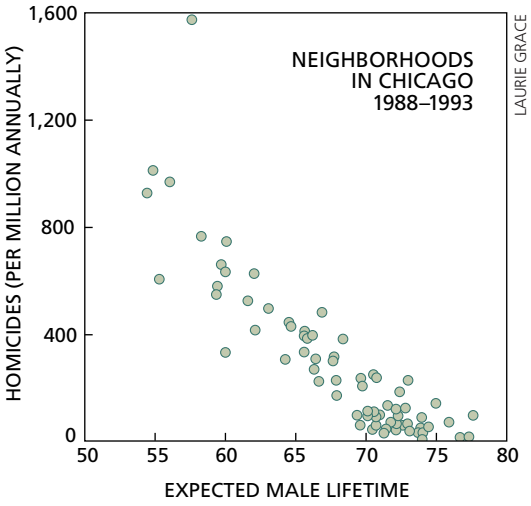
A recent analysis of the life spans of monkeys and apes in zoos inadvertently supports this idea. John Allman and his colleagues at the California Institute of Technology found that males die younger than females in precisely those species, such as gorillas and spider monkeys, in which effective polygyny is extreme. In contrast, male and female life expectancies are the same in the monogamous siamang and Goeldi's monkey, and males actually outlive females in another monogamous species, the owl monkey. White-handed gibbons, unlike the closely related siamang, have a mortality pattern like that of more polygynous apes, which was at first surprising because gibbons, too, had been considered monogamous. Recent observations of "adulterous" liaisons, however, indicate that wild gibbons are not such faithful monogamists after all.

In many species, males compete seasonally for mating opportunities and suffer injury and exhaustion in the process. When there are no more fertile females with which to mate, fighting loses its appeal and weapons such as antlers may be shed.

Such seasonally variable tactics are commonly controlled by changes in blood levels of androgens (testosterone and related hormones) produced in the testes, which affect muscularity, metabolism and motivational structures in the brain. Outside the mating season,



MEN AND WOMEN KILL unrelated persons of the same sex at greatly different rates. Most of these homicides arise from escalated disagreements over status and perceived insults. The huge difference between the sexes is seen everywhere, despite enormous differences in overall homicide rates.



LOCAL MALE LIFE EXPECTANCY is the best predictor of homicide rates in Chicago's 77 neighborhoods, even when it is computed with the effects of homicide removed* (graph). *Men who perceive an uncertain future may be more willing to take risks.

testes often shrink and may be withdrawn into the body.

Circulating testosterone has detrimental effects beyond promoting violence and risk taking. Prostate cancer, a leading cause of death in men, develops under the influence of testosterone and can be treated with drugs that inhibit androgens' effects. Testosterone also suppresses the immune system, which may explain why androgen-inhibiting drugs can apparently help male mammals combat infections. Furthermore, castration at an early age can increase the life span of some male mammals. (This might work for men, too, but we doubt that it will become a popular way to extend human lives.)

Testosterone Poisoning

The evolutionary theory of senescence makes it easier to understand the puzzle of why a naturally circulating substance like testosterone should constitute a health hazard. Moreover, recent work on the evolution of social signals suggests that "testosterone poisoning" may be more than just an unfortunate by-product of selection for success in reproductive competition.

Biologists have theorized that physical attributes used to intimidate rivals or to advertise health to potential mates must be features that a weakling could not fake, because natural selection favors those who respond correctly to "honest" signals of quality and ignore others. Individuals who are fooled by a fake signal will tend to have lower reproductive success in the long run, because their offspring with the faker will be less hardy than the offspring of genuinely healthy mates; gullible individuals will therefore become less common in succeeding generations while individuals who ignore the "dishonest" signal proliferate.

According to this "handicap theory," androgen-dependent decorations such as the peacock's tail are honest signals of male vigor that are attractive to females precisely because they require an animal to compromise its immune system or handicap itself in other ways that a male of lesser quality could not: they guarantee his physical toughness and suggest that offspring created with him will be tough, too. This initially controversial idea has gained support in studies on various animals, and researchers have just begun to investigate its possible relevance to human male attributes.

Several researchers, including Alan Booth of Pennsylvania State University, James M. Dabbs, Jr., of Georgia State University and Allan C. Mazur of Syracuse University, have shown that blood levels of male hormones are affected by competitive behavior. Testosterone begins to rise when a man is about to compete, whether in a strenuous athletic contest or something as cerebral as a chess match. The winner's testosterone continues to rise after the competition, but the loser's falls.

We hypothesize that such changes are part of a process by which competitive success or failure affects men's willingness to take a chance in a wide range of social actions, including approaching women. This idea has yet to be tested, but evidence already points to an association between changing social circumstances and testosterone levels. Mazur and his colleagues have used data from a study of 2,100 U.S. Air Force veterans to show that testosterone levels fall after marriage but rise again in those who divorce. Other studies show that levels fall lower still in new fathers who are helping to rear their infants. It is tempting to speculate that social circumstances such as competitive success, marital status and fatherhood influence assertiveness, violence and risk taking through their effects on testosterone. The behavioral effects of fluctuating hormone levels remain controversial, however, because the human data consist of correlations rather than experimental results, and the effects of hormones can be slow and cumulative rather than immediate.

Much remains to be learned about the links among men's physiology, psychology and behavior, but it is already apparent that men are more risk-prone than women in all these domains. The implication is certainly not that male recklessness and violence are universal or inevitable, for both evolutionary theory and the available evidence support the view that the more destructive forms of risk taking and competition are products of inequity and desperation. There is good reason to believe that the burdens that male risk taking imposes on society could be reduced by distributing material resources more equitably. SA

The Authors

MARTIN DALY and MARGO WILSON are professors of psychology at McMaster University in Hamilton, Ontario. Both began their scientific careers in animal behavior, Daly studying rodent socioecology and Wilson studying behavioral endocrinology of rhesus monkeys. They still do behavioral research on desert rodents, but their primary focus is now on epidemiological studies of homicides as an "assay" of interpersonal conflict. They are the co-editors of the journal *Evolution & Human Behavior,* and Wilson is just completing a term as president of the Human Behavior & Evolution Society.

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Maleness and aggression do not have to go together. A "culture of honor" underlies some high murder rates

Men, Honor and Murder

by Richard E. Nisbett and Dov Cohen

Homicide overwhelmingly involves males—as both perpetrators and victims. Evolutionary psychologists Martin Daly and Margo Wilson estimate that across a wide range of cultures a man is more than 20 times more likely to kill another man than a woman is to kill another woman, a finding they explain by arguing that men are more risk prone than women [see "Darwinism and the Roots of Machismo," on page 8]. Moreover, men are more likely to kill women than the other way around. When a woman does commit homicide, she usually kills a man who has repeatedly physically abused her.

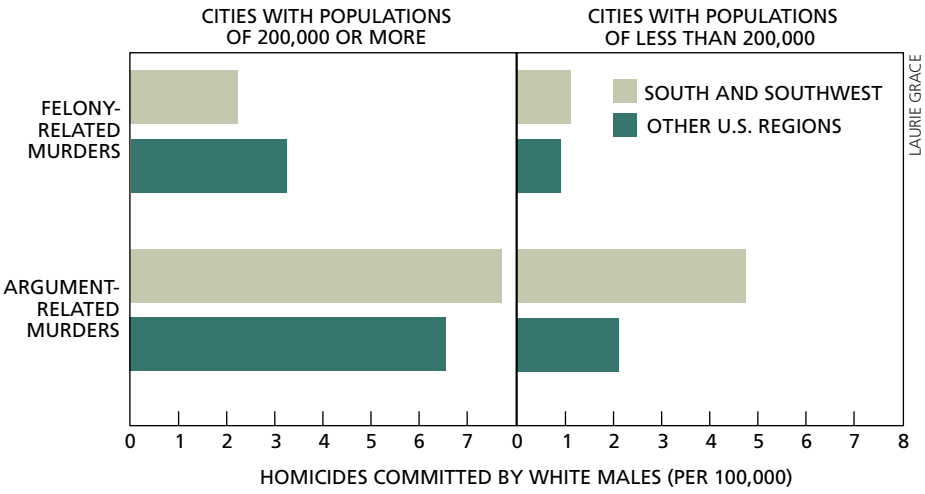
These facts, together with the observation that males are the more aggressive sex in nearly all mammals, have led many people to suppose that men are unavoidably aggressive and that homicide is a natural consequence of male biology. Yet the striking variation in homicide rates among different societies makes it clear that, whatever men's predispositions may be, cultures have a great influence on the likelihood that a man will kill. For example, Colombia's rate is 15 times

OUT OF MY WAY… *In a reenactment of a study of how southerners and northerners react to insults, an accomplice of the researchers* (man in foreground, far left and above) *rudely bumped into and swore at an unsuspecting participant passing him in a narrow corridor.*

I'M NOT BUDGING… *After the bump and insult, a bulky second accomplice of the experimenters* (foreground) *marched down the corridor, forcing unsuspecting passing subjects to step aside. A southerner who had previously been insulted waited until the last second to make way* (above). *A southerner who had not been insulted was far more gracious* (left). *Northerners showed no such difference.*

PHOTOGRAPHS BY WILL YURMAN *Gamma Liaison*

Rates of Homicide by White Males



***HIGHER RATES OF HOMICIDE** in the South and Southwest result from argument-related murders—not felony-related ones. The former are more common in those regions, especially in small cities and rural areas. Large cities in the South and Southwest have more argument-related but fewer felony-related murders than cities elsewhere.*

that of Costa Rica, and the U.S. rate is 10 times that of Norway. Marked regional differences exist even within the U.S. We and our colleague Andrew Reaves have established that in small U.S. cities in the South and the Southwest, the homicide rate for white males is about double that in the rest of the country. We also found that a white man living in a small county in the South is four times more likely to kill than one living in a small county in the Midwest. By making detailed regional comparisons, we have been able to rule out several explanations that have previously been offered to account for similar data, such as the history of slavery in the South, the higher temperatures there and the greater incidence of poverty.

Although there are surely many reasons for regional differences, we believe that one particular set of conditions reliably elicits high rates of homicide. It occurs when men face danger from the actions of other males and the state does not provide protection. Men respond by resorting to self-protection and demonstrating that they are strong enough to deter aggression.

This type of social system is known as a culture of honor. A man establishes his honor by tolerating no challenge or disrespect, responding to insults and threats to his property with threatened or actual violence. Such a code of behavior deters theft and wanton aggression, but it also requires that violence sometimes be employed: disputants cannot be too willing to back down, or honor will be compromised.

This type of culture dominates almost the entire Mediterranean basin and most of the New World countries influenced by Spanish culture. It is found among the Masai of East Africa, the horsemen of the central Asian steppes and the Native American horsemen of the plains. In the past, it also held sway in Ireland and Scotland, as well as in most of Scandinavia. We have found that it prevails in the U.S. South as well.

What characteristics do these disparate groups have in common? One we think is important is animal husbandry. It plays, or once played, a large role in their economies. Animals are easily stolen, so it is crucial for a man who owns livestock to establish that he is not someone to be challenged lightly. Ethnographer John K. Campbell illustrated the point when he described how critical the first quarrel is in the life of a young Greek shepherd: "Quarrels are necessarily public." To gain respect, a novice shepherd must challenge not only obvious insults but also subtly concocted slights. (The reader may recall people in high school who were gifted at constructing such insults: "You looking at my girlfriend?" "No." "What's a matter, she's not good-looking?")

The U.S. South was settled largely by herdsmen from Scotland and Ireland in the 17th and 18th centuries, when law enforcement was virtually nonexistent. Many of the settlers' descendants relied on keeping hogs and cattle, too. The northern U.S., in contrast, was colonized mainly by tillers of the soil from England, Germany and the Netherlands. Crop growers are at much less risk of having their capital assets stolen, and they must get along with their neighbors. The bluster of the herdsman would not serve them well. We think this is why homicide rates for white males are higher in the South than in the North. (All the statistics we discuss below make reference to white males.)

Many observers have assumed that the South is simply more brutal than the rest of the country. But its lead in the murder department is entirely the result of the number of homicides that, according to data from the Federal Bureau of Investigation, probably stemmed from insults, barroom brawls, lovers' triangles or neighbors' quarrels. Among cities that have a population of more than 200,000, those in the South and Southwest actually have fewer homicides that occur in the context of a felony such as a robbery or burglary than do those elsewhere. Sociologist John Shelton Reed of the University of North Carolina at Chapel Hill has commented that you are probably safer in the South than in the North if you avoid quarrels and stay out of other people's bedrooms.

Self-Defense in the South

Southerners favor violence in general no more than other Americans. They differ from northerners mainly over the use of force to protect home and property, to respond to insults and to socialize children. Our research shows, for example, that southerners are more likely to think it justifiable to kill to protect one's house. They are more likely to take offense at an insult and to think violence is an appropriate recourse. And they are much more inclined than northerners to say they would counsel their child to fight a bully rather than reason with him.

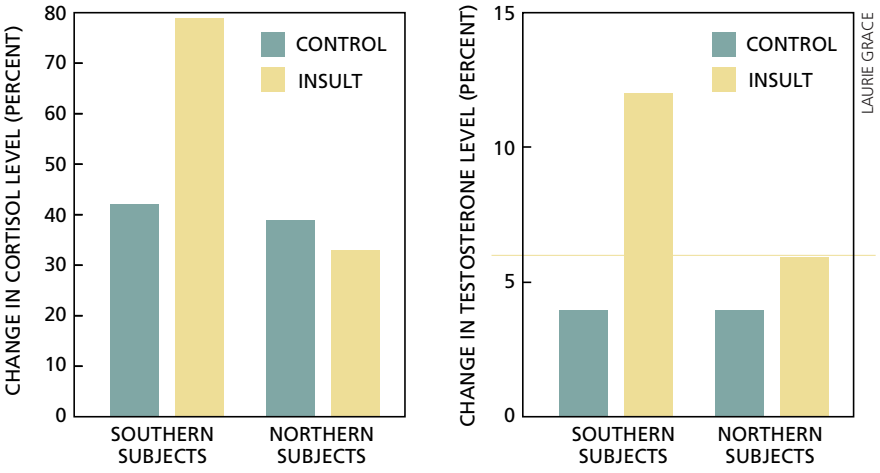
The differences go beyond attitudes. We conducted an experiment in which an accomplice insulted a college student by bumping him in a narrow hallway and swearing at him. (The students had agreed to participate in a study but were misled about its nature

and were given no clue that the corridor incident was staged.) Northerners tended to shrug off the episode. The angry faces of southerners revealed that they did not take it so lightly. Moreover, their cortisol and testosterone levels—but not those of northerners—surged after the insult, which suggests stress and preparedness for aggression.

For the clincher, we confronted some research subjects with another challenge immediately after the insult. As the subject was walking down the narrow hallway, a six-foot, three-inch, 250-pound accomplice of the experimenter walked toward him down the middle of the corridor. Southerners who had not been insulted stepped to one side when the bruiser was about nine feet away. But those who had been insulted walked to within three feet before they stood aside. Apparently the southerners who had just been offended were in no mood to be trifled with, even by someone else—a dangerous frame of mind when the new antagonist has a 100-pound weight advantage. In contrast, the northern students' decision on how close to approach before stepping aside was unaffected by whether they had been insulted.

We think we have some interesting evidence on what keeps the honor tradition alive. Southerners seem to think they will be regarded as unmanly if they do not respond to an insult, and compared with northerners they perceive more peer support for aggression.

Some of our research subjects knew that another person, whom they were just about to meet, had observed the bump-and-insult incident. After the meeting, we asked the subjects to assess what this observer thought of them. Southern participants, but not northern ones, reported that the observer probably thought they were weak because they had not responded forcefully enough. (They were most likely wrong in this. When shown videotapes of people responding to an insult, students from the South rated aggressive responders whom they watched to be just as unattractive as did northerners.)



HORMONE LEVELS surged in southerners who had been insulted in an experiment but changed much less in southerners in a control group who had not been insulted. Northerners in either group were relatively little affected.

In another version of our experiment, done with our colleague Joseph A. Vandello, the insult occurred in front of a group of people. Southerners judged this audience to be more encouraging of aggression than did northerners who watched the same interaction. Such a tendency to perceive support for aggression erroneously could be responsible for maintaining violence as an option.

Institutions in the South also reinforce the culture of honor. We sent retail outlets around the country a job-seeking letter purporting to be from a young man who had killed someone who had been sleeping with his fiancée. Responders from the South were more sympathetic than northerners were. In addition, we sent college newspaper editors around the country a police blotter–style account of a crime of passion that involved an insult. We asked the editors to write up the story for their paper for a fee. Northern accounts strongly condemned the insulted perpetrator; southern accounts were much more sympathetic. A version of the story that contained no insult elicited no comparable differences.

Furthermore, laws and social policies in the South reflect the culture of honor. Southern laws are more likely to exonerate people who shoot someone escaping with their property. And many statutes in the South endorse a "true man" rule, which allows someone to stand his ground and kill rather than forcing him to beat a cowardly retreat from an attacker.

The South's culture of honor will surely change. It has already come a long way since the era when a man would ask a prospective son-in-law if he had ever done any "sparkin'"—putting his life on the line in combat. (If the answer was no, the suit was over.) Economic and social changes, together with immigration from other regions, will eventually erode what remains of the tradition.

In the meantime, the contrast between North and South shows that violence by men is a matter of nurture as much as one of nature. Male aggression is not inevitable. Whether a man reaches for his gun or his civility when insulted is a matter of culture. SA

The Authors

RICHARD E. NISBETT and DOV COHEN study the relation between culture and thought processes. Nisbett is co-director of the Culture and Cognition Program at the University of Michigan. Most of his research focuses on differences in reasoning resulting from education and culture. He hails from Texas, and while doing the work reported here, he discovered that you can take the boy out of the South but not the South out of the boy. Cohen is assistant professor of psychology at the University of Illinois. He studies how culture affects people, and vice versa. Cohen abhors violence in all forms except heavy-metal rock music.

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The Y chromosome causes an embryo

The Key to Masculinity

ORIGINS OF MALENESS lie on the Y chromosome, shown in the inset with the much larger X chromosome. Males normally have one Y and one X chromosome, whereas females normally have two Xs. The dyed spots at the tops of the chromosomes mark the pseudoautosomal regions.

to become male by directing the development of the testes. But new research indicates that the Y does much more

by Bruce T. Lahn and Karin Jegalian

What a difference a Y can make. In humans, the tiny Y chromosome—one of the smallest of the 46 chromosomes that carry all our genes—essentially dictates a person's sex. Genes on the Y chromosome trigger the development of male features—everything from the formation of the testes and the ability to produce sperm to the emergence of secondary sexual characteristics, such as facial hair and a deep voice. Without a Y chromosome and its resident male-forming genes, an embryo will develop as a female. Thus, at the most fundamental level, the problem of understanding the biological differences between the sexes can be reduced to a problem of understanding the Y chromosome and how it encodes maleness.

Under a microscope, the Y chromosome appears as a small rod about one third the size of the X—the other sex chromosome, present in both males and females. (Males, who normally have one X and one Y chromosome, are designated XY; females normally have two Xs, hence the XX designation.) Although it has been known for decades that it takes a Y to make a male, until about 10 years ago scientists believed that the human Y chromosome contained few genes aside from those that determined maleness. This view stemmed, at least in part, from the relative abundance of "junk" DNA—repetitive DNA sequences that do not encode any proteins—on the Y chromosome.

But on closer examination, using powerful molecular techniques, we and other investigators have since discovered that the Y chromosome is not quite as genetically barren as previously thought. At last count, researchers have identified 21 genes on the human Y chromosome, a figure that is probably more than half the true total. These genes fall into three distinct groups based on the roles they play in the body. The first group contains a single gene that, on its own, steers an embryo into developing as a male by directing the formation of the testes. The second group consists of 10 genes, active only in the testes of adult males, that may be involved in sperm production. The remaining 10 genes perform mostly "housekeeping" functions that keep cells throughout the body running smoothly. These genes are closely related to genes found on the X chromosome. The presence of these "X-homologous" genes reinforces the theory that the X and Y chromosomes evolved from a common X-like ancestor before the Y acquired its male-specific genes and adopted its role in sex determination.

For much of human history, the riddle of what makes a baby a boy or a girl has been debated in nursery rhymes and folklore. Various legends attributed sex determination to the phases of the moon and the time of day when conception occurred. Scientists turned their attention to this question only about 100 years ago, when genetics emerged as a discipline.

At about that time, biologists first saw the sex chromosomes inside cells. Microscopic examination of cells had established that the chromosomes in most multicellular organisms exist in pairs and that the two partners line up side by side during meiosis—the type of cell division that occurs during the formation of eggs or sperm. But while studying insect cells, researchers noticed that in males, one chromosome did not seem to pair with any partner. In 1891 German biologist Hermann Henking labeled this anomalous structure "X," and a decade later American scientists identified the structure as a sex chromosome. A few years later Nettie M. Stevens of Bryn Mawr College and others, again studying cells from male insects, spotted a very small chromosome that appeared to be the X chromosome's missing partner. The mismatched chromosome pair subsequently became known as X and Y.

The Master Switch

That the Y chromosome on its own has the power to trigger male development in humans became clear in the late 1950s. In one study researchers discovered that individuals who possess three sex chromosomes—two Xs and one Y (XXY)—always develop as males. Conversely, individuals with only one X chromosome and no Y chromosome—designated as XO individuals—develop as females. These cases of unusual sex chromosome compositions demonstrate that in humans the presence of the Y leads to male development and its absence leads to female development.

These observations implied that the Y chromosome bears one or more male-determining genes that somehow set in motion the cascade of developmental events that makes a male. Discovery of the male-determining gene, however, did not happen until the 1980s, when researchers started to study sex-reversed individuals.

Sex reversal occurs when a person's morphological sex—the sex he or she appears to be—is the opposite of what his or her chromosomes seem to predict: in other words, an XY female or an XX male. Researchers estimate that about one in every 20,000 individuals is sex-reversed. Many such individuals grow up unaware of their condition; very often the first time they learn of it is when they go to a clinic with fertility problems (the sex reversal makes them unable to conceive). Using molecular analyses, two groups of researchers—one led by David C. Page of the Whitehead Institute for Biomedical Research and the other by Peter Goodfellow of the Imperial Cancer Research Fund—found that the sex chromosomes in many sex-reversed individuals have in fact undergone genetic rearrangements that are not detectable under a microscope. In many XX males, one of the X chromosomes

HORNICK/RIVLIN STUDIO (*photograph*); DEPARTMENT OF CLINICAL CYTOGENICS, ADDENBROOKS HOSPITAL/SPL/PHOTO RESEARCHERS, INC. (*inset*)

carries a small piece of the Y abnormally stitched onto it. Similarly, in many XY females, the Y chromosome is missing a small fragment. The male-determining gene or genes, the researchers reasoned, must therefore lie within that small region.

The search ended in 1990, when Goodfellow and his colleagues identified the *sex-determining region Y,* or *SRY.* This gene appears to be the master switch controlling male development in all mammals, including humans. Investigators led by Robin Lovell-Badge of the Medical Research Council's National Institute for Medical Research in London subsequently showed that injection of this single gene into fertilized mouse eggs is enough to turn a genetic female—an XX individual—into a male.

SRY encodes a protein that binds to DNA, suggesting that it exerts its effect on male development by regulating the activity of a number of genes. Those genes then somehow spur the embryonic bipotential gonad—the primitive tissue from which both male and female sex organs derive—to develop into testes rather than ovaries. The testes, once formed, in turn induce all other male features. In humans the two hormones secreted by the testes, testosterone and anti-Müllerian duct hormone, prompt the development of virtually all other male sex-specific characteristics, including the external genitalia, facial hair, deep voice and male skeletal structure.

Although researchers have had *SRY* in hand for nearly a decade, no one has yet identified any genes that are directly controlled by the master switch. In part, the fact that *SRY* acts only transiently in a highly complex system during early embryonic development has made it difficult to determine exactly how this gene functions to make a male.

Making Sperm

Given *SRY*'s pivotal role in dictating male development, it is tempting to think of the gene as being functionally interchangeable with the entire Y chromosome. But the situation is not that simple. Another critical aspect of maleness, the production of sperm, requires the participation of other genes on the Y chromosome.

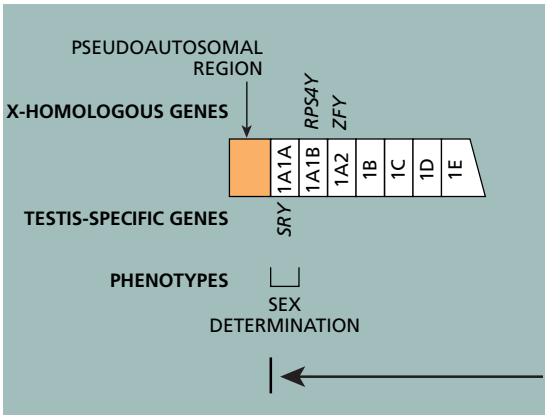
In 1976 clinicians Luciano Tiepolo and Orsetta Zuffardi of the University of Pavia in Italy first noticed that some infertile men who had no detectable sperm in their ejaculate—a condition called azoospermia—also had abnormally short Y chromosomes. The researchers reasoned that the part of the Y chromosome deleted in these patients harbored a gene or genes essential for making sperm. But these patients developed as males because their shortened Y chromosomes carried the *SRY* gene.

More recently, using molecular techniques for revealing much smaller deletions, our laboratory group and others have shown that at least three regions of the Y chromosome harbor genes essential for sperm production. Deletion of any one of these three regions—called azoospermia factors a, b and c—can lead to infertility caused by defective sperm production. One of the regions, azoospermia factor c, is deleted in one of every 5,000 to 10,000 newborn males; the other two regions are deleted much less frequently. To understand how the deletions in the Y chromosome block sperm development, the genes in the deleted regions have to be identified. Several laboratories, including our own, are trying to understand the precise functions of these genes in sperm development and how infertility may result from their deletion.

Because infertile men cannot father children, the deletions in the Y chromosome represent new mutations rather than inherited traits. But this may not always be the case, thanks to rapid advances in assisted-reproduction techniques. A small amount of normal sperm can be found in the testes of some infertile men with Y chromosome deletions. Using a procedure called intracytoplasmic sperm injection (ICSI), doctors can retrieve these isolated sperm cells and inject them directly into eggs to achieve fertilization. Although ICSI may offer these otherwise infertile men the only hope of having biologically related children, their sons will unfortunately carry the same abnormal Y chromosome and will in all likelihood be naturally infertile. In time, society may need to grapple with the long-term effects of such reproductive intervention [see "Of Babies and the Barren Man," on page 74].

The Y chromosome's contribution to biology is not limited to processes that are specific to males. This small chromosome also harbors genes that contribute to fundamental processes in each and every cell, processes that are common to the two sexes.

The existence of such general-function genes on the human Y chromosome was first postulated in 1965 by Scottish biologist Malcolm A. Ferguson-Smith, then at the University of Glasgow. Ferguson-Smith was studying Turner syndrome, a congenital disorder in which an individual possesses only one sex chromosome, the X. Such XO females are characterized by many anatomical abnormalities, including short stature, a webbed neck and a failure to develop secondary sexual characteristics, such as breasts and pubic hair. Although Turner syndrome occurs in approximately one in every 3,000 live births, an estimated 99 percent of XO embryos abort spontaneously. Ferguson-Smith proposed that the abnormalities seen in Turner syndrome were caused by insufficient levels of proteins that are produced by some specific "Turner genes" present on the missing sex chromosome.



Where X = Y

What does Turner syndrome tell us about the Y chromosome? First, let us review a bit of basic biology. In female mammals, one of the two X chromosomes in each cell is shut down so that its thousands of genes no longer direct the production of proteins. The rationale for this scheme—known as X inactivation—is simple. Females have two X chromosomes, whereas males have only one. And because the amount of protein produced from a gene is typically proportional to the number of copies of that gene in the cell, without X inactivation females would have twice as many X-encoded proteins as males. This could spell disaster for a complex organism that depends on tightly balanced levels of gene activity.

X inactivation thus allows the two sexes to achieve comparable amounts of activity from X genes.

Getting back to Turner syndrome: If the second X chromosome in females is shut down, why should an XO woman differ from an XX woman? As Ferguson-Smith hypothesized, and others later confirmed, X inactivation in females is not complete. A small subset of genes on the X chromosome always escapes inactivation and directs protein production from both chromosomal copies. So XO individuals wind up with half the normal amounts of these important proteins.

But males also have only one X, and yet they manage to evade the characteristics of Turner syndrome. Again, Ferguson-Smith hypothesized, and others later confirmed, that the genes that escape X inactivation have close counterparts, or homologues, on the Y chromosome. These genes are involved in processes fundamental to all cells, such as the production of essential proteins. In most cases, the homologues on the X and Y chromosomes encode proteins that are about 90 percent identical in their amino acid sequences. Although these homologous genes are considered possible "Turner genes," none of them has yet been definitively linked to a specific aspect of Turner syndrome.

It was not always the case that the presence of a Y chromosome dictated the sex of an organism. In many reptiles—crocodiles, alligators, and some turtles and lizards, for example—the sex of the embryo is determined by the ambient temperature. So how did the sex chromosomes arise?

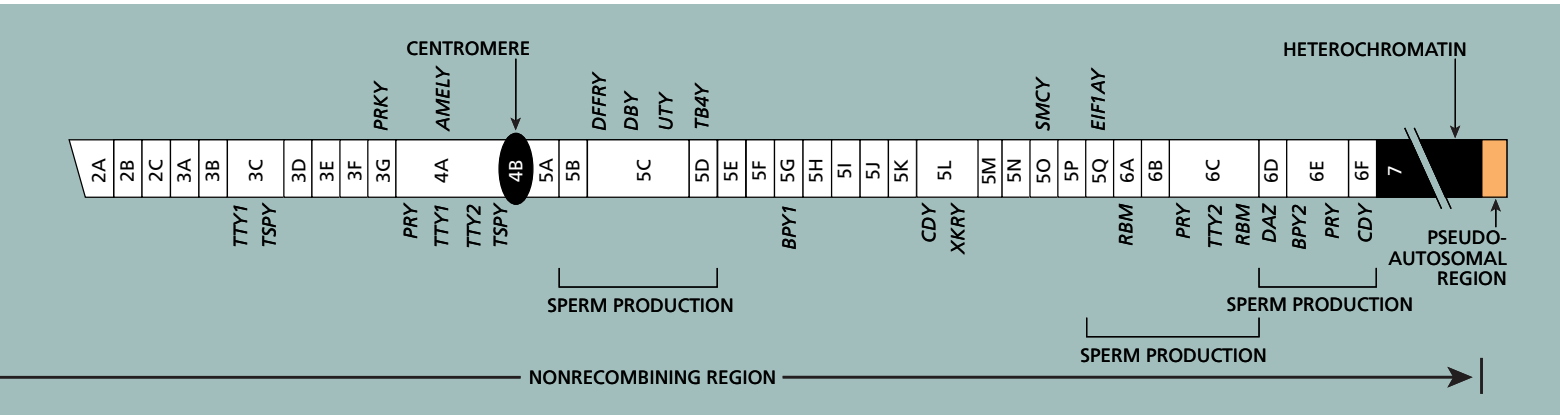
Where Did Y Come From?

Because the X and Y chromosomes share homologous genes, they are thought to have evolved from a pair of identical chromosomes. When mutations or genetic rearrangements gave rise to the male-determining *SRY* gene—or a factor that served a similar function—the Y chromosome was born. Its *SRY*-deficient partner became the X. The X and Y chromosomes most likely arose 200 to 300 million years ago, after mammals and the reptiles that lack sex chromosomes diverged.

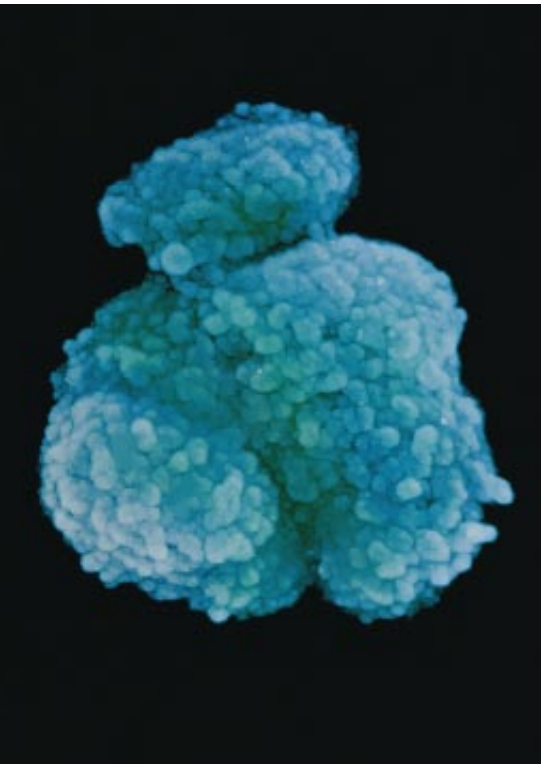
At first, the X and Y were basically identical except in the sex-determining region. But at some point the two chromosomes began to diverge. Evolutionary biologists believe that the X and Y went their separate ways when the two for some reason became unable to recombine—the process by which chromosome pairs line up and swap bits of DNA. Because recombination is essential for maintaining the integrity of DNA, the Y chromosome began to lose its genes. Genes on the X were maintained because X chromosomes could continue to recombine with one another in females. As genes on the Y degenerated, X inactivation emerged as a way of equalizing the dosage of X-linked genes—which lost their counterparts on the Y—between males and females. The X-homologous genes present on the Y today survived, most likely because they participate in the most basic cellular processes.

Less is known about the origin of the Y-specific genes, including those that may be involved in sperm production. Most of these genes have no homologues on the X chromosome. According to studies conducted in our laboratory, it appears that two of these Y-specific genes emerged on the Y chromosome much more recently, only 30 to 50 million years ago. In mammals that diverged from our primate ancestors before that time, the genes resided on other chromosomes, not on the X or the Y. These genes were then copied onto the Y chromosome in a creature that gave rise to humans and some of our primate relatives.

Why should these genes have sought to relocate on the Y chromosome? We think that these moves are not flukes. More likely, they represent a consistent trend in the evolution of the Y chromosome. There may be an advantage to storing genes that function only in males in the male-specific part of the genome. The possible advantage was first explored in 1931 by British geneticist Ronald A. Fisher. He suggested that if some genes benefit males but are inconsequential or even harmful to females, selective pressure might favor their sequestration in chromosomal regions present only in males, namely, the Y chromosome. The accumulation on the human Y of genes that function



GENE MAP of the human Y chromosome shows a large region that does not recombine during meiosis and the two small pseudoautosomal regions that recombine with portions of the X chromosome. The nonrecombining region is divided into 43 intervals defined by naturally occurring deletions. Researchers have identified genes in 17 intervals. The X-homologous genes, which have counterparts on the X chromosome, are shown above the map; the testis-specific genes, which are active only in the testes of males, are shown below. The phenotypes at the bottom of the map show the regions of the Y chromosome where deletions would cause sex reversal or defective sperm production.



***Y CHROMOSOME** is a bundle of tightly packed DNA, shown magnified 9,000 times in this scanning electron microscope image* **(left)**. *The chromosome's* **SRY** *gene encodes a protein that causes an embryo's gonads to develop into testes rather than ovaries. This sexual differentiation begins when the embryo is about six weeks old* **(right)**. *The embryo's testes then secrete testosterone and anti-Müllerian duct hormone, which in the following weeks stimulate the development of other male characteristics, such as the penis and scrotum* **(opposite page)**. *Without the* **SRY** *gene, the embryo would develop as a female.*

in sperm development may represent such an occurrence. Consistent with this notion, other species ranging from mice to fruit flies have also been shown to carry genes needed for male fertility on their Y chromosomes.

Such a setup could arguably benefit the species as a whole. But not everyone believes that the sex chromosomes always act in the best interest of the species. According to Lawrence Hurst of the University of Cambridge, sometimes a sex chromosome can harbor "selfish" genes that may enhance its probability of being transmitted to the next generation. A chromosome with such a selfish gene would then be passed along more than its fair share—that is, strictly half the time. Imagine, for example, that the X chromosome in an XY male acquires a selfish gene—say, one that encodes a toxin that selectively kills Y-bearing sperm. Most of this male's progeny will be female, as his X will be transmitted more often than his Y.

As this selfish X spreads, though, the sex balance of the population will be thrown off-kilter—a situation that can be harmful to the species as a whole. And the Y chromosome will be getting shortchanged. So to counter the effects of the selfish X, the Y would then evolve genes that can suppress the activity of the toxin—an antidote of some kind—as well as genes that will promote its own transmission. The result: a genetic arms race in which the X and Y try to outdo each other in their ability to gain entrance to the next generation.

In the long run, the X and Y might still be transmitted at a 1 to 1 ratio, more or less, but the underlying mechanism would be one of genetic hostility rather than cooperation. The idea might not be that far-fetched. Such genetic antagonism is believed to occur in certain species of flies. In a particularly interesting study, researchers led by Gerald Wilkinson of the University of Maryland found that in stalk-eyed flies with a selfish X, the X chromosome was passed along about twice as often as the Y, resulting in more female than male offspring. In humans, slightly more boys are born than girls. Could this bias be the result of a slight imbalance in the war between the X and Y chromosomes? Although the theory is controversial and there is no solid evi-

dence for the existence of selfish genes on human sex chromosomes, the possibility remains intriguing.

Multipurpose Y

For scientists, the Y chromosome is good for more than just making males. It can be used as a marker for tracking human evolution, for example. Because the Y chromosome, unlike all the other human chromosomes, does not undergo recombination with a partner during meiosis, it is passed on nearly unchanged from father to son. Along the way, the Y chromosome may accumulate mutations, but these are also passed down along the paternal line. By grouping different human populations based on the relatedness of their Y chromosomes, evolutionary biologists have been able to trace human lineages. The Y chromosome has thus helped biologists construct an evolutionary tree that shows how humans originated and diverged from a single source. According to this now famous tree, our ancestors arose in Africa between 200,000 and 100,000 years ago and subsequently migrated and dispersed into Europe, Asia and the Americas. Several teams of researchers have also noted how similar the Y chromosome is in men from different ethnic groups. They have argued, based on this consistency, that human populations have dispersed more recently than we might previously have supposed.

The Y has also been used to help unravel human genealogies. It was a study of Y chromosomes that led researchers to conclude that Thomas Jefferson, the third president of the U.S., could have fathered the child of one of his slaves. So despite its small size and its relatively limited complement of genes, the Y chromosome has made—and continues to make—unique and far-reaching contributions to human biology. SA

BIOPHOTO ASSOCIATES/PHOTO RESEARCHERS, INC. (*chromosome*); NEIL HARDING *Tony Stone Images (embryo)*; OWEN FRANKEN *Corbis (infant)*

The Authors

BRUCE T. LAHN and KARIN JEGALIAN did their doctoral work in the laboratory of renowned geneticist David C. Page at the Whitehead Institute for Biomedical Research and the Massachusetts Institute of Technology. Both researchers earned their doctorates in biology in 1998—Lahn for identifying and classifying genes on the human Y chromosome and Jegalian for studying the evolution of X and Y. Now, as a postdoc, Lahn analyzes the Y-based fertility genes to determine their precise function. Jegalian went on to complete the science writing program at the University of California, Santa Cruz, and is now a freelance science writer in Cambridge, Mass.

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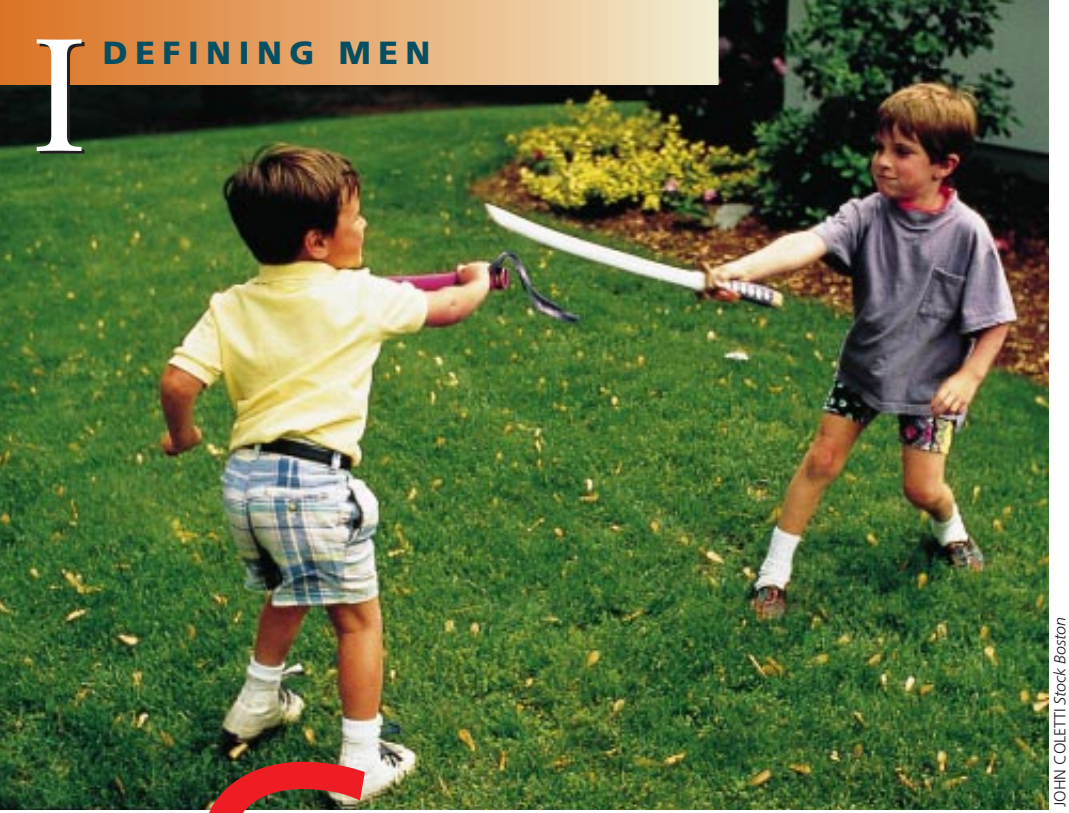


JOHN COLETTI Stock Boston

by Doreen Kimura

Sex Differences in the Brain

Men and women display patterns of behavioral and cognitive differences that reflect varying hormonal influences on brain development

SPENCER GRANT Stock Boston

DIVERGING PLAY STYLES *of boys and girls—boys' preference for mock fighting over playing house—may be dictated by hormonal differences.*

Men and women differ not only in their physical attributes and reproductive function but also in many other characteristics, including the way they solve intellectual problems. For the past few decades, it has been ideologically fashionable to insist that these behavioral differences are minimal and are the consequence of variations in experience during development before and after adolescence. Evidence accumulated more recently, however, suggests that the effects of sex hormones on brain organization occur so early in life that from the start the environment is acting on differently wired brains in boys and girls. Such effects make evaluating the role of experience, independent of physiological predisposition, a difficult if not dubious task. The biological bases of sex differences in brain and behavior have become much better known through increasing numbers of behavioral, neurological and endocrinological studies.

We know, for instance, from observations of both humans and nonhumans that males are more aggressive than females, that young males engage in more rough-and-tumble play than females and that females are more nurturing. We also know that in general males are better at a variety of spatial or navigational tasks. How do these and other sex differences come about? Much of our information and many of our ideas about how sexual differentiation takes place derive from research on animals. From such investigations, it appears that perhaps the most important factor in the differentiation of males and females is the level of exposure to various sex hormones early in life.

In most mammals, including humans, the developing organism has the potential to be male or female. Producing a male, however, is a complex process. When a Y chromosome is present, testes, or male gonads, form. This development is the critical first step toward becoming a male. When no Y chromosome is present, ovaries form [see "The Key to Masculinity," on page 20].

Testes produce male hormones, or androgens (testosterone chief among them), which are responsible not only for transformation of the genitals into male organs but also for organization of corresponding male behaviors early in life. As with genital formation, the intrinsic tendency that occurs in the absence of masculinizing hormonal influence, according to seminal studies by Robert W. Goy of the University of Wisconsin, is to develop female genital structures and behavior. Female anatomy and probably most behavior associated with females are thus the default modes in the absence of androgens.

If a rodent with functional male genitals is deprived of androgens immediately after birth (either by castration or by the administration of a compound that blocks androgens), male sexual behavior, such as mounting, will be reduced, and more female sexual behavior, such as lordosis (arching of the back when receptive to coitus), will be expressed. Similarly, if androgens are administered to a female directly after birth, she will display more male sexual behavior and less female behavior in adulthood. These lifelong effects of early exposure to sex hormones are characterized as "organizational" because they appear to alter brain function permanently during a critical period in prenatal or early postnatal development. Administering the same sex hormones at later stages or in the adult has no such effect.

Not all the behaviors that categorize males are organized at the same time, however. Organization by androgens of the male-typical behaviors of mounting and of rough-and-tumble play, for example, occur at different times prenatally in rhesus monkeys.

The area in the brain that regulates female and male reproductive behavior is the hypothalamus. This tiny structure at the base of the brain connects to the pituitary, the master endocrine gland. It has been shown that a region of the hypothalamus is visibly larger in male rats than in females and that this size difference is under hormonal control. Scientists have also found parallel sex differences in a clump of nerve cells in the human brain—parts of the interstitial nucleus of the anterior hypothalamus—that is larger in men than in women. Even sexual orientation and gender identity have been related to anatomical variation in the hypothalamus. In 1991, while at the Salk Institute for Biological Studies in San Diego, Simon Levay reported that one of the interstitial nuclei of the anterior hypothalamus that is usually larger in human males than in females is smaller in homosexual than in heterosexual men. Other researchers, Jiang-Ning Zhou of the Netherlands Institute of Brain Research and his colleagues there and at Free University in Amsterdam, observed another part of the hypothalamus to be smaller in male-to-female transsexuals than in a male control group. These findings are consistent with suggestions that sexual orientation and gender identity have a significant biological component.

Hormones and Intellect

What of differences in intellectual function between men and women? Major sex differences in function seem to lie in patterns of ability rather than in overall level of intelligence (measured as IQ), although some researchers, such as Richard Lynn of the University of Ulster in Northern Ireland, have argued that there exists a small IQ difference favoring human males. Differences in intellectual pattern refer to the fact that people have different intellectual strengths. For example, some people are especially good at using words, whereas others are better at dealing with external stimuli, such as identifying an object in a different orientation. Individuals may have the same overall intelligence but differing abilities.

Sex differences in problem solving have been systematically studied in adults in laboratory situations. On average, men perform better than women at certain spatial tasks. In particular, men seem to have an advantage in tests that require the subject to imagine rotating an object or manipulating it in some other way. They also outperform women in mathematical reasoning tests and in navigating their way through a route. Further, men exhibit more accuracy in tests of target-directed motor skills—that is, in guiding or intercepting projectiles.

Women, on average, excel on tests that measure recall of words and on tests that challenge the person to find words that begin with a specific letter or fulfill some other constraint. They also tend to be better than men at rapidly identifying matching items and performing certain precision manual tasks, such as placing pegs in designated holes on a board.

In examining the nature of sex differences in navigating routes, one study found that men completed a computer simulation of a maze or labyrinth task more quickly and with fewer errors than women did. Another study by different researchers used a path on a tabletop map to measure route learning. Their

results showed that although men learned the route in fewer trials and with fewer errors, women remembered more of the landmarks, such as pictures of different types of buildings, than men did. These results and others suggest that women tend to use landmarks as a strategy to orient themselves in everyday life more than men do.

Other findings seemed also to point to female superiority in landmark memory. Researchers tested the ability of individuals to recall objects and their locations within a confined space—such as in a room or on a tabletop. In these studies, women were better able to remember whether items had changed places or not. Other investigators found that women were superior at a memory task where they had to remember the locations of pictures on cards that were turned over in pairs. At this kind of object location, in contrast to other spatial tasks, women appeared to have the advantage.

It is important to keep in mind that some of the average sex differences in cognition vary from slight to quite large and that men and women overlap enormously on many cognitive tests that show average differences. For example, whereas women perform better than men in both verbal memory (recalling words from lists or paragraphs) and verbal fluency (finding words that begin with a specific letter), there was a large difference in memory ability but only a small disparity for the fluency tasks. On the whole, variation between men and women tends to be smaller than deviations within each sex, but very large differences between the groups do exist—in men's high level of visual-spatial targeting ability, for one.

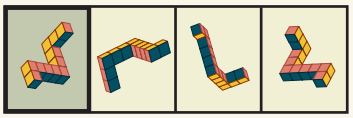
Although it used to be thought that sex differences in problem solving did not appear until puberty, the accumulated evidence now suggests that some cognitive and skill differences are present much earlier. For example, researchers have found that three- and four-year-old boys were better at targeting and mentally rotating figures within a clock face than girls of the same age were. Prepubescent girls, however, excelled at recalling lists of words.

Male and female rodents have also been found to solve problems differently. Christina L. Williams of Duke University has shown that female rats have a greater tendency to use landmarks in spatial learning tasks, as it appears women do. In Williams's experiment, female rats used landmark cues, such as pictures on the wall, in preference to geometric cues: angles and the shape of the room, for instance. If no landmarks were available, however, females used the geometric cues. In contrast, males did not use landmarks at all, preferring geometric cues almost exclusively.

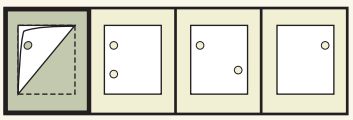
Williams also found that hormonal manipulation during the critical period could alter these behaviors. Depriving newborn males of sex hormones by castrating them or administering hormones to newborn females resulted in

Problem-Solving Tasks Favoring Men

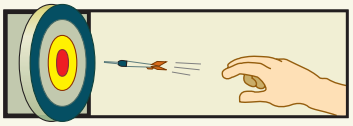
Men tend to perform better than women on certain spatial tasks. They do well on tests that involve mentally rotating an object or manipulating it in some fashion, such as imagining turning this three-dimensional object



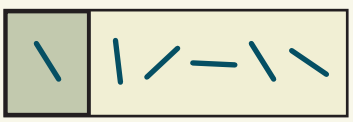
or determining where the holes punched in a folded piece of paper will fall when the paper is unfolded:



Men also are more accurate than women at target-directed motor skills, such as guiding or intercepting projectiles:



They do better at matching lines with identical slopes:



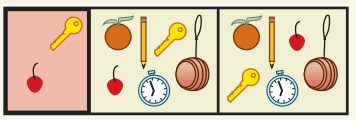
And men tend to do better than women on tests of mathematical reasoning:

1,100	If only 60 percent of seedlings will survive, how many must be planted to obtain 660 trees?

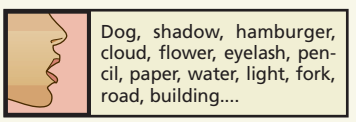
Problem-Solving Tasks Favoring Women

Women tend to perform better than men on tests of perceptual speed in which subjects must rapidly identify matching items—for example, pairing the house on the far left with its twin:

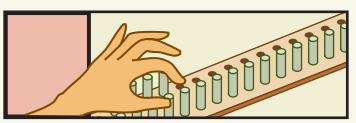
In addition, women remember whether an object, or a series of objects, has been displaced:



When read a story, paragraph or a list of unrelated words, women demonstrate better recall:



Women do better on precision manual tasks—that is, those involving fine-motor coordination—such as placing the pegs in holes on a board:

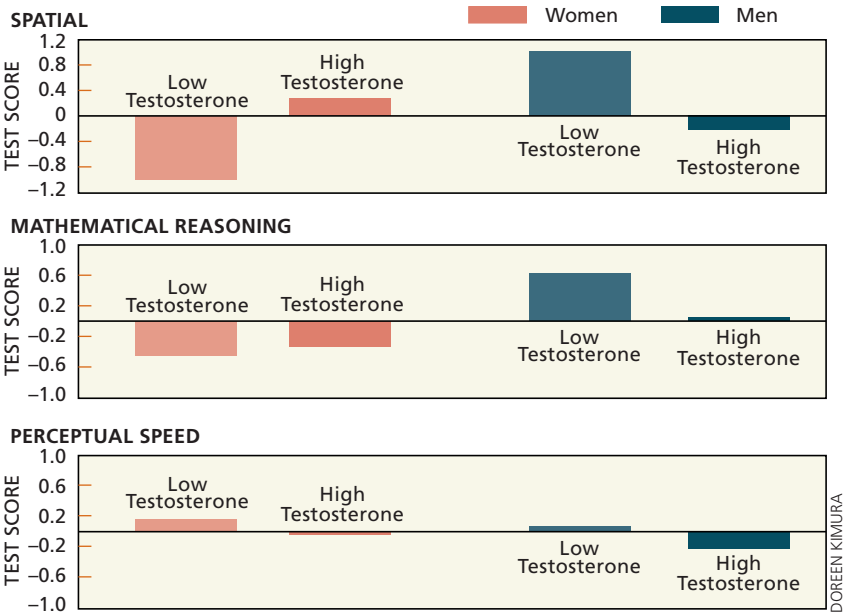


And women do better than men on mathematical calculation tests:

77	$14 \times 3 - 17 + 52$
43	$2\,(15 + 3) + 12 - \frac{15}{3}$

DOREEN KIMURA AND JOHN MENGEL

***TESTOSTERONE LEVELS** can affect performance on some tests* [see boxes on opposite page for examples of tests]. *Women with high levels of testosterone perform better on spatial tasks* (top) *than women with low levels do, but men with low levels outperform men with high levels. On a mathematical reasoning test* (middle), *low testosterone corresponds to better performance in men; in women there is no such relation. On a test of perceptual speed in which women usually excel* (bottom), *no relation is found between testosterone and performance.*



a complete reversal of sex-typed behaviors in the adult animals. Treated males behaved like females and treated females like males.

Structural differences may parallel behavioral ones. Lucia F. Jacobs, then at the University of Pittsburgh, discovered that the hippocampus—a region thought to be involved in spatial learning in both birds and mammals—is larger in several male species of rodents than in females. At present, there are insufficient data on possible sex differences in hippocampal size in human subjects.

One of the most compelling areas of evidence for hormonally influenced sex differences in humans comes from studies of girls exposed to excess androgens in the prenatal or neonatal stage. The production of abnormally large quantities of adrenal androgens can occur because of a genetic defect in a condition called congenital adrenal hyperplasia (CAH). Before the 1970s a similar condition also unexpectedly appeared in the offspring of pregnant women who took various synthetic steroids. Although the consequent masculinization of the genitals can be corrected by surgery and drug therapy can stop the overproduction of androgens, the effects of prenatal exposure on the brain cannot be reversed.

Sheri A. Berenbaum of Southern Illinois University at Carbondale and Melissa Hines of the University of California at Los Angeles observed the play behavior of CAH girls and compared it with that of their male and female siblings. Given a choice of transportation and construction toys, dolls and kitchen supplies, or books and board games, the CAH girls preferred the more typically masculine toys—for example, they played with cars for the same amount of time that boys did. Both the CAH girls and the boys differed from unaffected girls in their patterns of choice. Berenbaum also found that CAH girls had greater interest in male-typical activities and careers. Because there is every reason to think parents would be at least as likely to encourage feminine preferences in their CAH daughters as in their unaffected daughters, these findings suggest that these preferences were actually altered in some way by the early hormonal environment.

Other researchers also found that spatial abilities that are typically better in males are enhanced in CAH girls. But the reverse was reported in one study of CAH-affected boys—they performed worse than unaffected boys on the spatial tests males usually excel at.

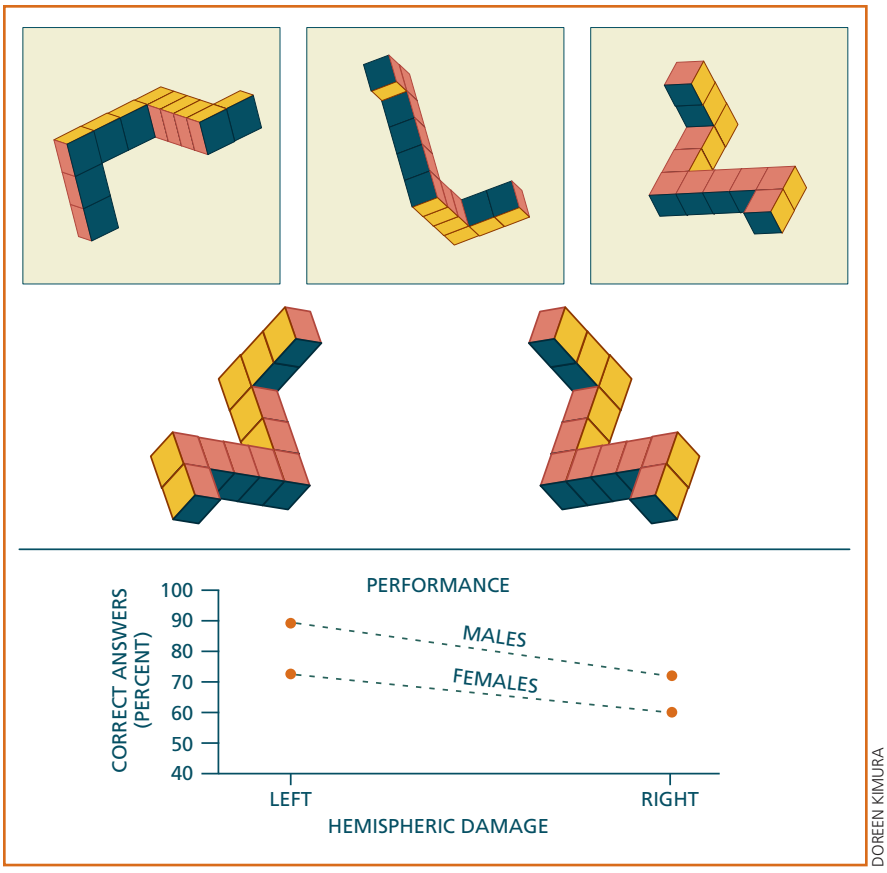
Such studies suggest that although levels of androgen relate to spatial ability, it is not simply the case that the higher the levels, the better the spatial scores. Rather studies point to some optimal level of androgen (in the low male range) for maximal spatial ability. This finding may also be true with men and mathematical reasoning; low-androgen men tested higher. There was no obvious correlation between hormone levels and women's math scores, however.

These findings are relevant to the suggestion by Camilla P. Benbow of Iowa State University that high mathematical ability has a significant biological determinant. Benbow and her colleagues have reported consistent sex differences in mathematical reasoning ability that favor males. In mathematically talented youth, the differences were especially sharp at the upper end of the distribution, where males outnumbered females 13 to one. Benbow argues that these differences are not readily explained by socialization.

It is important to keep in mind that the relation between natural hormone levels and problem solving is based on correlational data. Although some form of connection between the two measures exists, we do not necessarily know how the association is determined nor what its causal basis is. We also know little at present about the relation between adult levels of hormones and those in early life, when abilities appear to become organized in the nervous system.

Hormonal Highs and Lows

One of the most intriguing findings in adults is that cognitive patterns may remain sensitive to hormonal fluctuations throughout life. Elizabeth Hampson of the University of Western Ontario showed that women's performances at certain tasks changed throughout the menstrual cycle as levels of estrogen varied. High levels of the hormone were associated not only with relatively depressed spatial ability but also with enhanced speech and manual skill tasks. In addition, I have observed seasonal fluctuations in spatial ability in men: their performance improves in the spring, when testosterone levels are lower. Whether these hormonally linked fluctuations in intellectual ability represent useful evolutionary adaptations or merely highs and lows of an average test level remains to be seen



DOREEN KIMURA

RIGHT HEMISPHERIC DAMAGE affects spatial ability to the same degree in both sexes* (graph at bottom), *suggesting that women and men rely equally on that hemisphere for certain spatial tasks. In one test of spatial-rotation performance, photographs of a three-dimensional object must be matched to one of two mirror images of the same object.

through further research endeavors.

A long history of studying people with damage to one half of their brain indicates that in most people the left hemisphere of the brain is critical for speech and the right for certain perceptual and spatial functions. Researchers studying sex differences have widely assumed that the right and left hemispheres of the brain are more asymmetrically organized for speech and spatial functions in men than in women.

This belief rests on several lines of research. Parts of the corpus callosum, a major neural system connecting the two hemispheres, as well as another connector, the anterior commissure, appear to be larger in women, which may permit better communication between hemispheres. Perceptual techniques that measure brain asymmetry in normal-functioning people sometimes show smaller asymmetries in women than in men, and damage to one brain hemisphere sometimes has a lesser effect in women than the comparable injury in men does. My own data on patients with damage to one hemisphere of the brain suggest that for functions such as basic speech and spatial ability, there are no major sex differences in hemispheric asymmetry, although there may be such disparities in certain more abstract abilities, such as defining words.

If the known overall differences between men and women in spatial ability were related to differing dependence on the right brain hemisphere for such functions, then damage to that hemisphere might be expected to have a more devastating effect on spatial performance in men. My laboratory has studied the ability of patients with damage to one hemisphere of the brain to visualize the rotation of certain objects. As expected, for both sexes, those with damage to the right hemisphere got lower scores on these tests than those with damage to the left hemisphere did. Also, as anticipated, women did less well than men on this test. Damage to the right hemisphere, however, had no greater effect on men than on women.

The results of this study and others suggest that the normal differences between men and women on rotational and line orientation tasks need not be the result of different degrees of dependence on the right hemisphere. Some other brain systems may be mediating the higher performance by men.

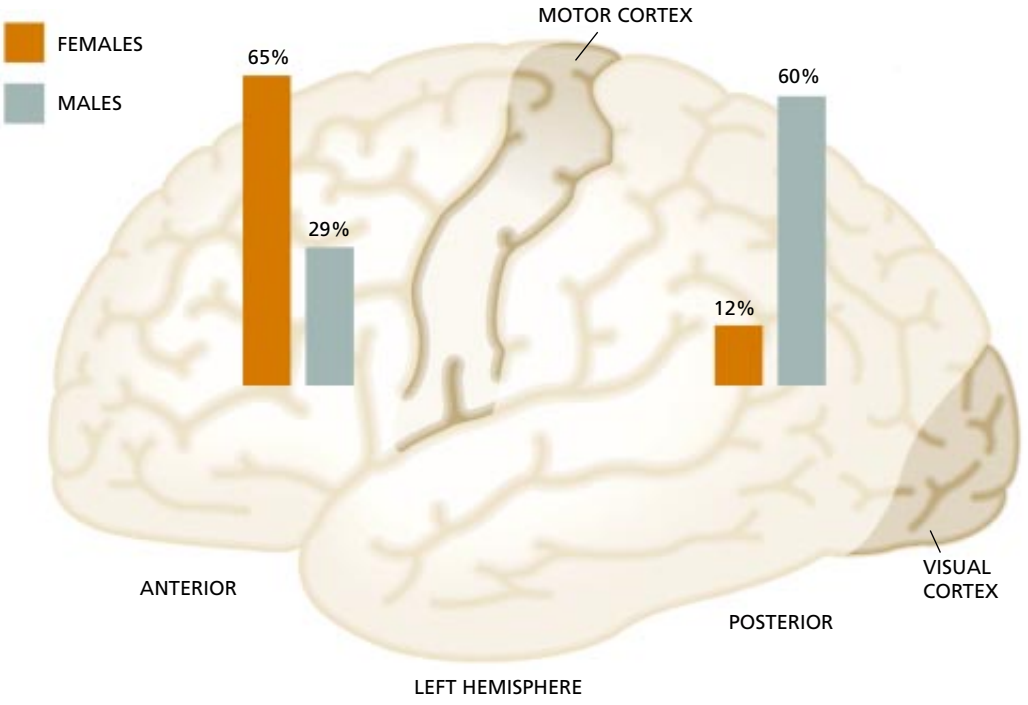
Another brain difference between the sexes has been shown for speech and certain manual functions. Women incur aphasia (impairment of the power to produce and understand speech) more often after anterior damage than after posterior damage to the brain. In men, posterior damage more often affects speech. A similar pattern is seen in apraxia, difficulty in selecting appropriate hand movements, such as showing how to manipulate a particular object or copying the movements of the experimenter. Women seldom experience apraxia after left posterior damage, whereas men often do.

Men also incur aphasia from left hemisphere damage more often than women do. One explanation suggests that restricted damage within a hemisphere after a stroke more often affects the posterior region of the left hemisphere. Because men rely more on this region for speech than women do, they are more likely to be affected. We do not yet understand the effects on cognitive differences of such divergent patterns of speech and manual functions.

Although my laboratory has not found evidence of sex differences in functional brain asymmetry with regard to basic speech, movement or spatial-rotation abilities, we have found slight differences in some verbal skills. Scores on a vocabulary test and on a verbal fluency test, for instance, were slightly affected by damage to either hemisphere in women, but such scores were affected only by left hemisphere damage in men. These findings suggest that when using some more abstract verbal skills, women do use their hemispheres more equally than men do. But we have not found this to be true for all word-related tasks; for example, verbal memory appears to depend just as much on the left hemisphere in women as in men.

In recent years, new techniques for assessing the brain's activity—including functional magnetic resonance imaging (fMRI) and positron emission

APHASIAS, or speech disorders, occur most often in women when damage is sustained in the anterior of the brain. In men, they occur more frequently when damage is in the posterior region. The data presented at the right derive from one set of patients.



JARED SCHNEIDMAN

tomography (PET), when used during various problem-solving activities—have shown promise for providing more information about how brain function may vary among normal, healthy individuals. The research using these two techniques has so far yielded interesting, yet at times seemingly conflicting, results.

Some research has shown greater differences in activity between the hemispheres of men than of women during certain language tasks, such as judging if two words rhyme and creating past tenses of verbs. Other research has failed to find sex differences in functional asymmetry. The different results may be attributed in part to different language tasks being used in the various studies, perhaps showing that the sexes may differ in brain organization for some language tasks but not for others.

The varying results may also reflect the complexity of these techniques. The brain is always active to some degree. So for any activity, such as reading aloud, the comparison activity—here, reading silently—is intended to be very similar. We then "subtract" the brain pattern that occurs during silent reading to find the brain pattern present while reading aloud. Yet such methods require dubious assumptions about what the subject is doing during either activity. In addition, the more complex the activity, the more difficult it is to know what is actually being measured after subtracting the comparison activity.

Looking Back

To understand human behavior—how men and women differ from one another, for instance—we must look beyond the demands of modern life. Our brains are essentially like those of our ancestors of 50,000 and more years ago, and we can gain some insight into sex differences by studying the differing roles men and women have played in evolutionary history. Men were responsible for hunting and scavenging, defending the group against predators and enemies, and shaping and using weapons. Women gathered food near the home base, tended the home, prepared food and clothing, and cared for small children. Such specialization would put different selection pressures on men and women.

Any behavioral differences between individuals or groups must somehow be mediated by the brain. Sex differences have been reported in brain structure and organization, and studies have been done on the role of sex hormones in influencing human behavior. But questions remain regarding how hormones act on human brain systems to produce the sex differences we described, such as in play behavior or in cognitive patterns.

The information we have from laboratory animals helps to guide our explanations, but ultimately these hypotheses must be tested on people. Refinements in brain-imaging techniques, when used in conjunction with our knowledge of hormonal influences and with continuing studies on the behavioral deficits after damage to various brain regions, should provide insight into some of these questions. SA

The Author

DOREEN KIMURA studies the neural and hormonal basis of human intellectual functions. She is professor of psychology at Simon Fraser University. Until recently, she was professor of psychology and honorary lecturer in the department of clinical neurological sciences at the University of Western Ontario. Kimura is a fellow of the Royal Society of Canada.

Further Reading

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Lessons Learned from Living

by George E. Vaillant

Vigorous octogenarians offer us rare role models for growing old. An appreciation of how they become that way provides object lessons for coming generations. After all, the demographers have noted that about half of the children born after 1970 can expect to live past the age of 80. But to truly understand successful adaptation to aging requires more than mere supposition and anecdote to shape our prescriptions for the future.

For the first time in the history of science, both the physical and mental health of a group of men have been studied from adolescence to age 80. The final chapters are now being written on the life history studies that have already allowed us to gain an understanding of what constitutes successful adaptation to the process of living. These investigations have made major contributions to our understanding of the stages of adult development, psychological defense mechanisms and the causes of alcoholism, perhaps the strongest predictive factor of early mortality and arrested adult maturation. The lives studied also suggest that factors within a person's control—drinking, smoking and maintaining productive relationships, among others—are more important than genetic makeup in determining whether someone reaches a vigorous old age.

More than 60 years ago, in 1938, the Grant Study of Adult Development began at the Harvard University Health Services. Two Harvard physicians, Arlie Bock and Clark Heath, received the first-ever research award from philanthropist William T. Grant to initiate a "systematic inquiry into the kinds of people who are well and do well."

From 1939 to 1942 Bock, Heath and later investigators selected 268 Harvard sophomores for study. In the original selection process, about 70 percent of the 1,000 students in each college class were arbitrarily excluded because of concerns about their academic achievement or their physical or psychological health. The names of the remaining 300 sophomores went to the college deans who every year selected about 70 boys whom they recognized to be "sound." Ever since then, those men have been sent biennial questionnaires. The choices were well made. By age 70 the mortality of the Harvard College sample has been only half that expected of white males of the same age. Half of the original study group have survived to become octogenarians. Four

Life history studies begun more than 60 years ago have started to reveal the components of successful maturation and aging

have run for the U.S. Senate, and others have been leaders in industry, journalism and the judiciary.

To control for sample bias—the fact that Harvard sophomores are unrepresentative—the Grant study of Harvard College men was broadened in 1970 to become the Study of Adult Development. Besides the Harvard men, the Study of Adult Development began following 456 urban young men—referred to informally as the Inner-City men—who had been selected in 1940 as the nondelinquent control group for the landmark study of juvenile delinquency by Sheldon and Eleanor Glueck of Harvard Law School. The study also reviewed the lives of 40 women between the ages of 75 and 80 from Lewis Terman's work at Stanford University on gifted children. The Terman study participants had been followed continuously since 1920. Thus, the findings from the Study of Adult Development are founded on the scrutiny of three diverse groups from adolescence until old age.

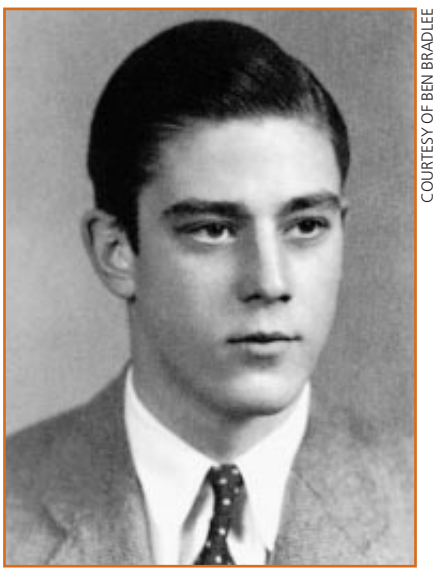
A prospective study—tracking a group throughout a lifetime—avoids the limitations of cross-sectional research. We never can accurately assess what happened "yesteryear" by asking a person today; maturation makes liars of us all. As a sophomore, one Harvard College man said of his father, "I like him as well as any man I have known. He is interesting and fun to be with." At middle life he rewrote history: "My and my father's entire life together had been a tortured relationship. We cordially hated each other." Both answers were probably half right.

Studying men's lives over long periods can also overcome shame and reveal when earlier reports have been consciously falsified. At age 50, one man finally admitted his mother's suicide when he was 14. Another man explained, "My replies have been frank, but with a period of delay. Whenever anything was badly wrong I tried to suppress it. If you want to find out what is really happening with me—read the next questionnaire or the one after that."

By far the most fascinating contribution of the Study of Adult Development has been the opportunity to observe adolescents become grandparents. Asked how he had changed between college and middle life, one unusually wise Harvard College–sample man wrote, "From age 20 to 30 I learned how to get along with my wife; from age 30 to 40 I learned how to be a success at my job; and since I have been 40, I have worried less about myself and more about the children." He succinctly summarized the model that the study conceived of for adult development influenced by the work of psychoanalyst Erik H. Erikson. The study model focused on five linked life tasks of Intimacy, Career Consolidation, Generativity, Keeper of the Meaning and Integrity. Empirical confirmation of these tasks has come through the experiences of study participants.

Developing a Sense of Self

Mastery of the task of Intimacy serves as the gateway to adult development. For this research, Intimacy was defined as living with another adult in an interdependent, mutually responsible, committed and intimate fashion for 10 years or more. Some individuals were well on their way to this process by 25; some not until age 60; and some, usually those with schizophrenia or severe maturational deficit, never.



COURTESY OF BEN BRADLEE

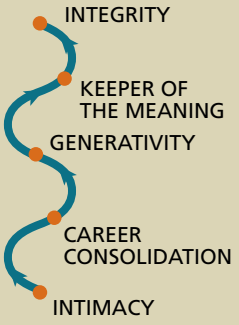
MARK GODFREY *The Image Works*

***BEN BRADLEE, former editor of the* Washington Post *and a participant in the Grant Study of Adult Development, poses just before entering Harvard in 1939* (left). *He confers with reporters Bernstein and Woodward during the Watergate scandal* (above, at right) *and relaxes in recent years* (opposite page).**

The task of Career Consolidation involves making a clear, specialized career identification that was characterized by contentment, commitment (attachment to one's work), compensation (a job valued by others) and competence (pride in one's work). These four Cs distinguish a career from a job or a hobby. Put differently, Career Consolidation involves the transformation of preoccupation with self and private (autistic) play and fantasy into a specialized role valued by *both* self and society.

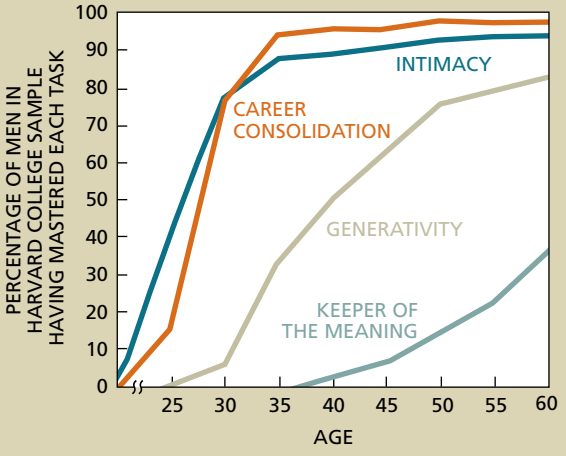
The task of Generativity means assuming sustained responsibility for the growth, well-being and leadership of others—in short, community building. Depending on the opportunities that the society makes available, Generativity can mean serving as a consultant, guide, mentor or coach to young adults in the larger society. Paradoxically, "selfless" Generativity cannot be achieved unless the adult has been able to master the "selfishness" of achieving a stable identity *and* the "selfishness" of Career Consolidation. In a developmental framework, to be selfish (to develop a sense of self) can be good, and to be selfless too early in life can lead to emptiness in old age.

The next task, Keeper of the Meaning, involves a more



***DEVELOPMENTAL LIFE TASKS** mark a winding path from Intimacy to Integrity. An increasingly smaller percentage of the Harvard College–sample men reached the later stages. The final stage, Integrity, was not measured.*

Mastery of Developmental Tasks



LAURIE GRACE

nonpartisan and removed approach to the world. This task was mastered by only a small fraction of our sample. To preserve one's culture involves developing concern for a social radius extending beyond one's immediate community. The Generative individual cares for young adults in a direct, future-oriented relationship—as, for example, coach or teacher. In contrast, the Keeper of the Meaning speaks for the less partisan preservation of past tradition. This is not a trivial distinction. The task of a Generative coach or parent of adolescent children is to take sides; the task of a judge, a referee or a conservationist is to be more impartial.

The final life stage in the model, Integrity, is well defined by Erikson as self-reconciliation: "The acceptance of one's one and only life cycle as something that had to be and of necessity permitted no substitutions." Put differently, when asked how he felt about growing old, Carl Jung, another psychoanalyst whose work dealt with life-stage development, allegedly replied, "I am old, so I be's old."

Some may offer the argument that such a model of adult development, particularly the stage of Career Consolidation, applies only to a modern technological society or only to educated, upper-middle-class professional men. But this is not the case. The medieval hierarchy that led from apprentice to journeyman to master craftsman was as clear 1,000 years ago as the developmental path that leads an Inner-City man from rookie cop to detective to precinct captain today. A like comparison across time or even culture holds for any of the other life stages, from Intimacy to Integrity. Despite their differences in gender, education and intelligence, the Harvard College sample, the Inner-City men and the Terman women all followed similar trajectories.

Empirical tests have supported this model of adult development. First, if a model of development is to be taken seriously, like embryology, it must conform to a relatively fixed sequence rather than either to free choice and social mores or to chronological age. As with shaving and menstruation, not everybody will reach that developmental stage at a fixed chronological age, but such development occurs cross-culturally and is necessary if not sufficient for parenthood to occur. Unlike physical or cognitive development, however, the Eriksonian developmental model requires support from biology *and* society *and* psychology.

In the Harvard College sample, some men reached 60 still mastering developmental tasks left unfinished earlier in life [*see graph at left*]. Yet of the 77 men who eventually mastered Generativity, 57 (74 percent) first mastered Intimacy, then Career Consolidation and only then Generativity. A few men achieved Career Consolidation and Generativity before Intimacy was reached. But for the Terman women and the Harvard College–sample men, *selfish* Career Consolidation always preceded *selfless* Generativity.

Second, if a psychobiological developmental model is to be taken seriously, it should be generally the same for women as for men and be relatively independent of social class, educational opportunity and intellectual capacity. The Inner-City men and Terman women were as likely to achieve Generativity as the Harvard graduates.

The third test is predictive validity. Of the 17 surviving Terman women who were rated as Generative at 60 years old, 100 percent were seen as aging well at 77 by an independent observer blind to the women's past. Of the 23 women not meeting criteria for Generativity, 39 percent did not meet criteria for successful aging. Successful aging was defined as "enjoys life, is open to new ideas, helps others, is graceful about dependency and maintains a sense of humor and acceptance of what has been." At age 75 the surviving Harvard College–sample men rated as *not* Generative at age 47 were three times as likely as those rated Generative to be viewed as aging badly by an independent rater.

Another hallmark of aging well is the ability to be ill without feeling sick: thriving in life even after being struck by physical malady. A pediatrician among the Harvard College men serves to illustrate this paradox as well as to demonstrate the model for successful aging. His life, though short, encompassed all the five stages of adult development.

Dr. Martin Carey (a pseudonym) came from a close-knit family, and by age 13 he had made his own commitment to a life of service to others. At 23 Carey married, and he and his wife remained devoted to each other until death. At age 26, when asked what was stimulating about his still embryonic career, Carey mentioned "the opportunity to provide aid to children through increasing parental understanding." Even in medical school, Carey identified with what a Generative pediatrician twice his age might do to care for the community as well as for the child.

At age 33 Carey developed poliomyelitis. For months he was totally helpless but then resumed an active social and professional life. For the rest of his life, Carey, like Franklin D. Roosevelt, provided a precocious example of successful aging: both men were "ill" and confined to wheelchairs, but they were not "sick."

One of the tasks of a Keeper of the Meaning is to model the meaning and dignity of maturity or old age for the young. By age 35, crippled by polio, Carey shared with his patients the advantages of working as an active clinician from a wheelchair: "Others can get not only professional

help but some measure of comfort from my carrying on as if nothing had happened." Twenty years later the progressively crippled Carey illustrated Erikson's last stage of Integrity and acceptance of the indignities usually associated with old age. He experienced, in his own words, "the frustration of seeing what needs to be done and how to do it but being unable to carry it out because of physical limitations imposed by bedsores on top of paraplegia." But three years later, at age 55, he wrote without bitterness, "I have coped . . . by limiting my activities (occupational and social) to the essential ones and the ones that are within the scope of my abilities."

At 57, slowly dying from pulmonary failure, Carey told the study that the past five years had been the happiest of his life: "I came to a new sense of fruition and peace with self, wife and children." A dying Carey told his interviewer, "Every group gives percentages for people who will die: one out of three will get cancer, one out of five will get heart disease—but in reality one out of one will die." Although still only middle-aged, he fully accepted that there is a time to be born and a time to die. It takes a longitudinal study to differentiate between a person's real-life behavior and his or her facility with platitudes. That Carey's words over the years were intimations of immortality was confirmed by continued study. After Carey died, an endowment for a professorship in his name was raised to perpetuate his lifelong contribution to pediatrics.

Healthy Defenses

The Study of Adult Development has played a pivotal role in elucidating the specific ways in which people cope with the inevitable stresses confronted during life. When we face unmanageable stress, three quite different methods can help us cope to avoid being overwhelmed. First, we can employ prerehearsed coping strategies that permit conscious and voluntary mastery of our problems (the equivalent of applying a tourniquet to a bleeding arm). Second, we can turn to other people for help (going to the emergency room). Third, we can use involuntary (unconscious) mechanisms (like our blood's innate clotting ability).

The third class of coping strategies, often termed defense mechanisms, reflects the involuntary ways in which the central nervous system denies and distorts inner and outer reality to reduce stress. Although such involuntary defensive behavior may strike us, the observers, as downright peculiar, defenses are often creative, healthy and comforting. Certain defense mechanisms—projection, repression, displacement and sublimation—have entered popular language. Some defenses are generally maladaptive: the projection of the paranoid bigot; the hypochondriasis of the angry, help-rejecting complainer; the passive aggression of the adolescent; and the acting out of the sociopath. Other defenses that also distort inner and outer reality are adaptive: the sublimation of a depressed Beethoven writing his Ninth Symphony, the suppression and stoicism of an astronaut with the "right stuff" and the humor of successful comediennes (Marilyn Monroe) or comics (Charlie Chaplin) who had miserable childhoods.

By 1970, however, defense mechanisms, popularized by psychoanalysis, appeared too metaphysical to empirical psychopathologists, and in 1977 all mention of defenses was dropped from psychiatric diagnostic manuals. Since 1970 the contribution of the Study of Adult Development to psychopathology has reduced the metaphysical aspects of defense mechanisms. We have achieved this through the prospective observation of behavior rather than through reports of free association in psychotherapy.

Let me offer an illustration of a defense. An internist who had participated in the study for 30 years told me, with vividness and enthusiasm, about his hobby—growing tissue cultures in his basement. With still more interest and enthusiasm, he told me that the cells from one culture came from a lesion on his mother's leg. Although he described his interest as if it were the most ordinary hobby in the world, I have yet to describe his hobby to an audience without laughter sweeping the room. The physician viewed his hobby as unremarkable; outsiders saw growing one's mother in the basement as bizarre. At the end of the interview, he revealed—in the most matter-of-fact way—that his mother had died only three weeks earlier. Knowing from longitudinal study that he had been very attached to her, I asked how he had coped with his grief. His conscious explanation was that he had spent his time comforting his father, thus employing the defense of altruism. Behaviorally, however, he had been tending a tissue culture with the enthusiasm and warmth usually allotted to people and had just described the recent death of his mother with a blandness usually reserved for tissue cultures. In other words, a grown child's very real love was displaced from his deceased mother and reattached to a tissue culture—an example of the defense mechanism of displacement. Twenty-five years after his mother's death, he had moved on with his life and had forgotten all about his hobby.

PHYSICAL HEALTH

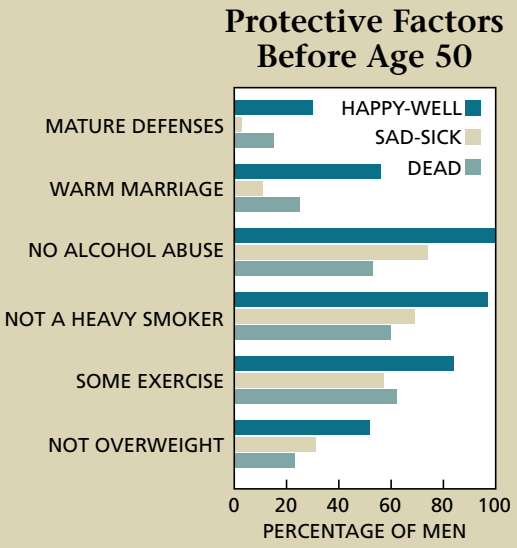
	HAPPY-WELL	SAD-SICK	DEAD
AVERAGE NUMBER OF YEARS DEAD OR DISABLED BEFORE AGE 80	0	9	18
IN GOOD HEALTH AT AGE 75	38%	15%	N/A
PHYSICALLY ACTIVE DAILY AT AGE 75 Still able to chop wood, climb stairs, move furniture, walk two miles, etc.	100%	0%	N/A

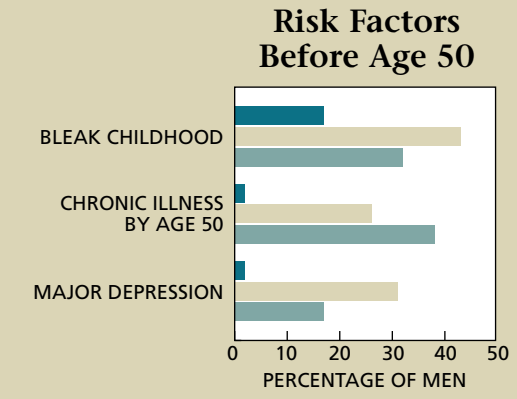
MENTAL HEALTH

	HAPPY-WELL	SAD-SICK	DEAD
POOR MENTAL HEALTH: AGES 50 TO 65 Men in bottom quarter in ability to work, love, play and remain free of psychiatric care	0%	54%	37%
POOR SOCIAL SUPPORTS: AGES 60 TO 80 Men in bottom quarter in quality of relationship with wives, children, siblings and others	0%	51%	44%
LOW LIFE SATISFACTION: AGES 55 TO 75 Men in bottom third in self-assessment of marriage, job, hobbies and other activities	0%	68%	N/A

LAURIE GRACE

***SUCCESSFUL AGING** was achieved by the "happy-well," 64 of the 268 Harvard College–sample men who thrived in six domains of physical and psychological health when surveyed between the ages of 50 and 80; meanwhile 35 men in poor health were categorized as "sad-sick." There were also 60 men who died before age 75, and another 109 who fell into an intermediate category* (not shown).





LAURIE GRACE

MATURE DEFENSES, such as altruism and humor, were among the most important predictive variables of psychological health for the Harvard College–sample men. But absence of alcohol abuse and smoking before age 50 figured most strongly in predicting physical health in later years.

Behavioral vignettes, obtained through longitudinal observation, made it possible to obtain a reliable rating of defenses—a scientific safeguard not possible in psychoanalytic studies. By contrasting the defensive styles of the longitudinally studied Inner-City men, of the Terman women and of the Harvard College–sample men, the study reached several surprising conclusions. Like the immune system, the relative adaptiveness of defense choice—rated by comparing how often subjects used mature instead of immature defenses—was not the product of social class, IQ, gender or education. At present, the source of mature defenses, like the workings of some aspects of immune function, remains a mystery. But an individual can enhance the use of mature defenses by actively changing his behavior or through a process of self-discovery, as often happens in therapy. Nevertheless, adaptiveness of defenses from ages 20 to 50 provided the best measure that the Study of Adult Development had to predict the men's adaptation to life 20 or even 30 years later. Such findings contributed to the reincorporation of defense mechanisms in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (1994).

The length of the study permits the contrast of men who have aged well with men who have aged less successfully. Few people grow old without some illness, but a key to successful old age is to be ill without feeling sick. Between the ages of 75 and 80, there were 64 of the 268 Harvard College–sample men who still remained unambiguously healthy—objectively and subjectively, physically and psychosocially—and there were 35 men who were still alive but clearly "sick" as well as ill [*see chart on preceding page*]. To achieve this contrast, then, the Harvard College men who fell somewhere in the gray zone of being "healthy" or "sick" and, of course, the 60 who had died prematurely were excluded.

Aging Well

To assess the different facets of successful adaptation, the study investigators divided the lives of the Harvard College men into six categories. Curtailment of an active physical life characterized the first domain evaluated. It was quantified by a measurement of the disability and mortality that the men experienced between the ages of 40 and 80 years old. None of the happy-well men and all the sad-sick men had spent some years disabled. Biological health, the second domain, was based on a complete physical examination at age 75 by an internist and uniformly assessed by an independent observer blind to the individual's psychosocial adjustment. Although twice as many of the happy-well as the sad-sick were still without any life-shortening irreversible illness—such as coronary thrombosis, diabetes or multiple sclerosis—some were nonetheless chronically ill. Yet none were disabled.

The third domain was reported activities of daily living. At 75, all the happy-well men could still climb two flights of stairs, walk two miles, carry suitcases through airports and pursue favorite strenuous activities such as heavy gardening, singles tennis, downhill skiing and chopping wood. All the sad-sick men saw their lives as severely curtailed. Sometimes, however, their disability reflected major depression, arthritis or other psychological or physical illnesses that were not life-threatening.

The fourth domain was mental health. This area, too, was assessed by an independent observer reviewing the men's lives from ages 50 to 65 and quantifying their ability to work, to love, to play and to remain free from psychiatric care. The fifth domain was objective social supports. This was assessed by another independent observer evaluating the men's relationships with their wives, their children, their siblings, their playmates (bridge and golf partners, for instance), their religion, their social networks (civic organizations) and their confidants.

The sixth, and final, domain was subjective life satisfaction. On two occasions between ages 70 and 80 the men were asked: "Over the past 20 years how satisfying was your marriage? Your job? Your children? Your friends? Your hobbies? Your community activities? Your religious participation? Your recreational activities?"

The happy-well were the men who scored high in all domains. The sad-sick were men who before age 80 experienced at least five years (the average was nine years) of disability *and* were classified as unhappy in at least one of the three domains of mental health, psychosocial efficacy or life satisfaction. Significantly, the 60 men who died too young for such categorizations to be made had been almost as psychosocially impaired as the surviving sad-sick men.

Six protective variables appeared in the pasts of men who

were among the happy-well. The use of mature defenses before age 50—by that I mean the capacity to make lemons into lemonade and not make mountains out of molehills—was among the most important predictors of successful aging later in life. A third of the happy-well, one sixth of the prematurely dead and only one of the sad-sick men had adopted mature, positive defenses such as humor and altruism before age 50. Yet adaptiveness of defenses did not predict the men's physical health, only their psychosocial health.

Absence of alcohol abuse and of heavy smoking before age 50 were the two most important protective factors for physical health. Two fifths of the dead, one fourth of the sad-sick but not a single one of the happy-well had abused alcohol, and only two had been heavy smokers. Warm marriages and exercise also predicted good health at 80. Bleak childhoods and depression were strongly associated with poor outcome [*see graph on opposite page*].

Unlike many earlier studies linking mental health with physical health outcome, the Study of Adult Development controlled for many confounding influences that could affect physical and mental health and included long-term observation of behavior at work and at home. But the most valuable aspect of the study was that it controlled for alcohol abuse among the lives it tracked.

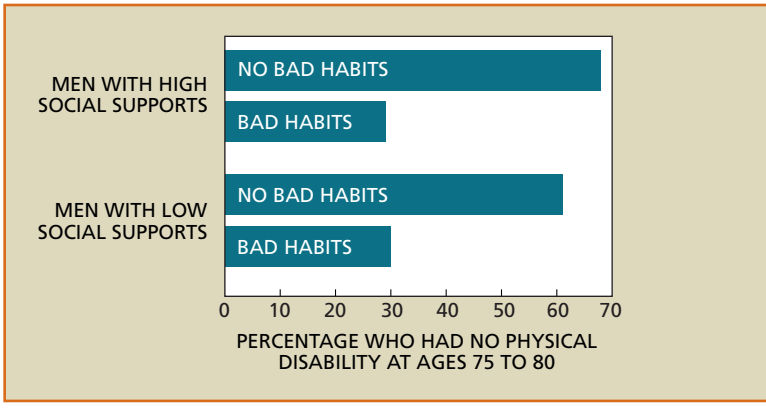
Perils of Alcoholism

Until now, most major longitudinal studies of health have controlled only for reported alcohol consumption, which unfortunately predicts alcohol abuse almost as poorly as reported food consumption predicts obesity. Reported consumption of alcohol is not a strong predictor of poor aging. In contrast, the Study of Adult Development measured alcohol abuse by reported alcohol-related problems and found alcohol abuse strongly predictive of poor health.

Men who were the most socially isolated were twice as likely to be disabled as the men with good social supports. The association between social supports and physical health disappeared, however, if alcohol and cigarette abuse were controlled [*see graph at right*]. One reason may be because alcohol abuse not only is a direct cause of cancer and heart disease but also causes increased life stress, depression and decline in social supports. Another study of the data involving the Inner-City men found that alcoholism is more hereditary than the result of an unhappy childhood. It also found that alcoholism is a cause of life distress rather than a form of self-medication administered in reaction to an adverse life situation, such as a troubled family. These discoveries proved counterintuitive and at variance with almost the entire literature based on short-term studies of alcoholics.

Significantly, prolonged follow-up of both the Harvard College and the Inner-City men established that seemingly incurable alcoholics (analogous to two-pack-a-day cigarette smokers who quit) often achieved lifelong recoveries of two decades or more. These recoveries (analogous to those of heavy cigarette smokers) were achieved almost always through lifelong abstinence, often facilitated by Alcoholics Anonymous, and not by a return to controlled drinking.

It is true that genes are very important in researching the longevity of fruit flies. Therefore, one of the first variables we looked at was the genetic predictors of aging. Ancestral longevity was estimated by computing the age at death of the subject's parents and four grandparents. To our surprise, although study participants with short-lived ancestors were more likely to encounter poor health at age 50, those with long-lived ancestors had only a slightly better chance of being in vigorous health at age 75 and had no better chance of rating highly on scales of psychological or social well-being.



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BAD HABITS—defined as heavy smoking and drinking to excess—removed any benefit to physical health that the Harvard College–sample men received from social supports, such as a warm marriage.

Ancestral longevity also failed to predict vigorous late-life adaptation for the Terman women ages 75 to 79.

Thus, there is a hopeful message for the younger generation—destined by actuarial tables to live past age 80. Most of the protective factors that distinguished the happy-well from the sad-sick are under personal control. It is true that we cannot voluntarily change our childhoods or avoid major depression—but we can control our weight, our exercise and our abuse of cigarettes and alcohol. With hard work, and perhaps with therapy, our relationship with our most significant other and our coping styles can be modified. Two thirds of the men with five or six protective factors at age 50 were among the happy-well at 75; only one man was among the sad-sick or deceased. Of men who maintained two or fewer protective factors, not even one was among the happy-well and two thirds were among the sad-sick or prematurely dead. Put simply, whether we live to a vigorous or to a "sick" old age may not be so much in our stars or in our genes but in ourselves. SA

The Author

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Further Reading

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Balancing Work and Family

by Joseph H. Pleck

Stories in the media often portray contemporary men balancing an active family role with the breadwinning responsibilities of a career. At the same time, commonly held wisdom suggests that yesterday's men—even those from just a few decades ago—often failed at that juggling act, serving primarily as full-time workers and participating in few, if any, family activities. These images of present and past men, however, might arise more from folklore than fact. By studying exactly what activities American men do now, and have done in the past, social scientists find an interrelated web of trends that are changing men's roles.

In 1956 Swedish sociologist Alva Myrdal and British historian Viola Klein published *Women's Two Roles: Home and Work*. Their title introduced what became the leading understanding of the change in adult women's lives in industrial societies over the first half of the 20th century. In addition to their traditional child-rearing and homemaking role within the family, women were increasingly engaging in a second role: paid employment outside the family. In the decades subsequent to *Women's Two Roles,* Myrdal and other sociologists have tentatively suggested that in the long run, women could not succeed at both roles unless men also took on more family responsibilities. Our society is still just beginning to recognize that men, too, face the challenge of dual roles.

Are Men Doing More in the Family?

Since the mid-1970s other social scientists and I have systematically studied the changing ways in which contemporary American men combine and prioritize their work and family responsibilities. In attempting to analyze these changes, many people—especially students, journalists and scholars—often ask: Are men doing more in the family now than they did in the past? That question can be examined on many levels. For example, beyond simply knowing how much time men spend with their families, one might examine what men do during their family time and what it means to them. This changing role for men also leads to larger social implications.

Today's American men spend less of their lives working than their predecessors did. In comparison to men of the early 20th century, they now enter the labor force later and retire earlier. In addition, the average number of hours that men work each week also decreased substantially during the first half of this century, but there is some controversy about whether such decreases have continued. Even more interest—and controversy—surrounds a related question: Do today's men spend more time taking care of children and doing housework?

One long-term comparison came from the so-called Middletown project, in which sociologists Robert and Helen Merrill Lynd studied Muncie, Ind., in the 1920s. In 1924 about 10 percent of Muncie's working-class wives reported that their husbands spent no time with their children, and 68 percent said that their husbands spent more than an hour a day. In 1978 Theodore Caplow of the University of Virginia and Bruce A. Chadwick of Brigham Young University repeated most of the Lynds' interview procedures with a similar sample in Muncie. In their study, only 2 percent of working-class wives reported that their husbands spent no time with their children, and 77 percent reported that their husbands spent more than an hour a day. In both studies, the figures were similar for what the Lynds called "business-class" families, in which the husbands held white-collar jobs.

Many more comparisons can be made with data collected since 1965. Some of the most important of these studies have used so-called time diaries. Home economists developed this technique in the 1920s, but it fell into disuse until

Fathers who live with their families are spending more time with their children. At the same time, more fathers are not living with their families

WORKING FATHERS are now struggling with the same dilemma that has bedeviled working mothers: how to balance the needs of family with the demands of a career.

BERND AUERS

its reinvention in the 1960s. With this method, respondents report—in their own words—what they were doing at each moment of the previous day, starting at 12 A.M. The respondents list each activity, when that activity stopped, what they did next, when that stopped, what they did after that and so on, until reaching the following midnight. They might also be asked other questions about each activity, such as whether a television was on or who was with them. Responses are then coded into specific categories, such as baby care and indoor playing, which can be combined into broader categories, such as child care.

In the studies that do not use time diaries, fathers are often asked to simply estimate how much time they spend with their children each day. To make sense of the more recent data collected with time diaries as well as with other methods for estimating time-use patterns, Michael Lamb of the National Institute of Child Health and Human Development, James Levine of the Families and Work Institute and I proposed two categories: paternal engagement and paternal availability. Paternal engagement consists of direct interaction with a child, which is described by the father in language indicating that he thought of the activity as taking care of the child. Paternal availability adds to this the amount of time the father and child are in the same vicinity but engaging in different activities.

Lamb, Levine and I discovered that different time-diary studies often interpret the same behavior differently. For example, "talking with children" might be considered part of child care in some studies but not in others. To identify trends across studies, we converted the data about fathers' time with children in each study from an absolute amount, such as 76 minutes a day, to a percentage of the mothers' interactions, such as 43 percent. Consequently, results of the different studies could be converted to a common standard of measurement—fathers' time as a proportion of mothers'.

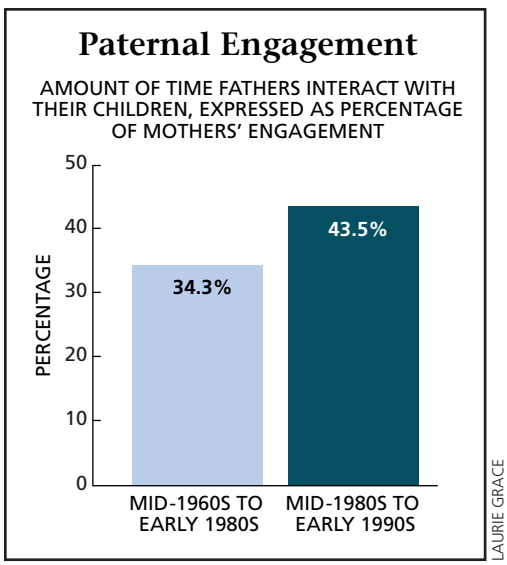
Using this approach to review 11 national or local studies that collected data between the mid-1960s and the early 1980s, Lamb, Levine and I found that fathers' engagement was on average about one third of mothers' and their availability was about half of mothers'. When I recently examined 13 similar studies that reported data collected between the mid-1980s and the early 1990s, fathers' engagement had risen to 43.5 percent of mothers', and paternal availability had risen to 65.6 percent. In addition, many studies have shown that when fathers are more involved with their children because they want to be, the fathers' involvement benefits the children's cognitive and social development.

Although men still perform less child care than women, good evidence indicates that the participation of men in family activities is increasing. Nevertheless, most of the data come from studies of married fathers, which overlook a substantial part of the adult male population.

More Diverse Family Roles

Even though some data show that U.S. men's involvement with the family has risen, other indicators suggest the contrary. For example, the increase in divorce rates since the 1950s has weakened many men's family ties. Most divorced fathers' contact with their children drops off rapidly after divorce. Almost half of all divorced fathers have not seen their children in the past year, and high proportions of them do not pay child support. (More than 80 percent of court-ordered child-support money is never actually paid.) What is more, the recent increase in the proportion of men who never marry also indi-

Although men still perform less child care than women, good evidence



LAURIE GRACE

BERND AUERS

***PATERNAL ENGAGEMENT** is the category of activities in which fathers interact with their children. Examples include playing with children* (right)*, reading to them and helping with their homework. Paternal engagement is increasing, but mothers still spend more than twice as much time interacting with their children* (above)*.*

cates decreasing family involvement. Most unmarried fathers—teen and adult—refuse to accept any responsibility for their children.

These phenomena, however, are more complex than they first appear. For example, although the increase in divorce during the 1960s and 1970s appeared dramatic compared with the unusually stable divorce rate during the 1950s, rates of divorce have actually been relatively stable at about 50 percent for nearly two decades. In addition, divorced fathers' loss of interest in their children is not the only possible source of the rapid decrease in contact. For instance, many divorced mothers do not want continuing contact between their ex-spouses and their children.

In their 1991 book *New Families, No Families?,* Frances K. Goldscheider of Brown University and Linda J. Waite of the University of Chicago perceptively argue that American family life is now changing in two contradictory directions. In two-parent families, fathers' involvement with children and overall gender equality are increasing; however, two-parent families have become a smaller proportion of all families. Families headed by single mothers are becoming more common, and thus,

***PATERNAL AVAILABILITY** is a measurement of the amount of time fathers spend in the vicinity of their children, either interacting with them or not. The category covers activities such as working on the computer while the children play video games* (below). *In recent years, paternal availability has risen to nearly two thirds of maternal availability* (bottom).

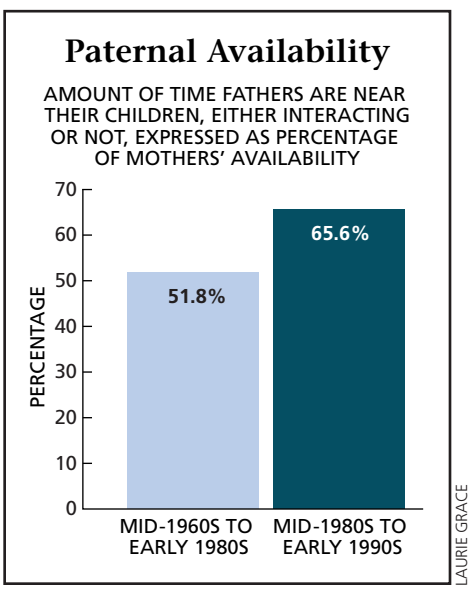
BERND AUERS

indicates that the participation of men in family activities is increasing.

more children overall do not have a resident father.

Goldscheider and Waite's analysis helps to make sense of the perhaps surprising finding that ethnicity and socioeconomic status show little if any consistent association with the amount of child care performed by married fathers. These variables primarily influence fathers' behavior by determining whether fathers get and remain married, not by affecting how fathers act when they are married.

How might these demographic and behavioral trends play out in the future? The downside trend—more children in single-parent families—has leveled off, because the divorce rate has been stable for nearly two decades and the out-of-wedlock birth rate has also leveled off in recent years. The upside trend—greater father involvement in married two-parent families—appears to be continuing. This produces a positive overall trend toward greater paternal involvement. Nevertheless, the disparity between the experiences of children growing up in married two-parent families and those of children in single-parent families will continue to grow.



LAURIE GRACE

This discussion usually contrasts two groups—resident, married fathers versus nonresident, never-married or divorced fathers—but my research suggests that there is a surprisingly large and unrecognized third group: resident, unmarried fathers. Jeffrey L. Stueve of the University of Illinois and I analyzed a nationally representative sample of fathers between the ages of 22 and 26 who live with their children. Nearly 60 percent were the children's biological father, residing with and married to the children's biological mother, but more than 40 percent were not. Resident, unmarried fathers have several subtypes: cohabiting biological fathers (13 percent of the total number of resident fathers), cohabiting stepfathers (8 percent) and fathers raising biological or unrelated children alone (6 percent). Married stepfathers have been studied more than any of these subgroups but are less frequent (5 percent). Fathers in "blended" families—in which they are living with children *and* stepchildren—make up 8 percent of the total. Men were defined as "cohabiting" if they were living with a female partner at

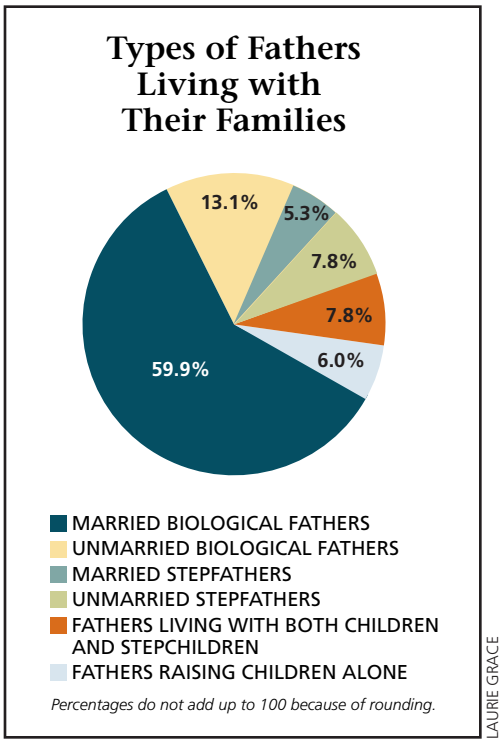
the time of the study; there was no minimum length of time for the relationship. This wide variety of family types suggests that researchers need to broaden their studies to include all kinds of fathers.

For a long time, social scientists assumed that men's and women's experiences must be opposite in all respects. For example, past researchers often thought that if family is more central than work for women's identities, work must be more central than family for men's identities. Nevertheless, research has never borne out this expectation. My research in the 1970s, using self-report questionnaires, showed that family is far more psychologically central to men than work, just as is true for women. Other recent studies concur.

Someone might say that men merely report the socially desirable response. To sidestep that potential criticism, one could compare how strongly men's overall psychological well-being is linked to their satisfaction with either family life or work life. Using two mid-1970s surveys, I found that men's levels of family satisfaction explained twice as much variance in their psychological well-being as their levels of work satisfaction did—just like women. Rosalind C. Barnett of Brandeis University replicated my findings with more recent samples.

Of course, more subtle differences might exist between the family identities of men and women. In studies of so-called emotional transmission from work to family, for example, Reed W. Larson of the University of Illinois showed that a father's mood at the end of a workday influences a mother's mood when they're together at home far more than her prior mood affects him. In fact, a father's mood at work more strongly influences a mother's mood at home than her own mood at work affects her mood at home. Larson's findings suggest an important difference in the place of work and family in fathers' and mothers' personalities: fathers carry their workplace emotions home with them, but mothers keep their family experience insulated from workplace pressures.

Other research, however, suggests unexpected similarities. For example, Ellen Hock and Wilma Lutz of Ohio State University found that fathers and mothers experienced similar levels of anxiety over separation from their children during the first two years of parenthood. Research today is just beginning to flesh out a full understanding of the differences and similarities in men's and women's family identities.



LAURIE GRACE

***UNCONVENTIONAL FATHERS** make up about 40 percent of all fathers who live with their children. Studies show that cohabiting fathers and stepfathers are particularly common, at 13.1 and 7.8 percent, respectively.*

Actions and Expectations

Less evidence exists about how the character of men's behavior in the family has changed. What is available continues to find gross differences between fathers' and mothers' behavior with children. With infants, mothers' behavior is more soothing and predictable, and fathers' is more stimulating and unpredictable. With older children, mothers provide more caregiving, and fathers engage in more play.

Some conservatives suggest that a new social pressure encourages fathers to "act like mothers." For instance, David Blankenhorn of the Institute for American Values says that a new cultural "script" pushes dad toward androgyny under the label of "Mr. Mom." I see little evidence, though, of this alleged new ideal. Other researchers and I recognize the importance of fathers' providing children with financial support and developmental guidance as well as supporting the mother in her relationship with the children. Moreover, we have not claimed that greater paternal involvement necessarily has positive effects, and we have not recommended that fathers should act like mothers. Indeed, several of my colleagues and I contend that fathers' play with children might have more positive consequences for their children's development than fathers' caretaking time, because play interaction is more socially and cognitively stimulating. In any event, no recent evidence finds fathers actually acting more like mothers in terms of their specific activities or behavioral style, so conservatives need not be so concerned.

I also question whether the current cultural script about fathering really has shifted in favor of greater involvement with children. Within the general belief that it is desirable for fathers to be more involved lurks a hidden qualification: not if it negatively impacts their jobs. For example, a recent survey of large companies showed that fathers are usually entitled to parental leave on the same basis as mothers—but when company employees were asked how many days a father should be entitled to take, 90 percent said none.

Social Implications

Although men's changing work-family balance affects their children, their spouses and the men themselves, we must also consider broader effects: the consequences of these changes on social institutions. The two different directions in which men's work-family patterns have changed—an increase in paternal involvement among married men and a simultaneous increase in divorce and fatherhood outside marriage—must be considered separately.

Men's decreasing tendency to be married fathers forces more children to face significant risks in their development. In recent years, our society has developed better strategies to increase the number of child-support court orders directed at absent fathers and to encourage their compliance with the orders. Nevertheless, even with the highest feasible child-support payments and maximum paternal compliance, many children in these families will live in poverty, and most of them will need some form of public assistance.

AP PHOTO

KEVIN KNUSSMAN, a helicopter paramedic with the Maryland State Police, won a $375,000 jury award in January 1999 after proving that he was denied parental leave.

Robert E. Emery of the University of Virginia found that court data over the past two decades indicate a large rise in the proportion of fathers who share legal custody but only a small increase in the proportion sharing physical custody—in other words, actually living with their children. Emery's studies, however, point to a possible intervention effort: divorce mediation, in which the couple negotiates a settlement instead of fighting it out in court. Emery found that divorce mediation leads to more contact between fathers and children 12 years after divorce than the standard divorce process does.

Other intervention efforts can effectively promote parental responsibility among teenage fathers and reduce the incidence of out-of-wedlock births, especially among teenage women. Unfortunately, our government's recent approach—eliminating increases in benefits to mothers who have additional children while on welfare—is not one of them. This approach has not resulted in lower rates of out-of-wedlock births in the states that have passed such laws. Recently attention has turned to possible ways of reducing the incidence of divorce by making it more difficult to obtain or by creating a class of marriage in which divorce is not permitted. These latter efforts are, at best, controversial in their feasibility and desirability.

Married fathers' increasing involvement with their children also has social ramifications for the workplace. In a 1977 national survey that I co-directed for the U.S. Department of Labor, I developed the first measures of the extent to which employed married men and women experience conflict between their work and family roles. In that survey, and in much of the research conducted subsequently by other investigators, the married mothers and fathers reported similar levels of conflict. Other studies show that parenthood is associated with increased absences or lateness at work to a similar degree for men and women and that work-family disruptions, such as a breakdown in child-care arrangements, affect men's well-being at least as much as women's.

Impetus for Change

Men's conflicts between their work and family responsibilities create pressure to change the workplace, which adds to the impetus for change already created by the rising numbers of employed mothers. Over the past two decades, for example, enough men fought for parental leave on the same basis as women—generally unpaid—to generate a well-established body of case and administrative law affirming this right. In fact, fathers initiate a significant proportion of the grievances regarding denial of parental leave filed with the U.S. Department of Labor under the 1993 Family and Medical Leave Act. In January 1999 one father—Kevin Knussman, a helicopter paramedic with the Maryland State Police—received a $375,000 jury award for denial of leave. Knussman's award was the largest ever granted to a father in a parental leave case.

Although men's changing work-family patterns are triggering demands for more flexible workplace policies, the changes are sure to be contested. In fact, considerable resistance to greater workplace flexibility exists today, despite the social attitudes favoring more involvement of fathers in family life. The resistance stems from the hidden qualification mentioned earlier: the belief that fathers' family involvement should not affect their job performance in any way.

As a result, the shifting pattern of work-family commitments for men will most likely mirror the pattern experienced by women. Policy changes in the workplace have been important, but we should remember that employed mothers have nonetheless needed to work out accommodations between their work and family lives largely on an individual basis, relatively invisible from public view. And the widespread resistance to paternity leave suggests that companies are even less sympathetic to their male employees' work-family problems. So it is likely that the accommodations that most employed fathers create to balance their work and family responsibilities will, to an even greater degree, be largely private and thereby socially unrecognized and unsupported. SA

The Author

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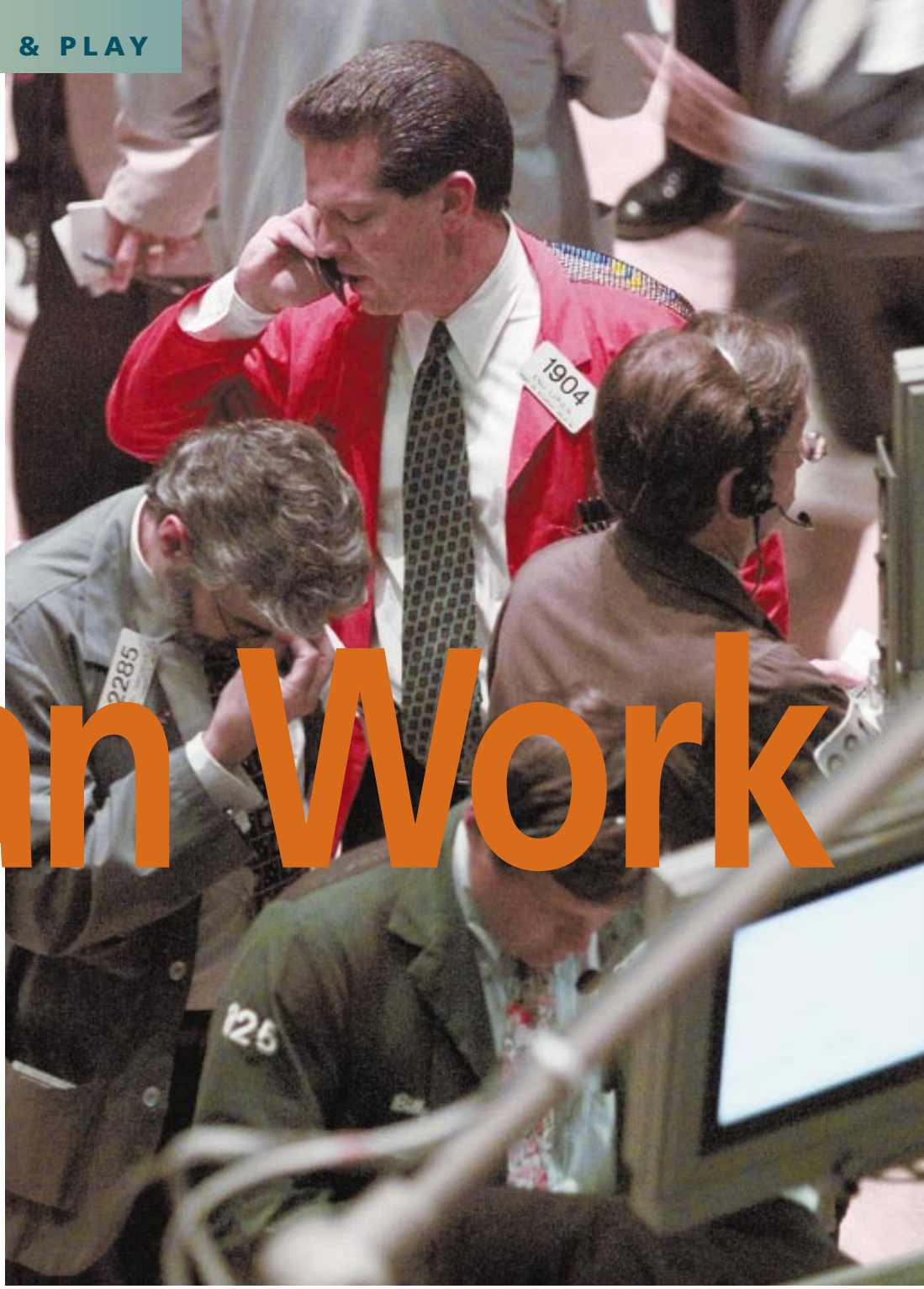

Recent studies suggest that stress on the job can be deadly

Can Work Kill?

by Harvey B. Simon

According to Sigmund Freud, a man's mission in life is "to work and to love." In this modern world, an excess of—or, at least, unprotected—love can be hazardous indeed. But what of work? Can a man literally work himself to death?

The Japanese think so; in fact, *karoshi,* or "death from overwork," is a recognized diagnosis that qualifies survivors of its victims to receive employee compensation payments. A 1998 survey of 526 Japanese men, aged 30 to 69, supported the idea that long working hours can be hazardous to a man's health. The subjects of the study included men who had been hospitalized with a heart attack as well as healthy men of similar ages and occupations. The results were striking: men from both groups who put in more than 11 hours of work on an average day were 2.4 times more likely to have a heart attack than were men who worked "just" seven to nine hours a day.

What accounts for the increased risk of heart attack among Japanese men who work very long hours? Mental stress is a logical explanation, but in this study psychological factors, as measured by what the researchers called the "burnout index," did not completely account for the trend. Nor

RICHARD DREW *AP Photo (far left);* KYODO NEWS *(left)*

***STRESS ON THE JOB** is a common complaint of many professionals, including Wall Street traders* (far left). *In Japan, hot lines* (left) *provide counseling for men suffering from work-related stress as part of an effort to reduce the incidence of* karoshi, *or "death from overwork."*

Kill?

did established risk factors. High blood pressure, high cholesterol levels, smoking, diabetes and obesity were linked to heart attack, but even after taking these variables into account, the number of hours worked itself was still closely related to the risk of heart attack.

The Japanese are notorious workaholics, but working conditions in Japan are actually designed to be predictable and to minimize stress among employees. In general, Western men do not enjoy such advantages, so one wonders just how working too hard affects their health. In 1997 an international team addressed the question by examining the results of over a dozen earlier studies on work and health, which looked at conditions ranging from heart attacks to exhaustion and mental stress. Analysis of the compiled data confirmed a correlation (in both men and women) between hours of work and ill health; the effect was small but consistent and significant.

Both of these studies focused on working hours but not on working conditions. Are such qualitative factors also important? A 1996 study from Sweden explored the possibility. The group of researchers observed more than 12,500 employed men over a 14-year period. The scientists evaluated the psychological and physical demands of each man's job; they also collected information about the age, smoking history, exercise habits, educational level and social class of each individual. When the results were analyzed, two occupational factors emerged as risk factors for death from cardiovascular disease. Men who had low control over the demands of their jobs were 1.8 times more likely to die from heart disease than men with more control were; men who also experienced a low level of social support from co-workers were 2.6 times more vulnerable to cardiovascular death.

These heart-stopping results do not stand alone. An earlier study of 2,465 Danish bus drivers linked the intensity of traffic on the drivers' routes to a two-fold increase in the risk of death and heart attack; lack of social support compounded the problem. Job strain was implicated as a predictor of mortality in a seven-year study of 500 Swedish men; high demands and low control combined to explain this effect as well. In a related survey, researchers who evaluated 99,029 Italian railway workers found that the combination of high job responsibility and low level of physical work was associated with an increased risk of heart attack.

More research will be needed to verify these observations. Even now, however, there is enough evidence to suggest that job stress may increase a man's risk of dying from heart disease. The combination of high mental demands, low personal control and inadequate social supports is particularly worrisome.

If stress at work kills, how does it happen? Nobody knows for certain. But we do know that mental stress increases blood levels of adrenaline and cortisone, two so-called stress hormones. Psychological stress raises the blood pressure and heart rate; it can also induce abnormalities in the heart's pumping rhythm, known as arrhythmias. Stress can also activate platelets in the blood, triggering clots that can block diseased coronary arteries. Furthermore, doctors have known for several years that anger in particular can trigger heart attacks and that mental stress tests can predict heart trouble more accurately than exercise stress tests.

Anger is an important component of stress on the job—and according to a recent study, men with the most anger and hostility have the highest risk of heart disease.

Since 1961 scientists at Harvard Medical School and the Harvard School of Public Health have been observing 2,280 men as part of the Normative Aging Study. In 1986, 1,305 men (with an average age of 61) completed the psychological test known as the Minnesota Multiphasic Personality Inventory (MMPI-2), which includes a section designed to quantify anger [*see box on next page*]. Each participant received a score that indicated his level of anger and hostility. The men returned for comprehensive medical examinations approximately every seven years, at

The Hostile Heart

EVERETT COLLECTION

ANGRY as a result of work-related stress, the character played by Michael Douglas in the 1993 film* Falling Down *vents his frustration violently.

Do you have an angry heart? To evaluate your overall tendency toward hostility, use the Minnesota Multiphasic Personality Inventory Anger Content Scale. Answer true or false to each of these questions:

T	F		
❍	❍	**1.**	At times I feel like **swearing**.
❍	❍	**2.**	At times I feel like **smashing** things.
❍	❍	**3.**	Often I can't understand why I've been so **irritable** and **grouchy**.
❍	❍	**4.**	At times I feel like picking a **fistfight** with someone.
❍	❍	**5.**	I easily become **impatient** with people.
❍	❍	**6.**	I am often said to be **hotheaded**.
❍	❍	**7.**	I am often so **annoyed** when someone tries to get ahead of me in a line of people that I speak to that person about it.
❍	❍	**8.**	I have at times had to be **rough** with people who were rude or annoying.
❍	❍	**9.**	I am often **sorry** because I am so irritable and grouchy.
❍	❍	**10.**	It makes me **angry** to have people hurry me.
❍	❍	**11.**	I am very **stubborn**.
❍	❍	**12.**	Sometimes I get so **angry** and **upset** I don't know what comes over me.
❍	❍	**13.**	I have gotten angry and broken furniture or dishes when I was **drinking**.
❍	❍	**14.**	I have become so angry with someone that I have felt as if I would **explode**.
❍	❍	**15.**	I've been so angry at times that I've hurt someone in a physical **fight**.
❍	❍	**16.**	I almost never lose **self-control**.

Questions 1–15: One point for each "true"
Question 16: One point for "false"

KEY

0–5: Anger is not a problem.
6–10: Anger level is moderate; work on ways to relax.
11–16: Anger level is a concern; your health may suffer the consequences if corrective measures are not taken.

—*H.B.S.*

which time they were checked for heart disease and cardiac risk factors such as smoking, hypertension and high cholesterol.

All the men were free of coronary artery disease when the study began, but during seven years of observation, 110 of them developed heart disease. The men with the highest anger scores were at the greatest risk for developing heart disease. And the risk was substantial: coronary artery disease was diagnosed three times more often in the angriest men than in the men with the least anger. The link between anger and heart disease was not explained by differences in blood pressure, smoking or other cardiac risk factors; hostility was heartbreaking in its own right.

As it turns out, hostility is not so good for the brain, either. In a report published this spring, Susan A. Everson and her colleagues at the University of Michigan School of Public Health reported that hostility increases a patient's risk of stroke. The effect is significant. In a seven-year study of more than 2,000 men, the scientists found that men who showed high levels of anger on standard tests of anger expression were two times more likely to have strokes than were their calm peers. Other factors such as age, smoking, high blood pressure, excessive alcohol consumption, diabetes, obesity and high cholesterol levels did not account for the increased risk.

Men do not have to retire to protect their health. They should, however, certainly eat right, exercise often and avoid smoking to keep their hearts healthy. They should have regular medical care and be sure their blood pressure and cholesterol levels are okay. But they should also seek a work environment that provides a healthy degree of autonomy and control without sacrificing social supports. At its best, work should be challenging without being stressful; it should also be balanced by a healthy amount of play. SA

The Author

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The Most Dangerous Occupations

Aircraft pilots, truckers and construction laborers make the top 10. Women would prefer to work at Microsoft

If you're destined to die on the job, odds are overwhelmingly good that you're a man. Although women make up nearly half of the workforce, they account for only about 8 percent of the 6,000 or so annual job-related fatalities tracked by the Bureau of Labor Statistics (BLS). Why this difference? The answer is less tightly linked to a male craze for death-defying occupations than one might think.

Bomb squad technicians, plague fighters, volcanologists—the list goes on—risk death routinely. But because few people are employed in these lines of work, the absolute number of casualties is quite small; thus, the BLS and other agencies do not include these data. Deaths rack up far more ominously among transportation workers, construction workers and other laborers. Those are not jobs that women typically occupy.

One explanation for this occupational gender gap, according to several studies, is that women have generally moved into those sectors of the job market in which employment has expanded. Writing in the April 1997 *Monthly Labor Review,* economist Barbara H. Wootton observed that between 1975 and 1995, job growth climbed fastest among managers and professionals, more than doubling for managers, for instance. Women now hold about half of all managerial and professional positions. During that same interval, growth was slowest for some more hazardous jobs such as laborers and farmers, and women gained fewer places in these occupations.

Based on the fatality rate for men and women combined, fishers and timber cutters hold the most dangerous jobs, although truck drivers sustained the highest number of deaths. Indeed, highway traffic accidents accounted for 22 percent of fatal work-related injuries and have increased in number nearly 20 percent over the past five years, according to the National Safety Council. Beyond this worrisome trend, the overall rate of fatal occupational injuries—4.7 per 100,000 employed—has decreased by about 10 percent over the same period. In general, both men and women are facing less danger of becoming a statistic. —*Kate Wong,* staff writer

ZIGY KALUNZY *Tony Stone Images*

JIM NILSEN *Tony Stone Images*

The 10 Most Dangerous Occupations

Occupation	Employed (in thousands)	Employment % Men	Employment % Women	Fatality Count	Fatality Rate*	Leading Fatal Events
Timber cutters	79	97.0	3.0	121	128.7	Felled tree
Fishers	47	95.7	4.3	58	123.4	Drowning
Water transportation	52	96.6	3.4	49	94.2	Fall from ship
Aircraft pilots	120	98.8	1.2	100	83.3	Air crash
Structural metal workers	66	100.0	0	45	68.2	Fall
Mining and other extractive occupations	145	98.7	1.3	75	51.7	Vehicle-related
Construction laborers	811	95.4	4.6	333	41.1	Fall
Taxicab drivers	248	91.7	8.3	100	40.3	Homicide
Truck drivers	3,075	94.3	5.7	857	27.9	Highway crash, jackknifing
Farm occupations	2,177	78.4	21.6	615	27.5	Tractor-related

SOURCE: Bureau of Labor Statistics. Data are from 1997.

*per 100,000 workers

by Glenn Zorpette, staff writer

The Mystery of Muscle

A little over two decades ago a grinning, oiled Arnold Schwarzenegger, with the motion picture *Pumping Iron*, hauled bodybuilding out of the dingy gyms and into the mainstream of U.S. popular culture. During more or less the same period, anabolic steroids started infiltrating bodybuilding, turning musclemen into big-jawed, moon-faced freaks, and strength-training machines began making weight training safer and more appealing to the masses.

The U.S. has not been the same since. Strength training has persisted as few movements have in recent U.S. history, reshaping popular views of physical beauty and male feelings of self-esteem. In 1994 an article in *Psychology Today* declared that "there seems to be emerging a single standard of beauty for men today: a hypermasculine, muscled, powerfully shaped body." Since then, the trend has only intensified.

In 1995 weight training replaced riding a stationary bicycle as the most popular kind of exercise among American adults. The same year the number of males in the U.S. who worked out with weights at least 100 days a year reached 11.6 million, up from 7.4 million in 1987, according to American Sports Data in Hartsdale, N.Y. And more recently, the market for dietary supplements aimed at weight lifters and bodybuilders has grown explosively, led by a chalky powder called creatine monohydrate [see "Sports Supplements: Bigger Muscles without the Acne," on page 52].

Although the number of women who regularly use weights has roughly tripled in the past decade, the superior ability of men to add muscle to their bodies has ensured that weight training remains inextricably linked to the male image and feelings of self-worth. And in recent years, several disturbing aspects of this link have become clear. Use of anabolic steroids is up, as are cases of muscle dysmorphia, a puzzling disorder in which abundantly muscled people see themselves as scrawny and become increasingly obsessed with weight training [see "You See Brawny, I See Scrawny," on page 54].

Along with the cultural appreciation of muscle has come a surge of work aimed at understanding the biology of muscles. The vast majority of researchers in this area are studying anatomical or physiological aspects of exercise related to aging, the effects of diet, dietary supplements and so on. A large group is also studying heart muscle tissue, a subject that bears strongly on cardiac diseases. Oddly enough, what might seem to be the most compelling issue in muscle science in this physique-obsessed era—the biochemistry of bulking up—has but a tiny band of full-time devotees.

Nevertheless, their research has yielded some impressive and even startling results of late. For example, researchers at the Royal Free and University College Medical School of University College London recently cloned a kind of hormone, which they call mechano-growth factor, that appears to be a significant link in the still largely mysterious ways in which muscle cells respond biochemically to mechanical stress by becoming stronger and thicker.

The University College researchers themselves view their discovery with a mixture of enthusiasm and uneasiness. On the one hand, the findings could be invaluable for treating muscular dystrophy and possibly age-related muscle loss. At the same time, the discovery seems likely to usher in a new age in performance-enhancing drugs, one that sports officials have anticipated with dread.

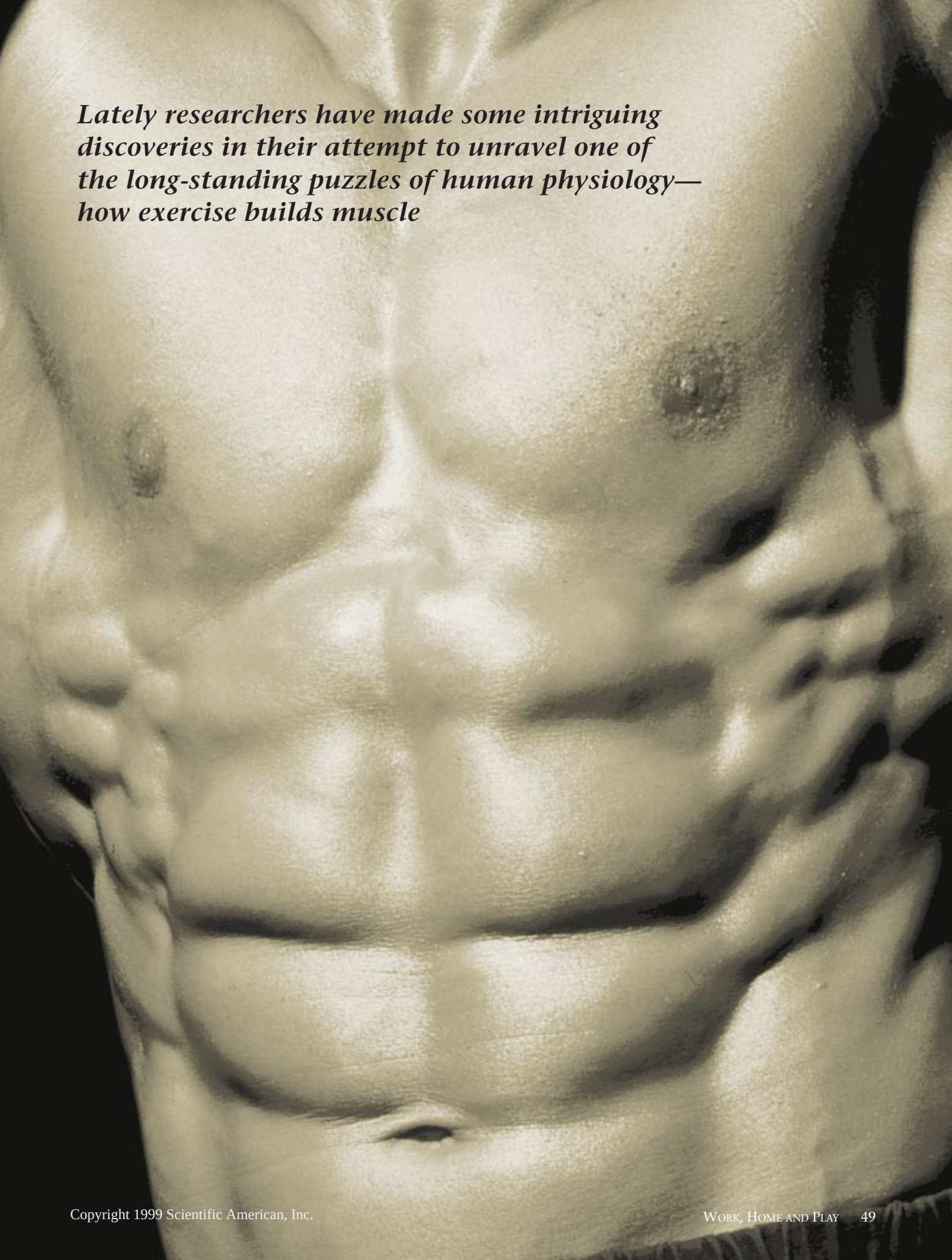
Stimulating the production of mechano-growth factor in specific muscles would increase their mass. Doing so would require only the injection of bits of human DNA into the muscles. Because the muscle cells would have already contained the DNA naturally, sports officials would find it difficult, if not impossible, to detect the injections. Thus, the development promises to create the ultimate muscle-building drug—one that, like anabolic steroids, could build muscles even without strenuous exercise.

"We've cloned the magic substance that makes muscles grow," says Geoffrey Goldspink, the leader of the University College group that identified and reproduced the growth factor. In the not too distant future, he adds, "American footballers and athletes in all countries will probably be using this method. It will be abused, I'm sure. It is a great worry to me."

How Muscles Contract

The recent findings at University College and elsewhere on skeletal muscle are the latest in a chain of discoveries stretching back at least to the 1950s. Researchers have laid out a detailed if incomplete understanding of skeletal muscle: what it is, how it works, how it grows and develops, and—most intriguingly—how it alters itself in response to exercise.

Although it is only one of three categories of muscle in the human body, skeletal muscle is what most people think of as "muscle." The other two kinds are cardiac muscle, which



Lately researchers have made some intriguing discoveries in their attempt to unravel one of the long-standing puzzles of human physiology—how exercise builds muscle

powers the heart, and smooth muscle, which lines the arteries and parts of the stomach, intestine, uterus and other bodily components (its relatively slow, sustained contractions move food through the digestive system, for example).

Groups of skeletal muscles contracting against a scaffold of bone, all coordinated by the nervous system, do the work of lifting, playing the piano, moving an eyeball or throwing a right cross. Muscle is the most abundant tissue in the body, a distinction that makes it the body's largest store of a variety of key substances, such as amino acids, which are the building blocks of protein. For this reason, among others, the consequences of muscle loss in the elderly go beyond frailty to include such problems as weakened immune systems.

Skeletal muscle cells, also known as muscle fibers, are rather unusual in many respects, not least of which is that they have multiple nuclei. They are also comparatively huge, at approximately 50 microns in diameter and up to tens of centimeters long. Most of the cells' cytoplasm (the gelatinous part outside the nucleus but within the membrane) consists of elements called myofibrils [*see illustration below*]. Organized by the hundreds or thousands inside the muscle fiber, myofibrils are often about the same length as the muscle cells but only one to two microns in diameter.

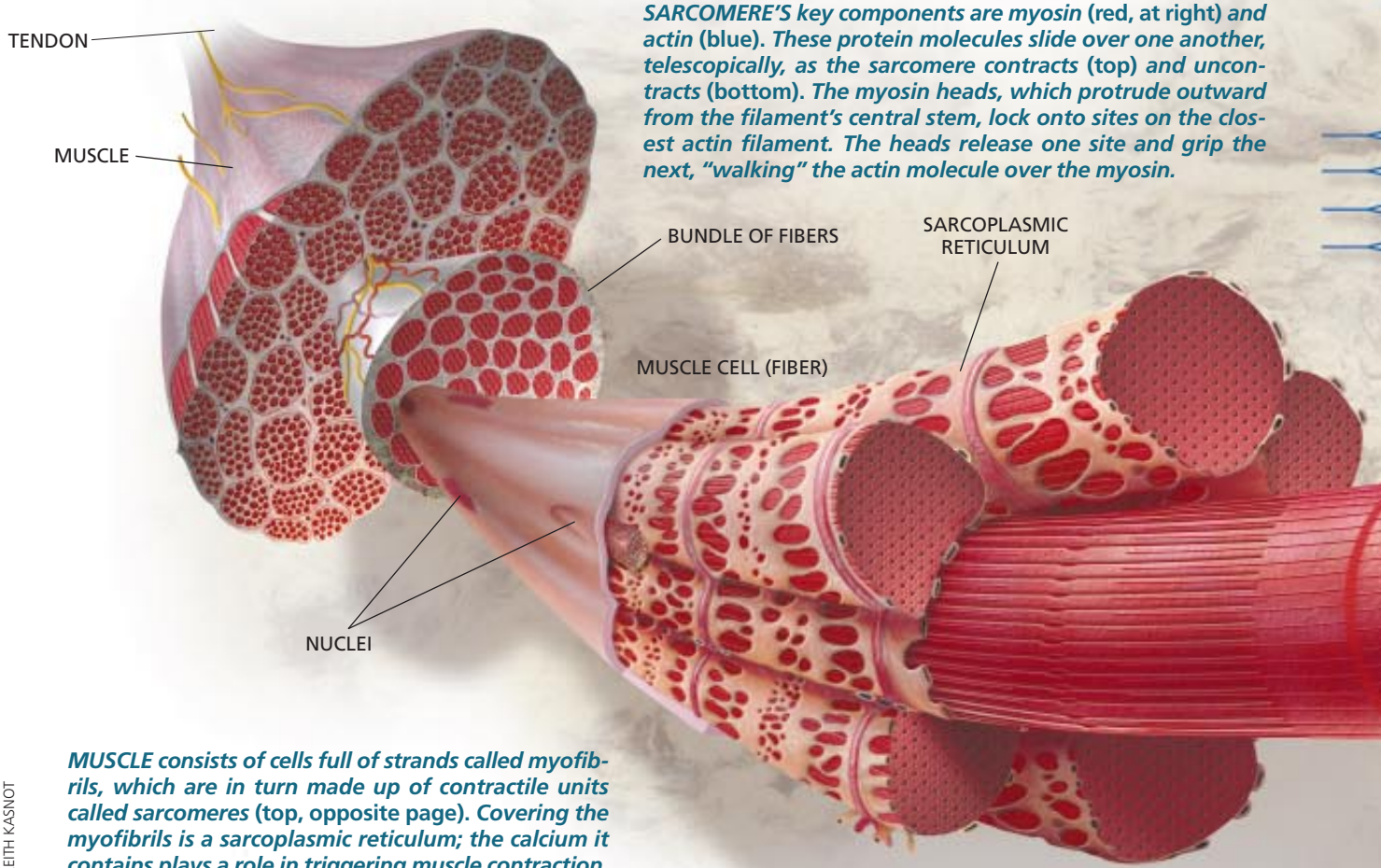
Myofibrils are the contractile elements of muscle. In other words, a muscle contracts—and does work—when the lengths of all its myofibrils shrink forcefully in response to nerve impulses. To understand how the myofibrils do this requires an understanding of yet smaller elements within the myofibrils. These components, called sarcomeres, are the contractile units of muscle; a myofibril contracts when all its sarcomeres do so. Sarcomeres are about 2.2 microns long and are linked end to end to make up a myofibril.

Like Russian nesting dolls, muscle's components keep getting smaller: within each sarcomere are two protein molecules, known as myosin and actin. It is the interaction of these two molecules, primarily, that makes a sarcomere contract.

Myosin, the most abundant protein in muscle, is shaped like a tadpole, with a large head and a long, thin tail. Many of these proteins make up what is known as a myosin thick filament, the central component of a sarcomere. In a thick filament the many myosin proteins are arranged with their tails bundled together, like a bunch of pencils held in a fist and with the heads sticking out to the side.

In the sarcomere the ends of the thick filament are surrounded by molecules of actin, also elongated and helical, and parallel to the myosin [*see illustration below*]. During muscle contraction, a sarcomere shortens like a collapsing telescope as the actin filaments at each end of the myosin thick filament slide toward the thick filament's center.

The motive force that pulls the actins inward is exerted by the myosin heads. Each myosin head locks onto specific sites on the actin molecule. The head "walks" the actin molecule over the bundles of myosin tails, step by step, by relinquishing its grip on one site on the actin and grabbing and pulling the adjacent site [*see illustration below, right*]. In effect, the myosin heads are like so many oars that, marvelously



SARCOMERE'S key components are myosin* (red, at right) *and actin* (blue). *These protein molecules slide over one another, telescopically, as the sarcomere contracts* (top) *and uncontracts* (bottom). *The myosin heads, which protrude outward from the filament's central stem, lock onto sites on the closest actin filament. The heads release one site and grip the next, "walking" the actin molecule over the myosin.

MUSCLE consists of cells full of strands called myofibrils, which are in turn made up of contractile units called sarcomeres* (top, opposite page). *Covering the myofibrils is a sarcoplasmic reticulum; the calcium it contains plays a role in triggering muscle contraction.

KEITH KASNOT

synchronized, paddle the actin filaments to move them.

The fuel for this molecular motor is adenosine triphosphate (ATP). In a contracting sarcomere, an ATP molecule combines with a myosin head and breaks down into adenosine diphosphate (ADP) and a phosphate ion. From this reaction comes the energy necessary to release the myosin head from the actin molecule, to move the head to the next binding site and to help pull the actin molecule that distance. The ratchetlike cycle can happen five times a second in a rapidly contracting muscle. As the cycles occur, various reactions convert the ADP back to ATP to keep fueling the contraction.

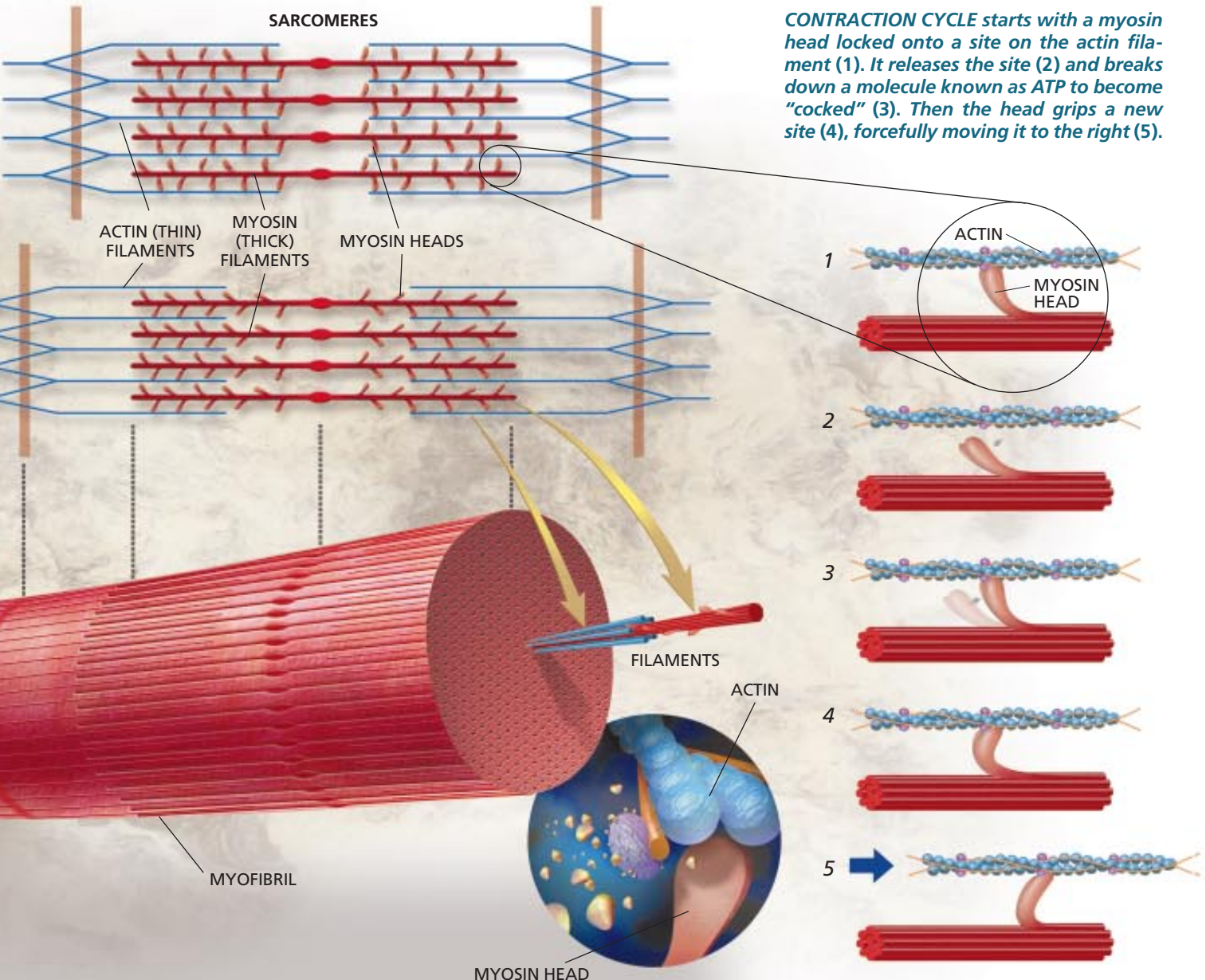
Three Kinds of Skeletal Muscle

Healthy adults have at least three main types of skeletal muscle cells, which differ primarily in the kind of myosin at the core of their sarcomeres. These three cell types, like the myosin variants they contain, are designated I, IIa and IIx (also known as IId).

Type I muscle cells are also known as slow fibers, because their kind of myosin converts ATP to ADP relatively slowly and derives energy from the reaction efficiently. Muscles that must contract repeatedly for long periods, such as those of the back and legs, are rich in type I fibers. For example, the soleus, which extends from the central calf area to the ankle, is almost entirely type I. It comes into play not only for walking and running but even for simply standing.

Type I muscle cells, which are critical for any kind of aerobic exertion, have large numbers of mitochondria, specialized cellular functionaries that use nutrients and oxygen to convert ADP back into ATP. Type I muscle fibers are therefore the narrowest, because their constant need to feed the mitochondria with nutrients and oxygen and to remove their waste limits how wide the fiber can be. These fibers also have a great deal of myoglobin, a protein that acts as a short-term store of oxygen for the cells. (The leg and thigh meat of a chicken, rich in type I muscle, gets its dark coloration from the myoglobin.)

The other two myosin varieties are "fast." They predominate in muscles, such as those of the biceps, capable of more powerful but less frequent contractions. One of the key necessities for sustaining high-power output even briefly is a method of rapidly replenishing ATP, the cells' energy source.



Sports Supplements:
Bigger Muscles without the Acne

Steroid alternatives have become an $800-million market

Weight lifting used to be pretty simple. You went to a dingy, seedy room on the other side of the railroad tracks, you put on ragged cotton clothes, and you hoisted, heaved and herniated to your heart's content. Of course, in those days, Burt Lancaster and Jack LaLanne were paragons of physical masculinity.

Today better understanding of nutrition and muscular development has complicated life for weight lifters. Most notably, it has given rise to so-called sports supplements, a category comprising hundreds of different pills, powders and the odd potion that supposedly enhance physical performance. Last year Americans spent some $800 million on sports supplements, not including sports nutrition bars and electrolyte replacement drinks, according to Grant Ferrier, editor of the *Nutrition Business Journal* in San Diego.

NAJLAH FEANNY *SABA*

***SPORTS SUPPLEMENTS** line the walls at the Elite Value Center in New York City, where acting student John Ostensoe, 26, shopped recently.*

Sports supplements aimed at weight lifters are doing particularly well, thanks in part to clinical trials that have proved that at least a few of the supplements actually do help increase strength and muscle mass or promote the repair of muscle tissue.

"Supplements are a tool for making an exercise program work," says Bill Phillips, the relentlessly motivational 34-year-old CEO of Experimental and Applied Sciences, the largest marketer of sports supplements. "And when an exercise program works, it is one of the most empowering things an adult can experience."

At best, supplements provide the elevated energy levels and possibly the tissue-repairing help that lets weight lifters lift a little more weight, do a few more repetitions or train a little more often. The muscle-mass gains possible are not on a par with those of anabolic steroids. But supplements have the advantages of being legal, much less expensive and a lot less harmful.

No two weight lifters seem to have the same supplement regimen. But the one thing almost all of them have in common is creatine, which accounted for $180 million of the $800 million spent on all sports supplements in 1998, according to Ferrier. Most weight lifters are also consuming some kind of protein supplement, such as whey powder or ordinary sports nutrition bars.

Creatine occurs naturally in the body. It plays a role in muscle contraction, which is energized by a molecule called adenosine triphosphate (ATP). When ATP breaks down, giving up one of its three phosphates, it releases the energy used by the muscle cell to contract. The small amount of ATP stored in a muscle is used up instantaneously during strenuous exertion. Fortunately, muscles contain creatine phosphate, which donates its phosphate and the necessary energy to replenish the ATP.

Eventually you tire out when, among other things, your supply of creatine phosphate dwindles. But by taking creatine supplements, weight lifters and sprinters can at least marginally increase the amount of creatine phosphate in their muscles, enabling them to exert themselves a little harder. Although no one has been able to prove that creatine has any harmful side effects, no study has lasted more than a few years.

The biggest seller in the prohormone category is 4-androstenedione, which became one of the longest and strangest household words in history after Mark McGwire's admission that he was using it. The substance is just one of a growing family of over-the-counter steroids; other products in this category include 5-androstenedione, 4-androstenediol, 5-androstenediol, 19-4-norandrostenedione and 19-5-norandrostenediol. Yet another product, DHEA (dehydroepiandrosterone), like 4-androstenedione, is often used by people seeking to boost their sex drive.

The main difference between these prohormones and traditional anabolic steroids is that the prohormones are converted in the liver and testes to testosterone, the body's key hormone for muscle building. Anabolic steroids, in contrast, are nothing more than synthetic versions of testosterone. Because of this hormonal action, prohormones can have mildly steroidal side effects, such as acne, a swollen prostate and hair growth in unusual places. Some evidence suggests that prohormones temporarily elevate testosterone levels, at least marginally, but no one knows if these higher levels translate into greater muscle mass. —*G.Z.*

Type II fibers have variable amounts of mitochondria, but they also exploit a much faster process, called glycolysis, to provide the energy the muscle needs. Basically, glycolysis releases energy for making ATP by breaking down sugars only partially but without need for oxygen.

The type II fibers differ mainly in their oxidative properties. Type IIa fibers have more mitochondria and are thus more similar to type I. Because of the extra mitochondria, type IIa can sustain an output of power longer than can the type IIx fibers, which are "faster," more powerful and more quickly fatigued.

Injections of genes will ***increase muscle mass—without exercise*** *and almost undetectably.*

The bodily distribution of the different muscle fiber types is not fixed. It depends on the body's regular activities, and it changes if they do. This ability of the body to alter itself is an important part of its complex, genetically based response to mechanical stressors and signals. Take an extreme example: a fitness enthusiast who gives up doing squat thrusts and begins training to run a marathon. According to Brenda Russell of the University of Illinois at Chicago, who did pioneering investigation in this area in the early 1980s, the runner would gradually replace much of the fast, type IIx fibers in his quadriceps and calves with the slower, more oxidative type IIa fiber. The change would occur because the nuclei of the muscle cells in his legs would stop specifying production of type IIx myosin and start prompting for the type IIa myosin. In more technical terms, the nuclei would stop "expressing" the gene that through a chain of events triggers the cell to assemble amino acids into the type IIx myosin. Instead the nuclei would express the gene that specifies the IIa type.

Bulking Up

Researchers know relatively little about how the body translates mechanical stresses into increased muscle mass. Recent findings, however, have shed light on parts of the process while generating some intriguing theories and a few controversies.

One of those areas of contention is whether the number of muscle cells in a body is fixed for life. Although a small group of researchers disagrees, the widely accepted view is that the number of muscle cells cannot increase significantly, because the cells cannot split apart to form completely new fibers. (Their multiple nuclei may make the process infeasible.) Because a muscle cannot produce more fibers, the only way it can grow in response to exercise is for the individual fibers to become thicker. This thickening can be thought of as the body defending itself against a mechanical stress by enlarging the structural members so that they can generate more contractile force.

With continued weight training, the type II muscle fibers grow ever thicker by adding more myofibrils. This thickening initially involves the longitudinal splitting of myofibrils into two daughter myofibrils, a process that occurs over and over if the mechanical stresses continue. Enormous amounts of myosin, actin and myriad other proteins are needed to create entirely new myofibrils. But the amount of protein, and therefore the number of myofibrils, that the existing muscle cell nuclei can help create and maintain is limited.

In cardiac muscle, that limit is absolute. In skeletal muscle, it is not. Scattered among the many nuclei on the surface of a skeletal muscle fiber are so-called satellite cells. They are largely separate from the muscle cell and, unlike it, have only the usual one nucleus apiece. Thus, they can replicate by dividing. In the mid-1970s Véra Hanzliková and her colleagues at the Czechoslovak Academy of Sciences in Prague discovered that these satellite cells proliferate in response to the stresses of muscle growth.

As they multiply, some of these cells remain as satellites on the fiber, but others, incredibly, become incorporated into it. Their nuclei become indistinguishable from the muscle cell's other nuclei. With these additional nuclei, the fiber is able to churn out more proteins and create more myofibrils. Most researchers now believe that this recruitment of satellite cells is a significant factor in the muscle growth that comes from weight lifting.

Satellite cells figure in another controversy: whether damage to muscles is necessary for enlargement (a phenomenon known as hypertrophy). A popular theory contends that it is: according to this view, rigorous exercise inflicts tiny "microtears" in muscle fibers. Calcium ions enter the ripped area, initiating biochemical cascades that break down the existing proteins to leave a less ragged gap. The tiny opening, meanwhile, releases a specific protein—the very same one that Goldspink has dubbed mechano-growth factor but that others have called hepatocyte growth factor or scatter factor. In the mid-1990s Richard Bischoff of Washington University found that at least in cultured cells, this growth factor attracts satellite cells to its source, which in muscle would be the damaged area.

Some of these satellite cells incorporate themselves into the muscle tissue and begin producing proteins to fill the gap. Significantly, the number of nuclei passing from the satellite cells into the damaged area of the fiber is greater than the number of nuclei lost when the gap opened up. As a result, in that part of the fiber, more protein can be produced and supported. Gradually, as more microtears are repaired, the overall number of nuclei grows—as does the fiber itself.

Muscle-Making Machinery

This "damage" model of muscle cell growth is by no means the only one that can explain hypertrophy; it is at best only one of many, perhaps dozens, of processes at work in exercise-induced muscle growth. For example, a fair amount of speculation, and at least a modest amount of research, focuses on the mechanical connections between muscle cells and surrounding tissue. These connectors are the tendons and the focal adhesion complex, a series of some 30 proteins that connects the cell's skeleton (the "cytoskeleton") with its exterior supportive "scaffolding," the extracellular matrix.

Mechanical stresses on the tendons and focal adhesion complex are believed to initiate intricate processes that affect the protein-making machinery of muscle cells. Understanding these theories requires some background on the machinery.

One of the key steps in the creation of a protein is transcription. It occurs in a cell's nucleus when a gene's information (encoded in DNA, the "blueprint" for protein production) is copied as a kind of molecule called messenger RNA

You See Brawny, I See Scrawny

Big bruisers with a self-image problem

The ascendance of muscle as a key ingredient of male allure has had ramifications both good and bad. Take the countless aging squires and he-men who've turned to weight training mainly out of vanity: they have unwittingly improved their metabolic rates, bone strength, connective tissue and other important bodily components. At the same time, though, a distressing self-image disorder—which afflicts men disproportionately—has become pervasive enough of late to be the subject of dozens of articles in the academic and general-interest press.

At first description, the malady seems almost comical: imagine a 250-pound bruiser with rippling, rocky muscles and a body-fat percentage hovering around 7.5. Now imagine that the guy thinks he is so scrawny that he only wears loose-fitting clothes to cover up what he sees as a shamefully skinny body. But muscle dysmorphia, as the condition is known, is not very funny. Like anorexia nervosa, the disproportionately feminine disorder to which it is often compared, muscle dysmorphia can lead to complete social withdrawal and, in the most extreme cases, to suicide.

Muscle dysmorphia and anorexia are both part of a larger group of disorders in which the afflicted fixate despairingly on a facial feature, body part or their entire bodies. Harrison G. Pope, Jr., the psychiatrist who has done more than anyone else to uncover and describe the condition, says you can spot muscle dysmorphics by their "pathological preoccupation with their degree of muscularity." Pope, who is probably the only Harvard Medical School professor who can squat 400 pounds, pumps iron six days a week. He himself does not have muscle dysmorphia, he says. (But he did ask Scientific American Presents not to disclose his height, weight and body-fat percentage.)

In his studies with volunteers recruited from Boston-area weight rooms, Pope has encountered people "who had not dined in a restaurant in years, because they could not tolerate eating something for which they did not know the precise protein, fat and carbohydrate content." Although use of anabolic steroids is not at all universal among muscle dysmorphics, Pope found "many who would persist in taking anabolic steroids or drugs for fat loss even if they were getting pronounced side effects." Such as? Well, high cholesterol, hard arteries and teeny testicles in men, and beards and rich baritone voices in women.

The anecdotes go on. Pope and his colleagues have encountered dysmorphics who left high-powered jobs in law or business because their careers were taking away too much time from the gym. They've come across muscle dysmorphics in the 230- to 290-pound range who were so ashamed of their puniness that they hardly ever left their homes, preferring instead to adhere to an indoor regimen of weight lifting in the basement interrupted mainly for periodic protein consumption. The underground nature of the condition makes it virtually impossible to estimate how many people have it, Pope says.

How do you distinguish muscle dysmorphia from good old hormone-fueled enthusiasm? One of Pope's experiences suggests a method. To recruit volunteers for a study a couple years back, he put up handbills in Boston-area weight rooms seeking out people who could bench press their own weight 10 times. Hardly any of the respondents had dysmorphia. He then repeated the procedure, again asking for people who could bench their own weight 10 times—but who also thought they were "small." This time, almost all the 24 respondents were dysmorphic. —*G.Z.*

DAVID TILLINGHAST

(mRNA). The mRNA then carries this information outside the nucleus to structures called ribosomes, which assemble amino acids into the protein—myosin or actin, say—specified by that gene. This latter process is called translation.

But what triggers transcription? For muscle and many other tissues, the answer is an array of extraordinarily complex biochemical pathways involving a dizzying number of proteins. Some of the key proteins are sex hormones, such as testosterone, thyroid hormones, insulinlike growth factors, fibroblast growth factor and transcription factors. Some of these proteins are produced in organs such as the liver and circulate throughout the body; others are created locally, in specific muscle tissue, in response to exercise or stretching of that tissue.

These hormones, growth factors and transcription factors act in a variety of ways, often in conjunction with one another, to promote protein production. For example, sex hormones appear to work with particular transcription factors to turn on certain genes. These transcription factors are generally in the cytoplasm or in the nucleus itself. Their combination with a testosterone molecule enables them to bind to locations on the chromosome, called promoter regions, that "turn on" a nearby gene and trigger transcription. Because anabolic steroids are merely synthetic versions of testosterone, this pathway is the one they initiate and exploit to build muscle.

Other factors work by doubling up. In 1995 Frank W. Booth and James Carson of the University of Texas–Houston Health Science Center found that when two identical molecules of serum response factor combine in a muscle cell, they form a kind of biochemical "key." The keyhole in this case is a gene in the nucleus. When the double molecule attaches itself, the gene becomes active and begins producing more mRNA for a certain protein. In this case, the protein is actin. "It's a pretty novel finding," Booth says. "It's only the seventh transcription factor described in hypertrophy."

Other pathways are more complex. Some crucial ones begin with the binding of growth factors to receptors. Receptors are specialized proteins that poke through a cell's membrane. When the part outside the cell binds with a specific molecule, it activates a series of chemical reactions inside the cell. For example, the binding of a growth factor to a receptor activates cascades of enzymes, called kinases, that modify other proteins in the cytoplasm that in turn bind to promoter regions on the chromosome and otherwise regulate the expression of genes.

One of the most important growth factors is insulinlike growth factor-1 (IGF-1). During the first few years of life, IGF-1 produced by the liver circulates throughout the body, rapidly expanding essentially all its muscle fibers. The amount of this circulating, liver-produced IGF-1 eventually declines sharply, ending the early-life spurt. For hypertrophy, the free ride is then over, and only exercise can add (and, eventually, merely maintain) muscle mass. According to University College's Goldspink, IGF-1 and other growth factors continue to play a major role, but they are released only locally in muscle during exercise. For example, IGF-1 concentrations are high around muscle-fiber microtears caused by exercise.

According to Goldspink, mechano-growth factor is one of the most important of these locally acting factors. The University College researchers cloned the gene that leads to the production of mechano-growth factor, using a standard biological technique to insert the gene into muscle cells. The gene for mechano-growth factor was incorporated into a plasmid, a circular piece of DNA, which acted like a teeny Trojan horse. Injected into a mouse's leg, the engineered gene infiltrated muscle cells and induced them to produce more of the growth factor. Within two weeks, the muscle mass in the mouse's leg increased by 15 percent—without exercise.

Goldspink's interest is in treating degenerative diseases such as muscular dystrophy. But he notes ruefully of his accomplishment: "This will be the way they reshape athletes in the future."

Mechanical-Chemical Link

Researchers know very little about the mechanical-chemical link that translates stress on muscle fibers into locally higher levels of mechano-growth factor and countless other biochemicals. But earlier this year Booth and Martin Flück, now at the University of Bern in Switzerland, made a significant discovery. The finding involved focal adhesion kinase, one of the 30 proteins in the focal adhesion complex that connects the structural elements inside cells with the matrix outside them. In muscle cells undergoing hypertrophy, the researchers learned, the amount of this enzyme doubled. "It could be the mechanical-chemical link," Booth speculates, "because the stress on the kinases could release signaling factors, which could go to the nucleus to trigger the production of more messenger RNA" and therefore more protein.

Anabolic steroids combine with transcription factors to turn on genes and make more protein.

Perhaps more important, the kinase could also trigger a cascade of biochemical reactions that ultimately signal ribosomes directly to produce proteins. These proteins would be the product of translation alone, without any immediately prior gene activity in the nucleus. "We think, and a lot of others think, that the initial response when a muscle is loaded is to increase translation," Booth says. He adds that this more efficient process would, instead of transcribing new mRNA "templates" from the genes, simply reuse existing mRNA already in the cytoplasm to direct protein production.

Although their numbers are small, researchers studying the cellular and molecular biology of skeletal muscle are making important gains as they attempt to unravel the complex mystery of muscle. Over the next decade or so, their work will produce a more complete picture of how one of the most basic of human systems grows, develops and alters itself in response to changing stimuli. In addition to intellectual satisfaction, there will almost certainly be treatments, if not cures, for a host of degenerative diseases.

And if the history of anabolic steroids is a guide, there will also be a new kind of drug abuse problem—one that will be exceedingly difficult to monitor. Science will soon bring high-stakes athletics to a troubling threshold, beyond which the ground rules of competition could be forever altered. SA

"Type T" personalities push themselves to the brink of death for the neuronal rush or to relieve the ennui of modern life

Extreme Sports,

by Glenn Zorpette, staff writer

Sensation Seeking and the Brain

JESS STOCK *Tony Stone Images*

Deep underwater off Grand Cayman Island, I hovered over an ethereal, sandy tableau that sloped steeply away into an inky void. I had dipped into the upper edge of a twilight world seen by relatively few scuba divers, where the abundant hard corals of shallower water begin giving way to a sparser assortment in which large soft corals predominate. Off to my left, a big eagle ray flapped slowly and serenely, its white-spotted black body undulating against the dark-blue background of the abyss.

I glanced at my depth gauge, saw that it read 200 feet (61 meters) and grinned. Breathing a mixture of helium, oxygen and nitrogen from two of the four large tanks strapped to my body, I was beyond the depths that could be visited safely with ordinary scuba equipment and techniques. I was oddly, ineffably elated.

Over the previous eight days I had made half a dozen dives to depths between 52 and 58 meters, to satisfy the requirements of two courses in technical diving. During all those dives I breathed ordinary air, and the high nitrogen content sometimes brought on a strange mix of drunkenness tinged with a vague unease, as though different parts of my brain were in a struggle over whether enjoyment or terror should prevail. This nitrogen narcosis was most intense on the deepest dives. As a reward for enduring them, my instructor, Kirk Krack, suggested a final dive with the much less narcotic helium mixture, so that I could experience the joy of being deep underwater with a clear head.

As it happened, the day of the dive was my 37th birthday. But down in that sunken realm, I felt very much like an adolescent boy getting away with something naughty. Looking around, I became an awestruck visitor to a beautiful, forbidden zone, to which only knowledge, experience and technology could grant access. I achieved a kind of focus that only the desire to survive can instill. The cares, petty worries and job stresses of my terrestrial life were, at least for the moment, in a different world.

I'm not alone. Fueled in part by television, a few glossy magazines and some best-selling nonfiction books, extreme sports have managed to seize and hang on to at least a sliver of the popular attention span. The various coteries of practitioners are overwhelmingly male, as is the larger group that follows the exploits of the top stars.

Psychologists view an affinity for extreme sports as a form of sensation seeking, a category whose other entries are mostly disturbing—alcoholism, drug addiction, compulsive gambling, reckless driving, and some kinds of violent criminality and suicide. Indeed, as recently as the 1950s the profession saw sport parachutists, mountain climbers and other adrenaline junkies as indulging self-destructive urges and unconscious death wishes.

Because their passions do not disrupt society, extreme sports enthusiasts have not had nearly the kind of scientific scrutiny that has been focused on other sensation seekers. Nevertheless, in recent years a few psychologists have come up with more sophisticated explanations for the behavior, ones that are now largely free of references to pathology.

Temple University psychologist Frank Farley, for instance, identifies people who crave novelty and thrills as "Type Ts." Farley also labels them as either intellectual (examples include mental iconoclasts such as Albert Einstein and Pablo Picasso) or—in the case of extreme sports devotees—physical. Farley further classifies extreme sports people as "Type T positive physical" to separate them from, say, barroom brawlers, whom he refers to as "Type T negative physical."

Farley and other psychologists have also distinguished a variety of motivations that prompt people to take up this kind of activity. There is the old saw about feeling most alive when closest to death; melodramatic though that may sound, many participants do speak of heightened awareness and stimulation accompanying a dangerous excursion. More generally, most want to know the limits of their mettle and experience deep satisfaction after pushing themselves to a new milestone.

BRET GILLIAM

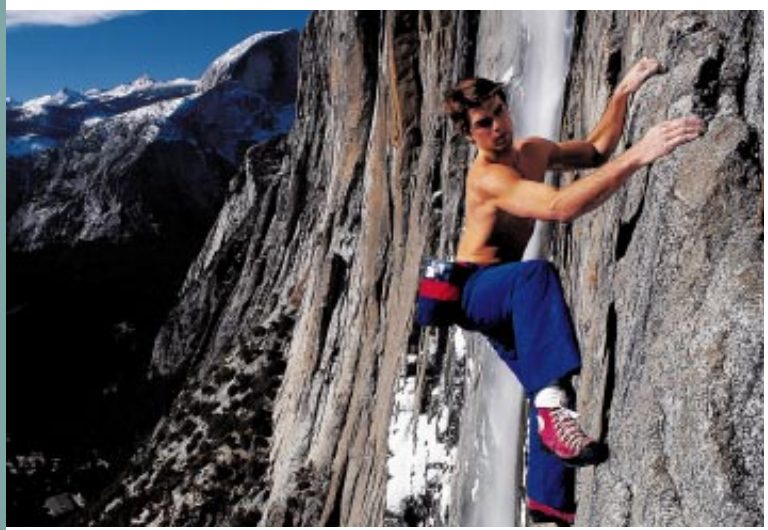
TECHNICAL DIVING

Another factor for some is a feeling of restlessness or even rebellion in the First World societies whose endless suburbs, comfortable routines, ubiquitous television and often oppressive liability laws seem to have created a way of life that is safe but deadening and culturally homogeneous and bland.

A minority of people, mainly otherwise mild-mannered men, appear to pursue extreme sports mainly to impress their friends or co-workers. And a smaller group of "counterphobics" engage in risky pastimes out of an almost obsessive agenda to confront deeply rooted fears. But other than these categories of people, participants report experiences pleasurable enough to compel them to engage in the activity over and over again. This fact suggests an underlying neurochem-

ical basis for the behavior, and indeed neuroscientists have begun identifying one.

Their studies have so far emphasized three neurotransmitters, small molecules that carry signals from cell to cell in the brain. Signaling occurs when a change in electrical potential causes one cell to release a neurotransmitter, which quickly defuses to a receptor on an adjacent cell. The receptor is a protein on the surface of a cell that binds specifically to the neurotransmitter. Each neurotransmitter can combine with



GALEN ROWELL

FREE SOLO CLIMBING

different types of receptors, which react characteristically when they bind to the neurotransmitter.

The three neurotransmitters implicated in sensation seeking are dopamine, which is associated with intensely pleasurable feelings; serotonin, linked to many types of extreme behavior; and norepinephrine, a key player in the "fight or flight" response. The levels of all three in the brain are regulated by an enzyme called monoamine oxidase (MAO). Dennis L. Murphy, a neuroscientist at the National Institute of Mental Health, found in 1980 that sensation seekers generally have low levels of MAO. Because MAO helps to break down and inactivate levels of dopamine, serotonin and norepinephrine, low MAO means higher levels of those neurotransmitters. And according to one speculative theory, people with high resting rates of the neurotransmitters need comparatively more stimulation to become aroused.

More recent theories have focused on the levels of the brain's receptors, rather than of the neurotransmitters. According to Kenneth Blum, a psychopharmacologist, the levels of two of the five receptors for dopamine are key "controlling factors" in sensation seeking. He says that people who have smaller numbers of these two receptors, designated D_2 and D_4, must spend more time stimulating the receptors with thrill-released dopamine to get a reasonable ration of excitement in their lives. Serotonin is important, too, he adds, because it stimulates the release of neurotransmitters called endorphins, which inhibit others called GABA, which finally allows the release of more dopamine.

Men are far more likely to have this neural need for excitement; the reason is a result of hundreds of thousands of years of evolution [see "Darwinism and the Roots of Machismo," on page 8]. Some psychologists contend that sensation seekers were crucial to primitive societies, because they could be counted on to reconnoiter areas no one else would visit, taste things that no one else would eat and pursue animals others would just as soon let alone.

Much of the thinking on the psychobiology of extreme sports is speculative, because most studies of the brain chemistry of humans are done indirectly. Moreover, there isn't even much agreement on what constitutes an extreme sport. But a thumbnail review such as the one offered below turns up a few consistencies. One is that most extreme sports evolved from existing pastimes as top practitioners pushed beyond the confines of the sport, oftentimes by borrowing equipment or methods from related disciplines.

These sketches might therefore be seen as snapshots of a work in progress. Its creators may think they are merely satisfying their own urges, but science suggests they are using the expanded technological opportunities of the late 20th century to respond to ancient, evolutionary motives. In time, these people—male and female—may give us more insights into the brain, evolution and why men are the way they are.

Technical diving

WHAT IT IS: A form of scuba diving that exploits technologies and techniques from commercial, cave and military diving to permit excursions to depths below 39 meters.
NUMBER OF REGULAR U.S. PARTICIPANTS: Roughly 10,000.
SPECIFIC DANGERS OF THE ACTIVITY: Decompression illness; oxygen toxicity; drowning after becoming lost in an enclosed environment, such as a cave or wreck.
FATALITY RATE: In 1998, 10 or 11 U.S. divers perished during technical dives, according to Joel Dovenbarger, vice president of medical services for Divers Alert Network in Durham, N.C.
THE "MOUNT EVEREST" OF THE ACTIVITY: The sunken ocean liner *Andrea Doria*, which sits in 73 meters of water off Nantucket Island, Mass. Even veteran divers have been overcome by the combination of strong currents, poor visibility, cold water and the wreck's labyrinthine interior, which presents many opportunities to become disoriented. (In the summer of 1998 three divers died on the wreck.)
LEGENDARY FIGURE, DECEASED: Sheck Exley, a veteran of 4,000 cave dives, died in 1994 during a 298-meter descent into a vertical cave in east-central Mexico.
LEGENDARY FIGURE, ALIVE: Tom Mount, a cave-diving pioneer and chairman of the International Association of Nitrox and Technical Divers. Mount has logged more than 10,000 dives, including an excursion to 145 meters off Andros Island in the Bahamas.

Free solo climbing

WHAT IT IS: Rock climbing without safety ropes or any other protective hardware.
NUMBER OF REGULAR U.S. PARTICIPANTS: Fewer than 2,000, estimates Jed Williamson, president of Sterling College and editor of *Accidents in North American Mountaineering*, an annual report published by the American Alpine Club.
SPECIFIC DANGERS OF THE ACTIVITY: Falling.
FATALITY RATE: About one every three or four years, according to Williamson.
THE "MOUNT EVEREST" OF THE ACTIVITY: Yosemite National Park's Half Dome, a 600-meter climb.

LEGENDARY FIGURE, DECEASED: Dan Osman, who died in 1998 while attempting a roped free fall from Yosemite's Leaning Tower, a 365-meter-high granite wall.
LEGENDARY FIGURE, ALIVE: Peter Croft, whose 450-meter ascent of the Astroman route on Washington Column in Yosemite still has not been repeated.

Extreme skiing

WHAT IT IS: A combination of mountaineering and skiing, it involves descents of high, rugged, very steep slopes reachable only by climbing.
NUMBER OF REGULAR U.S. PARTICIPANTS: 15, according to Dean Cummings, winner of the 1995 World Extreme Skiing Championship. A related activity, free skiing, includes other forms of aggressive skiing and has roughly 5,000 devotees in the U.S., according to Lhotse C. Merriam, vice president of the International Free Skiers Association.
SPECIFIC DANGERS OF THE ACTIVITY: Being buried by an avalanche; falling while climbing or skiing.
FATALITY RATE: Between 1993 and 1997, 25 "backcountry" skiers were killed in the U.S., according to Jim Frankenfield, director of the Cyberspace Snow and Avalanche Center; almost all could probably be considered free skiers.
THE "MOUNT EVEREST" OF THE ACTIVITY: Mount McKinley's Wickersham Wall, with its 4,000-vertical-meter drop and average pitch in excess of 40 degrees.
LEGENDARY FIGURE, DECEASED: Trevor Petersen, who died in 1996 in an avalanche in Chamonix, France.
LEGENDARY FIGURE, ALIVE: Doug Coombs, winner of the World Extreme Skiing Championship in 1991 and 1993.

BASE jumping

WHAT IT IS: Parachuting off tall buildings, bridges, sheer cliffs and the like, often at night. (BASE stands for "buildings, antennas, spans and earth.")
NUMBER OF REGULAR U.S. PARTICIPANTS: Fewer than 1,000.
SPECIFIC DANGERS OF THE ACTIVITY: "Overdelaying" opening of the chute.

KEN FISHER *Tony Stone Images*

BASE JUMPING

FATALITY RATE: Approximately 45 people have died since 1980, according to Frank Gambalie, an avid jumper.
THE "MOUNT EVEREST" OF THE ACTIVITY: Many newcomers strive to earn their "BASE award" by making at least one jump off an object in each of the four categories.
LEGENDARY FIGURE, DECEASED: Bob Neely, who died in 1998 jumping off a 381-meter tower in Lee County, Florida.
LEGENDARY FIGURE, ALIVE: Dennis McGlynn, who has made close to 800 jumps, including leaps from cable cars, lighthouses and smokestacks.

DAVID MADISON

DOWNHILL MOUNTAIN BIKING

Downhill mountain biking

WHAT IT IS: Time-trial race, generally down a ski slope in summer. Average time is about five minutes, during which competitors can hit speeds as high as 105 kilometers per hour (65 miles per hour).
NUMBER OF REGULAR U.S. PARTICIPANTS: A total of 4,666 people competed in the six national championship races held last year by the National Off-Road Bicycle Association (4,088 of these competitors were men).
SPECIFIC DANGERS OF THE ACTIVITY: Losing control of the bike; being thrown from it.
FATALITY RATE: Fewer than one a year, according to Patrice Quintero, communications director for NORBA.
THE "MOUNT EVEREST" OF THE ACTIVITY: The Kamikaze on Mammoth Mountain in Mammoth Lakes, Calif.
LEGENDARY FIGURE, DECEASED: Jake Watson, who was thrown from his bike during a practice run near Bakersfield, Calif., on March 12 of this year and died after hitting a boulder.
LEGENDARY FIGURE, ALIVE: Missy Giove. She was World Cup champion in 1996 and 1997, world champion in 1994 and the top finisher in nine U.S. races. (The premier male rider is John Tomac, who has won more races than any other competitor.) SA

Spokes Man for a Hard Problem

by Steve Mirsky, **staff writer**

The scientific evidence suggests that

To paraphrase the old song by Queen, "I want to ride my bicycle, I want to ride my bike. I want to ride my bicycle, but Irwin Goldstein doesn't like." Perhaps that's too strong. Goldstein, co-director of the Urology Research Laboratory at the Boston University School of Medicine, really has nothing against biking, although when I called him the first thing he said was, "I hope you're not biking." In fact, it is not the act of riding itself but the standard bike seat he has something against. He thinks that most men also have something against the seat—their perineum, the delicate area between the scrotum and the anus that contains the nerves and blood vessels that make erections possible.

Goldstein believes that conventional bicycle seats, with that narrow nose up front, may be making large numbers of men impotent by causing constant minor trauma to the perineum. He is on a crusade to arouse, if you will, what he calls "perineal phobia."

Most men have given plenty of thought, probably much too much in fact, to their penises and testicles. But few pay much attention to the perineum. Well, here's a flash: if you want running water and electricity, you had best make sure the plumbing and wiring are in order. "We pay very little attention to 'perineal health,' which is the other phrase I use," Goldstein says. "We play a sport and wear helmets and shoulder pads and elbow pads and gloves and kneepads and whatever else you think of, but there's absolutely no concept given to protecting the perineum from injury. It's high time we change that."

When I used to play baseball as a teenager, for example, I wore a cup that protected the goods, or so I thought. Little did I know that my perineum, protected from impact by only a thin layer or two of cotton clothing, was a sitting duck. One bad hop all those years ago and I might still be walking funny. And now what a shock to learn that when I became a serious cyclist 11 years ago at the age of 30, I may have endangered my perineum even more than when I hopped fences between houses to deliver papers as a kid.

Although Goldstein has been warning people about bicycles since the 1980s, the big impotence scare went through the riding community in 1997, when *Bicycling* magazine published an article about Goldstein's ideas. Alongside it was a report by Ed Pavelka, a former executive editor of the magazine, who owned up to the fact that he was not quite the man he used to be following a year in which he logged some 21,000 miles on the bike, about 7,000 more than his usual annual output and more odometer ticks than a lot of cars see in a year.

Pavelka went to Goldstein for tests that revealed a specific kind of blood vessel damage that Goldstein had seen in other cyclists. Obviously, there exists potential for serious injury if the perineum traumatically encounters the top tube, the horizontal metal bar that connects the front and back halves of the bike, another part of the bike's anatomy that Goldstein despises. It is the piece, ironically enough, that is missing in traditional women's bikes.

Goldstein and his colleagues did a study that found that a 150-pound man who suddenly lands on that top tube only inches below him might experience 500 pounds of force, a thought that should make you sleep in a fetal position for a few nights. Smacking hard into the seat nose after plunging

into a pothole is another frightening possibility. But in examining numerous impotent cyclists, Goldstein concluded that the same kinds of blood vessel insults he saw in traumatic injury were plaguing his cyclist patients who merely rode a lot, people like Pavelka. "The recurring minor traumatic episodes from bumps, from minor falls to the perineum, can lead to the same dysfunctions," Goldstein expostulates.

In a recent study, he found some provocative differences among cyclists and runners, the latter serving as a control group of active, athletic types who flatten their arches instead of their perineal arteries. Cyclists had about four times the impotence rate of runners, although both groups experienced a low incidence, about 4 percent versus about 1 percent. (Note to female readers or their male friends: the study also found more "clitoral numbness, difficulty urinating and diminished ability to achieve orgasm" among women cyclists as compared with runners.)

too much time in a bike saddle may leave your sex life in ruins

Here's a secret among cyclists that may explain part of the difference: some riders, even long-distance ones, are fat, which can be a risk factor for impotence. Actually, with the skintight Lycra outfits cyclists wear, the occasional potbellies really aren't a secret. And there was twice the rate of high cholesterol among the cyclists in the study compared with the runners. Nevertheless, Goldstein's numbers did further raise my eyebrows, if not any other parts of my anatomy.

I then dove into the medical literature, looking for other accounts linking cycling and impotence. To my surprise, such reports date back to at least 1975. A 1989 case study published in the *British Medical Journal,* for example, documents impotence in a 27-year-old who continued riding even after "severe perineal pain" that forced him to stop briefly only to find that "his penis was completely shriveled and had lost all sensation." Advice: pain, numbness and shriveling are nature's ways of telling you to take a ride in the sag wagon, the vehicle that collects fallen bikers. A 1985 study in the *American Journal of Sports Medicine* followed 132 riders over a 500-mile, eight-day ride. Some 45 percent experienced palm numbness, and 32 percent felt groin numbness. The authors noted that the hand discomfort was "relatively unimportant" but that groin numbness was "more important" and had driven 2 percent of riders off their bikes. After all, you have two hands.

When I first heard about the impotence issue, I was skeptical. I was averaging about 2,000 cycling miles a year, and I could produce witnesses to my perineal health. But I *had* experienced some numbness during rides. Naturally, the subject gets little discussion among biking buddies. "Hey, Peter, is your penis numb?" is a real conversation stopper. In fact, in 1989, after my first century—the 100-mile ride of passage among serious riders—I had a bit of numbness for more than 24 hours. It definitely got my attention. So I make a point of riding out of the saddle much more, especially when I see an obvious rough spot ahead. I have also made some minor adjustments in seat angle and in sitting position to put more weight on the bones of the backside. Numbness became a rarity, even during four subsequent century rides, and I'm out of the saddle at the first tingle. Because Goldstein found that arterial compression caused by jamming a bike seat into the perineum can block blood flow by as much as two thirds, not to mention the potential for damaging those delicate nerves, it turns out that I have been unwittingly practicing good preventive medicine. I now believe that cycling, which most likely prevents a lot of impotence by improving cardiovascular fitness, is nonetheless probably causing some cases, too.

The bottom line, if you will, is to ride smart. Although Pavelka loved cycling, the possibility of an erection-free future got his attention. "My first reaction was that I had to quit riding until I get this thing straightened out," he said, being both figurative and literal. He eschewed riding totally for a short while, experimented with different saddles and then rode a recumbent bicycle for much of 1997. The recumbent puts the rider in a full seat and puts the perineum completely out of harm's way. That change was a smart one: although nerve damage seems harder to treat, blood vessel problems appear to respond well to various treatments, including natural healing. The time off seems to have let nature do some damage control, and Pavelka is now back in the saddle. He also rides his bike. SA

PHOTOGRAPHS BY DAN WAGNER

STANDARD BICYCLE SEAT **(far left)** ***may contribute to some impotence among bicyclists. New alternative seats, such as a noseless model*** **(center left),** ***offer an alternative to recreational riders. Racers and other performance cyclists need the nose, as they press against it with their inner thigh when leaning into turns, and so may opt for a model with a cutout designed to remove the pressure from their perineum*** **(center right).** ***The optimal design, according to physician Irwin Goldstein, would be like a toilet seat, with support on the perimeter and no contact at all with the perineum. Racers, however, would still be faced with steering considerations.***

Impotence in the Age of Viagra

by Arnold Melman

Just as the birth-control pill ushered in the sexual revolution for many women, Viagra has brought about its own revolution for men. Since the introduction of the drug last year, millions of men have sought and received prescriptions of Viagra for the treatment of impotence, which doctors commonly refer to as erectile dysfunction. The rush for this medication and physicians' willingness to dispense it mark a sea change in how people view the condition, which decades ago was considered to be mainly of psychogenic origin—in other words, "it's all in your head."

This change has significant impact for the approximately 10 percent of the male population who will at some point in their lives face the complete inability to achieve or maintain an erection. This condition, which becomes more prevalent with age, has the effect of making sexual intercourse difficult, if not impossible. Although proved medical interventions have been available for more than 20 years, recent advances in the understanding of the processes that lead to an erection have spurred new treatments and promise even more targeted therapies in the future.

Before the advent of modern therapies, erectile dysfunction was often treated through psychoanalysis, when treated at all. Now many cases can be diagnosed as having organic causes, including nerve damage, hormonal imbalances and vascular diseases. The shift in diagnoses from psychogenic to organic has moved the primary responsibility for treating patients from psychiatrists to urologists. A second shift has recently taken place, spurred by the introduction of Viagra: family and general practitioners and internists now treat, with a simple prescription, most cases of erectile dysfunction in this country. A third change may take place in the future: with the aging of our population, geriatricians may become most responsible for treating the condition.

Although our understanding of the penis's erectile mechanism allows us to treat the organic causes of dysfunction in many ways, Viagra has become a catch-all cure. The famous blue pill is now the treatment of choice in approximately 95 percent of erectile dysfunction cases. This development raises some concerns: in many cases, other treatments aside from Viagra may be safer and just as effective. But on the positive side, Viagra has brought impotence out of society's closet and changed the way men and their doctors confront the condition.

Penile Anatomy

To understand the causes of erectile dysfunction, one must first know something about the anatomy of the penis. The organ's functions, of course, are to enable urine to exit the body and, when rigid, to help introduce sperm into the vaginal canal. An erection, however, is not absolutely necessary for impregnation of a female partner, because orgasm and ejaculation can occur in a semirigid state. The penis contains three well-vascularized cylinders of spongy tissue: the two corpora cavernosa and the corpus spongiosum [*see illustration on page 64*]. The latter has in its center the urethral channel, a tubular structure lined with specialized flattened cells through which urine passes. The three cylinders act as draining pools for the penis's blood supply, producing an erection when they are engorged. Smooth muscle and nerve beds line the entire phallus.

Blood flows toward the penis from the two pudendal arter-

A new understanding of the mechanism that causes erections has led to a wide range of options for treating impotence

ies, which emerge from the pelvis and then separately fork into two smaller branches, the dorsal and cavernous arteries, which run into the penis. Because the pudendal artery passes through the region between the anus and the base of the scrotum before reaching the penis, it is particularly vulnerable to injuries such as pelvic fracture or trauma from falling onto a post or bicycle bar [see "Spokes Man for a Hard Problem," on page 60]. The two branches of the pudendal artery branch off into smaller arteries once inside the penis, decreasing to a diameter of only 0.4 millimeter when the penis is flaccid. These relatively narrow blood vessels are susceptible to blockage from various arterial-narrowing conditions such as hypertension and atherosclerosis. The high incidence in our society of cardiovascular disease, which is exacerbated by diabetes and smoking, makes diminished blood flow to the penis the most common cause of organic erectile dysfunction.

Three primary types of cells live in the tissue of the penile corpora cavernosa: endothelial cells, smooth muscle cells and neurons. Endothelial cells line blood vessels and the sinusoids—the spaces within the corpora cavernosa—and secrete substances that aid in the relaxation and contraction of adjacent smooth muscle cells.

The penis has two states, flaccid and erect. The difference between the two depends on the filling of the penile chambers with blood up to the level of pressure in the major arteries of the body. For humans, this level is an average systolic blood pressure of 120 millimeters of mercury. If not sexually active, normal men are flaccid about 23 hours of the day, with approximately one aggregate hour of erection occurring during a part of rapid eye movement (REM) sleep. Men average four or five REM erections a night, each lasting about 15 minutes. Although the cause and function of these erections are not known, they are associated with dreaming. The frequency of REM erections usually diminishes with age. The number and duration of daytime erections for sexually active men varies greatly from person to person.

When flaccid, the penis's corporal sinuses have a blood pressure of only a few millimeters of mercury and blood flow of only five milliliters per minute (five milliliters is equivalent to one teaspoon). Whereas this is relatively low compared with other organs, such as the kidney—which receives about 500 milliliters per minute—it is sufficient to supply oxygen and nutrients to the penile tissue. The amount of blood entering the penis is regulated by the tone of the smooth muscle cells that line the three spongy corpora. When these muscle cells contract, blood flows freely in and out of the penis. When the cells relax, however, they press against the small veins that drain blood from the corpora. This pressure compresses the vessels like a closing valve; blood pools in the spongy tissues, and an erection occurs. But certain diseases and medications, as well as aging and anxiety—with its concomitant elevation of stress hormones in the blood—can prevent the smooth muscle cells from relaxing, thus keeping the valve partially or completely open. The corporal sinusoids then cannot fill with blood.

The Science of Stimulation

Most men do not walk around with a constant erection; this is because of the brain's inhibitory control over the erectile mechanism. (When that control is removed suddenly, as in the case of a hanging, a spontaneous erection sometimes occurs.) A stimulus is needed to begin the process. This sexual signal can be visual, tactile, auditory, gustatory or olfacto-

TREATMENTS FOR IMPOTENCE include **(clockwise from top)** ***a vacuum pump; a flexible penile implant; Viagra pills; a MUSE applicator, which inserts prostaglandin into the urethra; an inflatable penile implant; and Caverject, an injection of prostaglandin*** **(at center).**

SAM OGDEN

ry, or it may arise during dream-associated sleep. Conscious or unconscious neurological signals originating in the cerebral cortex and limbic system are sent to the hypothalamus and relayed down the spinal cord into the sympathetic and parasympathetic neurons of the penis. The nerve endings then release neurotransmitters that relax the smooth muscle cells lining the corporal bodies and the arteries supplying blood to the penis. More blood enters than exits, and the penis becomes rigid. The entire sequence of events, from stimulation to erection, can take place in seconds.

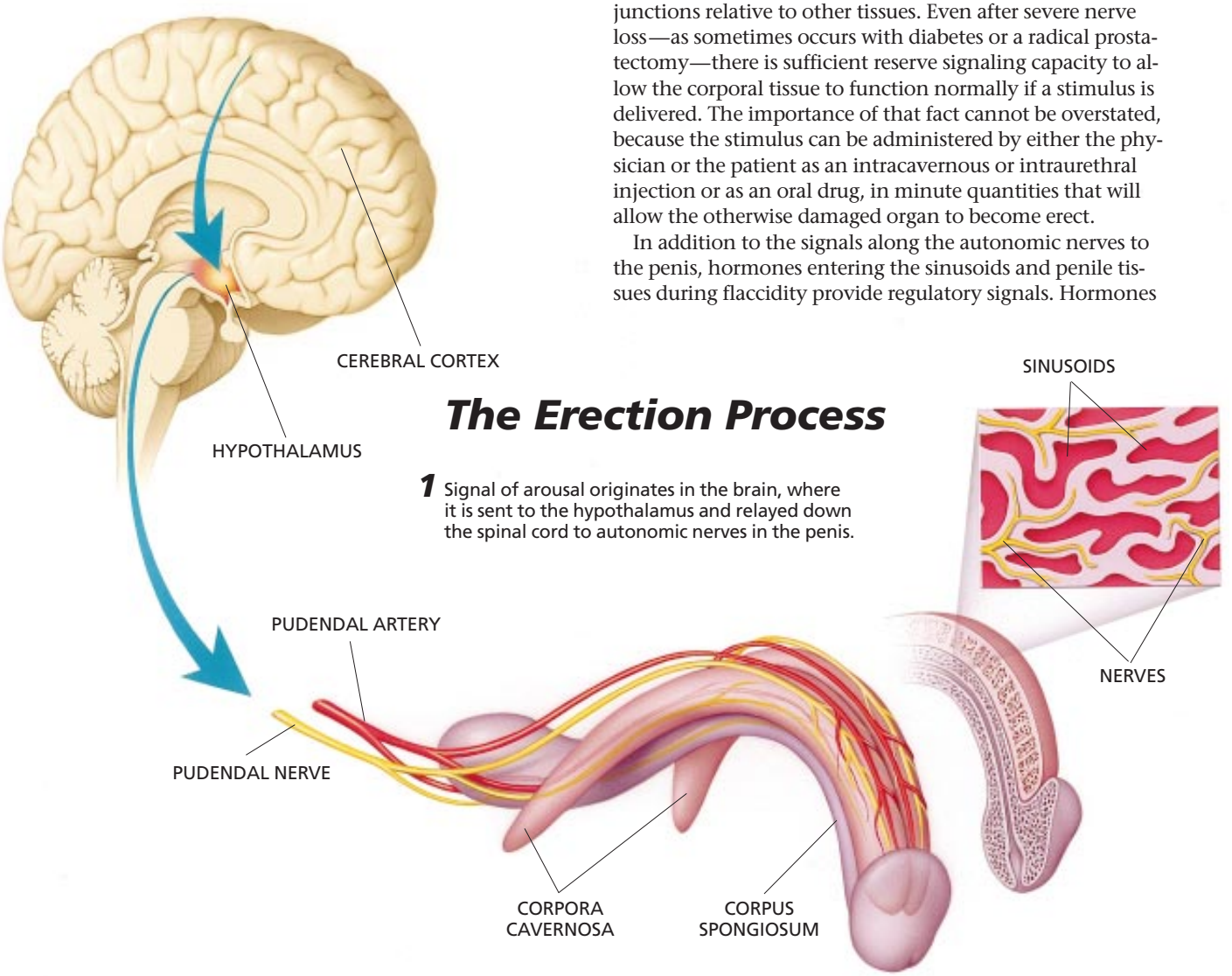
Many types of nerves and molecules participate in the signal transmission that culminates in an erection. The primary pathway is through autonomic nerve fibers that release molecules of nitric oxide near the smooth muscle cells of the penis. The nitric oxide diffuses through the cell membranes and begins a chemical cascade that culminates in the relaxation of the cells [*see illustration on opposite page*]. The secondary pathway is through cholinergic nerves, which release the neurotransmitter acetylcholine. This chemical stimulates endothelial cells to produce nitric oxide, which then seeps into the adjacent smooth muscle cells. But the most abundant nerves in the penis are actually adrenergic fibers, which provide brakes to the erection process in the absence of stimulation.

Regulation of the erection process depends on the concentrations of certain ions within the smooth muscle cells, and those concentrations can be affected by other neurotransmitters. For example, the neurotransmitter norepinephrine increases the amount of calcium ions (Ca^{++}) in the cells, prompting them to contract. Men who are anxious, cold or afraid sometimes secrete large quantities of norepinephrine, which causes transient contraction of the penile smooth muscle; the penis shrinks in length and cannot become erect. Potassium ions (K^{+}) also play an important role in regulating the contraction and relaxation of smooth muscle cells. When potassium ions leak out of a cell, the resulting electrical gradient prevents calcium ions from getting in, thus leading to the relaxation of the smooth muscle.

Specific therapies can target parts of this network of messages that enable an erection. Studies done in my lab, the Laboratory of Molecular and Integrative Urology at the Albert Einstein College of Medicine, have shown that the events in the penile corpora are coordinated via thousands of gap junctions—intercellular passages that allow ions and molecules to move from cell to cell. The coordination occurs in a precise order, developing into a synchronous wave of smooth muscle relaxation along the length and across the diameter of the penis, thus producing an erection.

Computer models developed by members of my laboratory team have shown that the penis has a great excess of gap junctions relative to other tissues. Even after severe nerve loss—as sometimes occurs with diabetes or a radical prostatectomy—there is sufficient reserve signaling capacity to allow the corporal tissue to function normally if a stimulus is delivered. The importance of that fact cannot be overstated, because the stimulus can be administered by either the physician or the patient as an intracavernous or intraurethral injection or as an oral drug, in minute quantities that will allow the otherwise damaged organ to become erect.

In addition to the signals along the autonomic nerves to the penis, hormones entering the sinusoids and penile tissues during flaccidity provide regulatory signals. Hormones

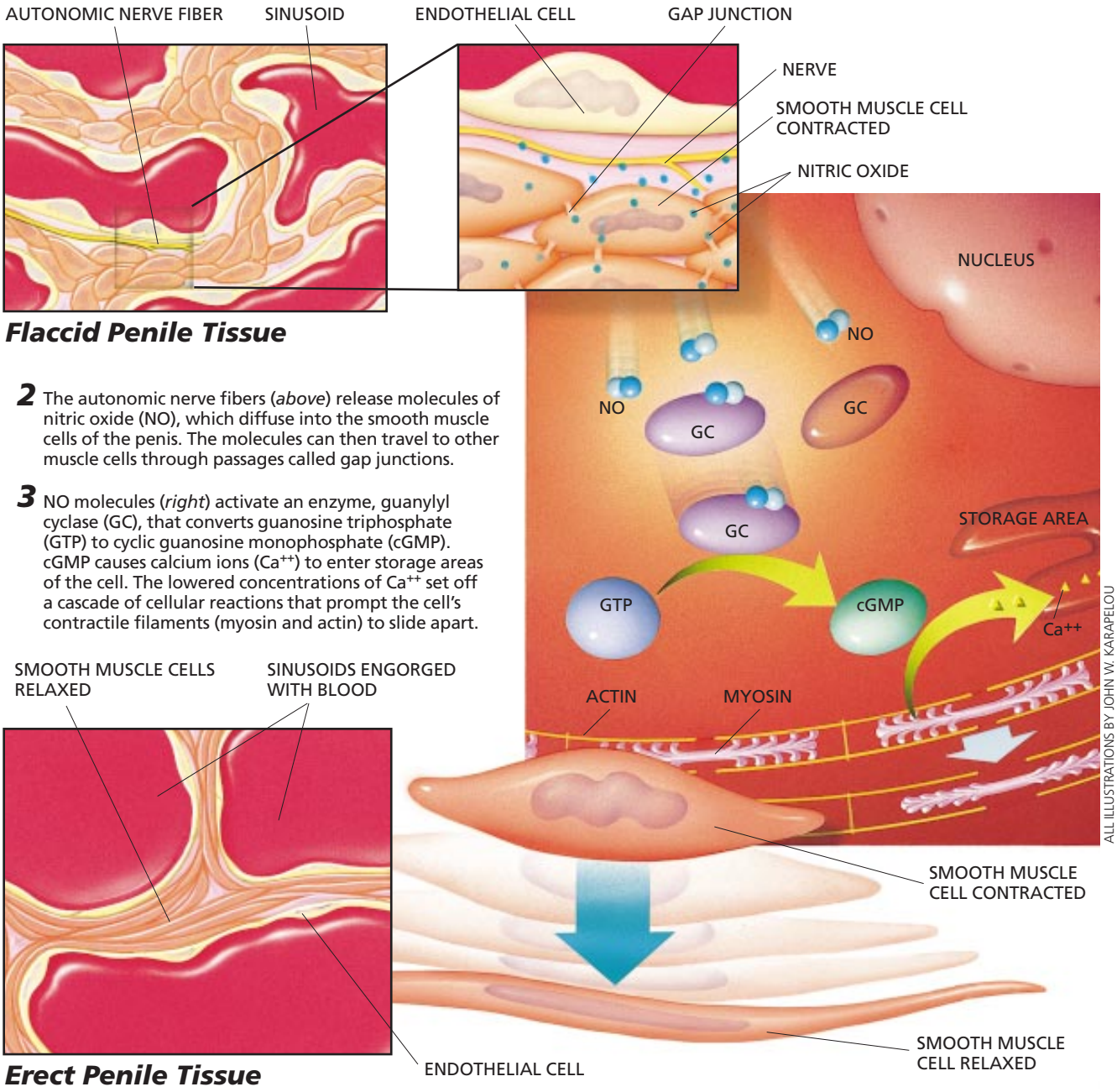


such as noradrenaline secreted from the adrenal glands and testosterone from the testes help to regulate the tone of the corporal smooth muscles and the secretory capacity of certain nerve fibers.

Causes of Dysfunction

Anything that interferes with the nerve pathway can cause erectile dysfunction. Trauma such as head and spinal cord injuries, stroke, Parkinson's disease, and diseases with systemic effects such as multiple sclerosis and diabetes can diminish nerve function and lead to impotence. Aging can be contributory, because it is often accompanied by a decrease in penile nerve endings and blood flow and by an increase in smooth muscle cell tone (making achieving an erection more difficult). Certain medications and alcoholism can also cause impotence. Vascular conditions such as hardening of the arteries can damage vessels supplying blood flow to the penis. Furthermore, anything impacting the primitive hypothalamic regions responsible for libido has the potential to cause erectile dysfunction. These factors include aging, depression, anxiety, chronic illness and medications that affect the central nervous system.

Finally, our new understanding of the erection process does not rule out the presence of secondary psychological problems emerging as a result of erectile dysfunction (which are often incorrectly blamed for the condition). In addition, certain psychological conditions, such as anxiety disorders,



Flaccid Penile Tissue

2 The autonomic nerve fibers (*above*) release molecules of nitric oxide (NO), which diffuse into the smooth muscle cells of the penis. The molecules can then travel to other muscle cells through passages called gap junctions.

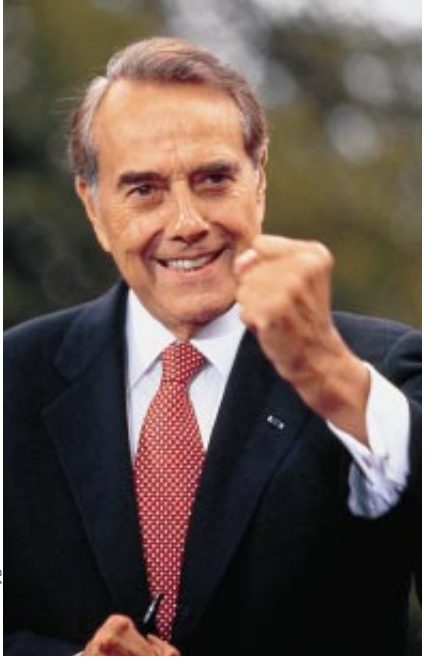
3 NO molecules (*right*) activate an enzyme, guanylyl cyclase (GC), that converts guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP). cGMP causes calcium ions (Ca^{++}) to enter storage areas of the cell. The lowered concentrations of Ca^{++} set off a cascade of cellular reactions that prompt the cell's contractile filaments (myosin and actin) to slide apart.

Erect Penile Tissue

4 The smooth muscle cells relax (*above, right*), pressing against the small veins that drain blood from the penis. Blood collects in the sinusoids (*above*), the spaces between the smooth muscle cells, and the penis becomes erect.

can be the primary cause of impotence.

The earliest effective treatment for organic impotence was the penile implant, successfully performed for the first time in 1947 using a single rigid plastic strut surgically inserted into the penis. Previous surgical efforts using a piece of rib or cartilage had failed because of rapid breakdown and absorption of the implant by the body. Although the plastic strut allowed some men to resume coitus, it was the introduction of medical-grade silicone in the 1960s that ushered in a truly practical surgical solution. The single flexible silicone rod was quickly followed by the introduction of more anatomically correct semirigid rods that bend like pipe cleaners, allowing manual positioning of the penis into an erection. Soon afterward, a three-component inflatable device was designed. The components include a bulb placed inside the scrotum, an inflatable cylinder positioned inside the penis and a saline sack inserted into the abdomen. Pumping the bulb causes fluid to fill the cylinder, bringing about rigidity. A release valve in the bulb allows a return to the flaccid state. Today three companies in the U.S. manufacture a variety of semirigid and inflatable prosthetic devices.



B. KRAFT *Sygma*

BOB DOLE, former presidential candidate, participated in the trials for Viagra and has appeared in ads for Pfizer, the drug's manufacturer.

The average age of a patient choosing a prosthetic is 50. Implants seldom wear out, even after decades of use; each implant carries a manufacturer's lifetime guarantee. Implants are safe and almost 100 percent effective. In addition, the approach offers a particular advantage not present in any other impotence treatment currently on the market: it allows coitus without prior planning. That fact greatly increases the overall satisfaction of the men and their partners who choose this option.

Another mechanical treatment is a vacuum pump, a temporary, nonsurgical approach that works on the same principle as milking machines placed over a cow's udder. Pumping air out of an airtight chamber covering the penis creates a vacuum, which draws blood into the penile sinusoids. A tourniquet is placed at the base of the penis to trap the blood in the phallus after removal of the vacuum chamber. Though safe, the instrument produces varying degrees of penile rigidity for each man and during each episode of use.

Penile Injections

The next major treatment advance was hit on by serendipity: in 1979 French vascular surgeon Ronald Virag accidentally injected papaverine rather than saline into a patient's penis during a diagnostic procedure. To his (and probably the patient's) surprise, the man became erect. Virag quickly recognized the utility of papaverine, a drug used to induce smooth muscle relaxation. After confirming the reproducibility of triggering an erection, which occurred minutes after intracorporal injection of the drug, Virag announced his findings. This discovery highlighted for the first time that smooth muscle relaxation was the key erectile mechanism and set the direction for the next generation of basic research. Of particular interest is that papaverine acts very far down in the chemical cascade needed for erection by increasing the concentration of cyclic adenosine monophosphate (cAMP), a chemical that helps to block the entry of calcium ions into the cell, which in turn results in smooth muscle relaxation. Activity at this point in the erectile process negates the need for sexual excitement in achieving erection. This discovery made available an inexpensive, safe, repeatable treatment that was effective in a very high percentage of men with diverse origins of impotence.

Other injectable agents soon followed, each affecting the erectile mechanism at different points in the signaling process. The drug phentolamine induces erections by blocking norepinephrine. Prostaglandin induces cAMP production, which then causes cell relaxation in the same way as papaverine. Because these drugs act at different points in the erection process, they can act to optimize one another's effects. Researchers have taken advantage of this, and now combinations of the drugs are widely used as an intracavernous injectable mixture.

Although these injectable drugs are effective in about 80 percent of patients, they require some advance planning, as there is about a 10-minute waiting period before erection. In addition, side effects, which are seen in a very small percentage of users, can include corporal scarring and penile pain. The most significant disincentive for their use, however, appears to be the psychological barrier to self-injection.

The inclusion of injectable treatments in the recommendations of a 1992 National Institutes of Health conference on impotence helped to legitimize the treatment of erectile dysfunction in the eyes of the government. Subsequent approval by the Food and Drug Administration of Caverject (an intracavernous injection of prostaglandin) and MUSE (a prostaglandin intraurethral pellet) brought about Medicare reimbursement for some nonsurgical treatments of erectile dysfunction.

Popping a Pill

In the tradition of previous erectile-dysfunction therapy discoveries, the erection-inducing effect of sildenafil—more commonly known by its brand name, Viagra—was discovered inadvertently. While performing clinical studies of sildenafil as a treatment for heart failure, researchers noticed that a statistically significant number of men were getting erections after taking the drug. Knowing a good thing when they saw it, the researchers began a separate clinical program to evaluate the drug as an impotence treatment. The heart treatment protocol was eventually dropped because of a high rate of fatal arrhythmias. But as a treatment for impotence, Viagra became the fastest-selling new drug on record, registering worldwide sales of some $700 million in its first nine months on the market.

Viagra works by inhibiting the degradation of cyclic guanosine monophosphate (cGMP), which is the last molecule in the chemical cascade that causes an erection. Viagra blocks

the activity of one type of phosphodiesterase, an intracellular enzyme found in vascular smooth muscle. This enzyme normally breaks down cGMP, but when Viagra inhibits the enzyme, the cGMP remains active, and the signal for smooth muscle relaxation is left in the "on" position. Viagra is effective in inducing erection in about 70 percent of men, as long as they have healthy penile blood flow, intact nerves and sufficient capacity to produce nitric oxide, a precursor to cGMP production. Because the drug is dependent on nitric oxide release, which is a result of nerve signals to the penis, sexual stimulation must occur for an effect to be seen.

Viagra acts not only on penile tissue but also throughout the body, potentially causing dose-related side effects such as facial flushing, headaches, gastrointestinal distress and a blue tinge to vision. The drug should be taken on an empty stomach and without alcohol. Some advance planning is needed because the drug does not take effect until up to an hour after pill ingestion. The major drawback with the medication may be the possibility of death: the FDA reported approximately 130 U.S. deaths potentially related to the use of Viagra in the first eight months that the drug was on the market. Although it can be argued that this represents a very small percentage of the men who have taken the drug, there are almost no reports of death with other therapies for penile dysfunction.

Viagra has affected more than just the treatment of impotence: it has also changed the way the condition is diagnosed. Before the introduction of the drug, a specialist would often seek to evaluate the number, duration and hardness of a patient's nocturnal erections with a Rigiscan, a device that includes a microcomputer strapped to the leg and contracting bands placed over the penis. Now, in most cases, the efficacy of Viagra is used to determine the cause of the condition. Questionnaires are also used to evaluate the drug's efficacy, although they provide only subjective data from the patients.

Other Approaches

Some treatments are designed to correct an imbalance that may exist in male sex hormones, which can also cause erectile dysfunction. Cases of significantly low levels of testosterone, often resulting from a congenital abnormality or from trauma or vascular injury to the testes, can be corrected with monthly intramuscular injections of the hormone or daily application of transdermal skin patches. Hyperprolactinemia, an overproduction of the hormone prolactin caused by an anterior pituitary tumor, can be treated with the drug bromocriptine or by surgical removal of the pituitary gland (pituitary hormones must be supplemented after surgery).

The use of topical agents for various types of erectile dysfunction, though not very effective in the past, are undergoing clinical trials. These vasodilating creams do not seem to show much promise, however, because the drugs probably need to enter general circulation to achieve a practical effect.

Pfizer, the pharmaceutical company that makes Viagra, is exploring various new ways of administering the drug, such as nasal and wafer delivery systems that may allow for more rapid absorption, thus reducing the waiting time for an erection. Meanwhile other researchers are testing different oral medications. A drug called apomorphine, which stimulates the hypothalamus to induce erection, is being tested in the form of a tablet that dissolves in the mouth—an attempt to minimize its main side effects of nausea and vomiting. Phentolamine, currently used as a stand-alone and combination injectable drug, is also being tested in an oral form.

Gene therapy represents a new area of research, one for which the penis is particularly well suited. Because the penis is external and easily accessible, a tourniquet can be readily applied (for up to 10 minutes) to prevent any injected genes from entering the rest of the body. Moreover, vascular smooth muscle cells, the probable targets for many gene therapies, have a low turnover rate, increasing the chances for the effects of the therapy to last for weeks or months. Gene therapy can be used in different ways, including the insertion of genes into penile cells to produce proteins that are lacking because of missing or defective genes. Injected DNA could also generate proteins that would make the penis more sensitive to compensate for an organic disorder.

Two gene therapy approaches are currently being tested. Jacob Rajfer of the University of California at Los Angeles Medical Center is attempting to introduce a precursor gene into the penis to boost nitric oxide production when the gene is activated by a chemical stimulant or irritant. My own lab is investigating the efficacy of inserting a gene subunit that would allow potassium ions to move freely out of the cells of the corpora cavernosa. This change would increase the relaxation of the smooth muscle cells and make the penis extremely sensitive to stimulation. In studies on rats, the inserted DNA remained active for at least four months. The penises of diabetic and aged rats receiving the gene responded to stimuli in the same manner as the organs of young or healthy rats did. There have been no adverse effects on the hundreds of rats tested. The potential for a safe, sustained therapy in humans that would allow spontaneous erections is truly encouraging and will be brought to clinical testing in the near future. SA

The Author

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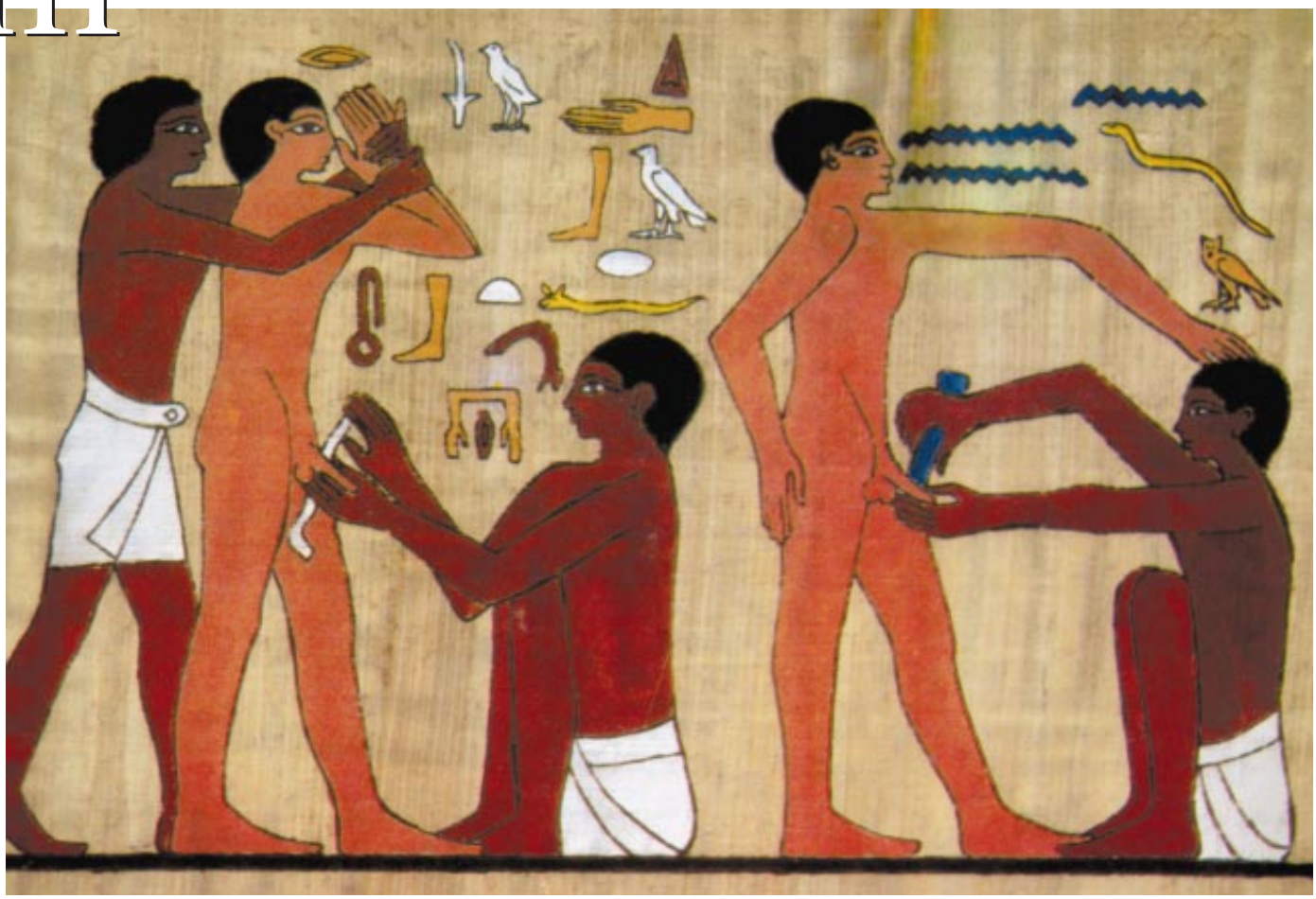


CHRISTINE OSBORNE *Corbis*

EGYPTIAN CIRCUMCISION RITES may have been practiced for reasons of hygiene.

The Circumcision Dilemma

Physicians in the U.S. are at odds over neonatal circumcision. Is it preventive medicine, cosmetic surgery or inhumane mutilation?

by Edward O. Laumann

The circumcision of newborn boys in the U.S. has been routine practice for more than 60 years, leaving an estimated 100 million of today's males without a foreskin. At the height of the practice in the 1950s and 1960s, the surgery became an automatic extension of hospital birth, especially for the sons of white, middle-class families.

In the past three decades, however, the debate surrounding routine circumcision has ignited. Proponents in the medical community contend that it is valid prophylaxis against certain forms of cancer and infection, much like vaccination; the detractors—both physicians and activist groups—argue that cutting healthy, sexually responsive tissue from a nonconsenting child is medically unnecessary and may be unethical. The most outspoken of these opponents maintain that circumcision amounts to nothing less than assault and battery. In this atmosphere of controversy, parents must decide whether or not to circumcise—a decision that recent results show may affect the sexuality of their sons throughout adult life.

An Ancient Ritual

Published debate on the merits of circumcision raged as early as the fifth century B.C., when Greek historian Herodotus described the millennial-old custom among Egyptians: "They practice circumcision for the sake of cleanliness, considering

it to be better to be clean than comely." The Jews adopted the practice from the Egyptians—but later were forced to hew to the Hellenistic ideal of an intact penis during the reign of Antiochus IV in the second century B.C. The Greeks outlawed circumcision and punished the ritual by death; to conform, some Jews stretched what remained of their foreskins with a weight called the Pondus Judaeus.

The tradition of circumcision survived, however, largely because the Old Testament prescribes it as a sign of the covenant between God and Abraham and his people. The Jewish ritual calls for a small ceremony, the Bris Milah, on the eighth day after birth; throughout Islam, boys are circumcised as well, often during puberty. In 16th-century Ottoman Turkey, the circumcision of the sultan's sons occasioned a lavish festival lasting several weeks, during which thousands of lower-class children underwent circumcision.

Native populations of the Americas, the aboriginal people of Australia and various African tribes also traditionally practiced circumcision, typically for cosmetic reasons or to prepare boys for manhood. Throughout most of the rest of the world, including China, Japan, northern Europe and modern South America, circumcision is uncommon. A survey of young German parents in 1992 revealed that 61 percent did not understand the term.

Remedying Epilepsy and Masturbation

How then did circumcision, once exclusively a religious and cultural rite, become a routine medical procedure in the hospitals of the U.S.? The custom began in the late 19th century, when practitioners touted circumcision as a remedy for ills ranging from epilepsy to asthma and also as a deterrent to masturbation, which many in the Victorian era believed to be harmful to health and sanity. One booster was John Harvey Kellogg of breakfast cereal fame, who recommended circumcision—preferably without anesthetic—as a reliable cure for masturbation in boys.

The practice continued during World War II, when the U.S. military would regularly circumcise soldiers who had trouble with penile irritation and hygiene in sandy or sultry battlegrounds. And the procedure received the imprimatur of the U.S. medical establishment in 1949, when a physician named Eugene Hand published an influential paper describing a lower susceptibility to venereal disease among the circumcised.

By the late 1950s and 1960s, insurance carriers were paying for the surgery, and 80 to 85 percent of all boys born in the U.S. were circumcised. In other English-speaking countries, the situation differed. A 1949 paper by British physician Douglas Gairdner that challenged routine circumcision as being of doubtful value and possibly harmful proved influential among health care policymakers. Whereas British circumcision rates before World War II were comparable to those in the U.S., by 1950 they began a marked decline.

The British National Health Service dropped coverage because it could find no medical benefit from routine circumcision. By 1985 the neonatal circumcision rate in Britain was estimated at 1 percent. Rates in Canada and Australia also tapered off, and only about 20 percent of Australian boys born in 1995 and 1996 underwent the surgery as infants. In the U.S., the rate has decreased somewhat since the 1960s, as the debate over the medical usefulness and the appropriateness of the procedure has seethed; still, in 1996, about 60.2 percent of newborn boys in the U.S. were circumcised, at an estimated annual cost of $150 million to $270 million.

Continuing popularity of routine circumcision in the U.S. can be partly attributed to its promotion as a simple public health measure that guards against a variety of diseases. That idea was strengthened in 1989, when the American Academy of Pediatrics (AAP) published a position paper that noted both risks and medical advantages to circumcision procedures.

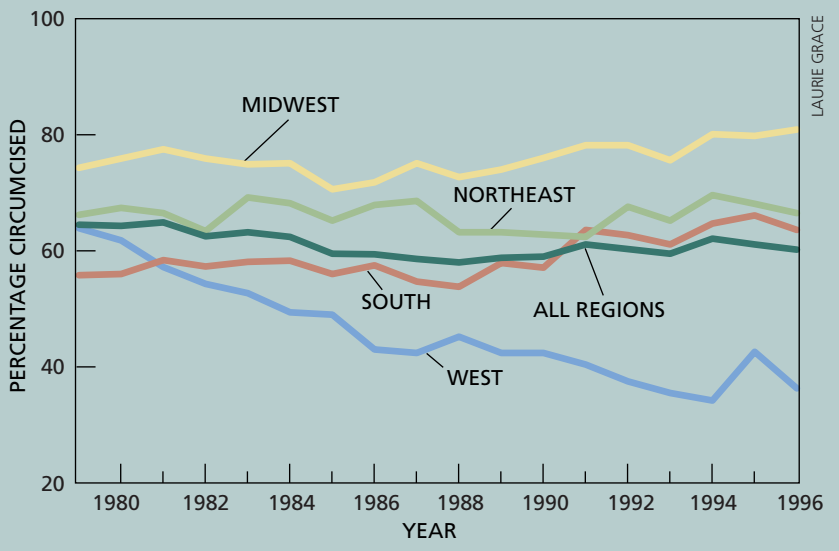
The 1989 AAP Task Force on Circumcision cited prevention of penile cancer as one benefit of circumcision. Several studies of groups of penile cancer patients in the U.S. have found that very few or none of the victims were circumcised as infants, an indication that neonatal circumcision protects against the disease. Parents considering circumcision as a preventive measure should be aware, however, that penile cancer is rare; incidence of the disease in uncircumcised men in the U.S. is estimated at perhaps 2.2 cases or fewer per 100,000 men a year.

In addition, there is more to penile cancer risk than simple circumcision status alone. Penile cancer rates among uncircumcised men also vary widely from country to country. Some developing nations experience rates as high as three to six cases per 100,000 uncircumcised men per year, markedly higher than the U.S. estimate. In Denmark, however, the overall incidence of penile cancer is only about 0.8 case per 100,000 men a year—although just 1.6 percent of the male population is circumcised. And in Japan, where circumcision is also rare, penile cancer rates dip to 0.3 case per 100,000 men a year, lower than the overall U.S. incidence (circumcised and uncircumcised) of 0.9 to 1.0 case per 100,000 men annually. Clearly, critics argue, other factors play a large role—they point to smoking, unprotected sex and poor hygiene as potential culprits for the discrepancies.

A second benefit of circumcision is a decreased rate of urinary tract infection (UTI) in circumcised infants. Studies that surveyed the records of several hundred thousand boys born in U.S. Army hospitals in the 1980s revealed approximately a 10-fold greater chance of hospitalization for UTI in the first year of life for uncircumcised than for circumcised boys. The hospitalization rate for UTI was about 1.4 percent of uncircumcised boys; because approximately 1 to 2 percent of UTIs in infants lead to serious kidney problems, many doctors argue for prevention by routine circumcision.

On the other side of the debate, some physicians question the design of these studies, which involved paging back through old medical records rather than observing a group of children prospectively. In comparison, a study that monitored a group of nearly 60,000 Canadian boys found that about 0.7 percent of uncircumcised boys were hospitalized for UTI in the first year of life. This rate was about 3.7 times that for circumcised boys. Because so many boys would need to be circumcised to prevent kidney disease in just a few, some opponents believe the risk of complications from the surgery also needs to be considered.

Fueled by a raft of conflicting reports, the connection between circumcision and venereal disease has generated heated debate for decades. Many studies have shown that uncircumcised men are more likely than those who are circumcised to suffer from sexually transmitted diseases (STDs), including gonorrhea, syphilis, herpes, papillomavirus, chlamydia and HIV. Risks for the uncircumcised increased twofold to fivefold for the range of STDs—and as much as eight times for HIV. To confuse matters, other investigations



SOURCE: National Center for Health Statistics Data, 1998

RATES OF CIRCUMCISION vary widely by region, but the national rate has decreased slightly since 1979.

have detected no link to these diseases. Still other publications suggest that circumcised men actually confront greater risk for STDs—among them, HIV and genital warts.

These studies are prone to methodological problems, though. Often they fail to control for social factors that might influence STD rates, including sexual practices and socioeconomic status. My own group examined data from the 1992 National Health and Social Life Survey (NHSLS), in which we surveyed a representative cross section of the U.S. population about health issues. This investigation allowed us to control for confounding factors such as religion, the number of sexual partners and education. Our analysis showed no discernible prophylactic effect of circumcision against various STDs, including chlamydia, gonorrhea and herpes. Certainly the relationship between STDs and circumcision does not seem particularly strong. And other, better-proved public health measures against STDs—such as regular condom use—are less invasive.

In 1999 the AAP reevaluated the medical arguments for circumcision. Its Task Force on Circumcision found that data on STDs in general are conflicting; they state that although circumcision does seem to lower the rate of HIV infection, behavioral risk factors are far more important. The task force also concluded that neonatal circumcision does decrease the incidence of UTI in infancy and of penile cancer in adulthood but that the number of males affected is small. Based on these findings, the AAP reversed its neutral stance on newborn circumcision, stating that evidence of medical benefits from the procedure is not sufficient to recommend routine circumcision of newborns.

Anatomy of a Circumcision

For many parents, whether their reasons to circumcise their sons are religious, cosmetic or medical, the most anxiety-laden aspect of the decision is the thought of the procedure itself. Circumcision is quick but also painful, and the image of knife against penis can be unsettling.

Done properly, circumcision takes from three to 10 minutes. Each procedure begins with the same first step: the foreskin is separated from the glans, to which it adheres tightly in infants. Next, a clamp is applied to shield the glans and crush the foreskin where the cut will be made, in an effort to seal blood vessels and prevent bleeding.

In the Jewish ceremony of Bris Milah, practitioners known as Mohels often use a simple metal clamp called a Mogen, which they slip onto the stretched foreskin and tighten. The glans is protected on one side of the clamp, and the cut is made on the other. This procedure is one of the quickest and is often performed in the home. Some Mohels use a traditional shield that does not crush the foreskin—a faster method but one that may increase bleeding.

In hospital circumcisions, the Gomco clamp is popular. After cutting a slit in the foreskin with scissors, the physician inserts a metal bell to protect the glans and draws the foreskin up around it [*see illustration on opposite page*]. The clamp crushes a circular section, and then a cut is made. The Plastibell device is similar, except that a string crushes the foreskin against a plastic bell. The bell remains in place for a few days, until the foreskin dies off and is sloughed away.

All these procedures draw criticism, even from the mainstream medical community, because they cause considerable pain, particularly during the first step of loosening the foreskin. A recent study showed that even four to six months later, babies circumcised without anesthesia exhibit greater pain reactions to vaccination than uncircumcised boys or babies whose circumcision pain was attenuated with anesthetics. Although many circumcisions are still done without anesthesia, most professional guidelines for physicians recommend attention to pain relief during the procedure.

Pain relief may come from topical anesthetic cream or injected local anesthetic. The latter option alleviates the pain of circumcision more effectively; although the injection hurts, studies have shown it to be less painful than the operation. Although this finding may seem obvious, the medical establishment believed until recently that the undeveloped nervous system of the newborn infant was incapable of experiencing pain. No method has been found yet that completely eliminates the discomfort of the surgery.

Just as doctors in the U.S. spar over the benefits of circumcision, they quarrel over the magnitude of the risks. Experts typically cite immediate complication rates ranging from 0.2 to 5 percent of procedures. These complications involve mostly minor bleeding, local infection or removal of too little skin, requiring repeat circumcision. Inadvertent damage to the glans or removal of too much skin happens more rarely. A few studies have reported a higher incidence of bleeding, in up to about 35 percent of cases.

Critics often mention another uncomfortable consequence of circumcision: the irritation experienced by the delicate glans of the penis once the protective foreskin is gone. Over time, the surface of the glans does become

tougher and thicker, but initially it is quite sensitive to irritation by constant rubbing against the diaper and ammonia generated by the bacteria in urine. Inflammation of the glans and urethral opening occurs in about 8 to 31 percent of circumcised infants.

Conversely, about 4 to 18 percent of uncircumcised boys experience inflammation of the foreskin and sometimes of the glans. In infants the foreskin adheres tightly to the glans, and the area requires no special care. As the boy grows, the foreskin and glans will slowly separate, but this may take a number of years. When the foreskin can be retracted easily, many doctors recommend washing underneath regularly.

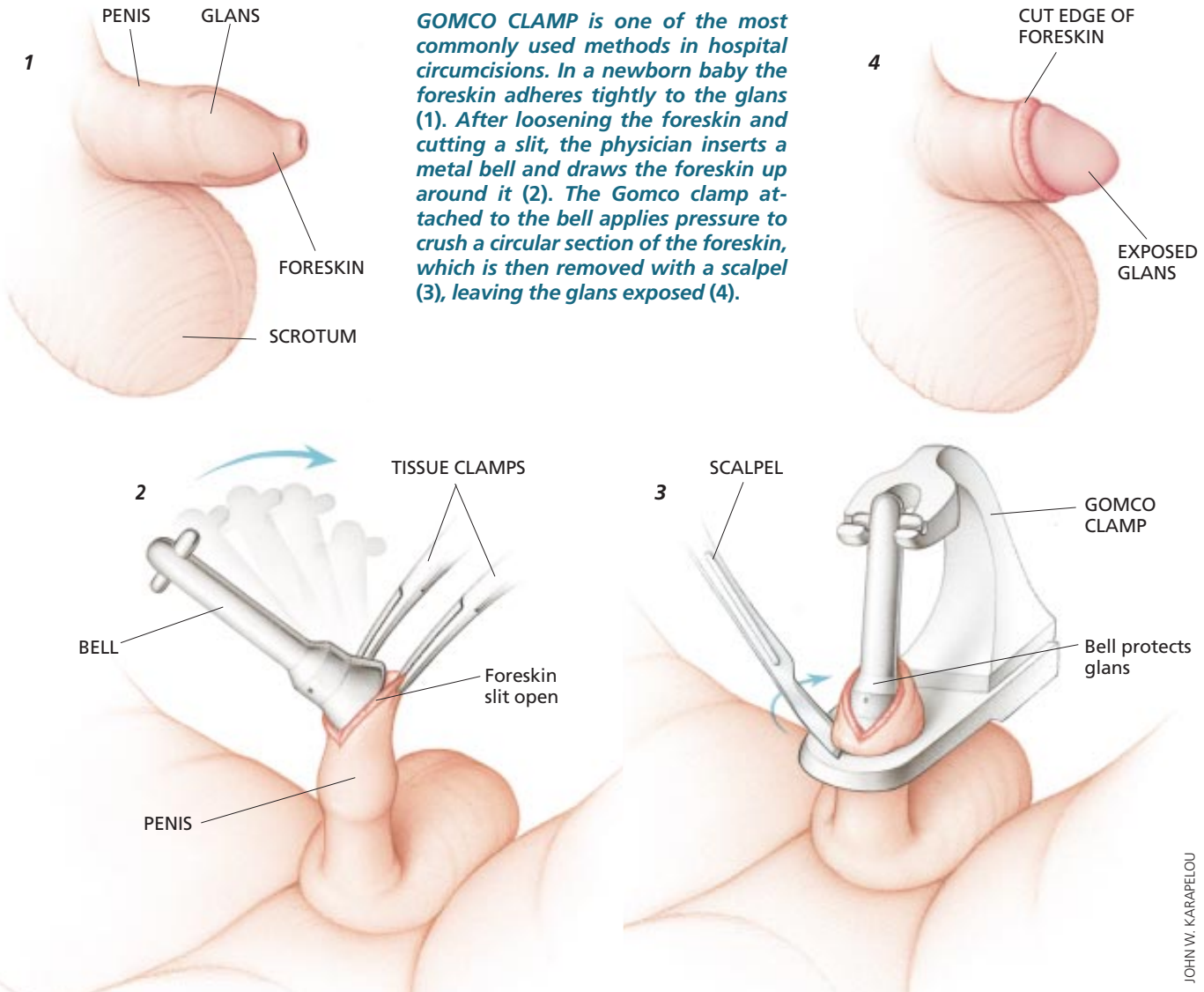
The foreskin should not be forcibly retracted before it has separated naturally, as this can cause scarring, which may lead to a condition called phimosis. In phimosis—from the Greek for "muzzling"—the foreskin is too tight on the penis, sometimes interfering with urine flow. As many as 1 to 10 percent of boys who keep their foreskins as infants may require circumcision at a later age—usually under general anesthesia—because of recurrent inflammation or phimosis.

The Decision

Looking at their baby boy, parents may not envision the child's future sex life, but perhaps they should consider it. Whereas a newborn's foreskin is just a few millimeters long, in an adult male there may be as much nerve-rich tissue in the foreskin as along the entire shaft of the penis. Some critics of routine circumcision argue that loss of this tissue greatly diminishes sexual pleasure [see "Anticircumcisionists Decry a Male's First Sacrifice," on page 73].

Research by my own group, using the NHSLS data, has revealed that circumcision does indeed have an impact on sex in adulthood. Contrary to the Victorian notion that circumcision weakens sex drive and prevents masturbation, we found that circumcised men actually engage in a somewhat more elaborate repertoire of sexual practices than uncircumcised men do. In particular, among whites the likelihood of a circumcised man masturbating at least once a month was 1.76 times that of an uncircumcised man; the lifetime odds of a circumcised white male receiving oral sex were similarly elevated.

Our findings may reflect a greater aesthetic appeal of the circumcised penis in cultures where circumcision is the norm, as similar trends were not found among black and Hispanic men. In our study sample, 81 percent of white men were circumcised, as op-



***GOMCO CLAMP** is one of the most commonly used methods in hospital circumcisions. In a newborn baby the foreskin adheres tightly to the glans* (1). *After loosening the foreskin and cutting a slit, the physician inserts a metal bell and draws the foreskin up around it* (2). *The Gomco clamp attached to the bell applies pressure to crush a circular section of the foreskin, which is then removed with a scalpel* (3), *leaving the glans exposed* (4).

JOHN W. KARAPELOU

HOSPITAL CIRCUMCISION may become less routine as parents weigh the medical benefits and risks. Concerns remain about the pain from the procedure, even when an anesthetic is used.

ARLENE COLLINS *The Image Works*

posed to only 65 percent of black men and 54 percent of Hispanic men. The more elaborate set of behaviors in circumcised men may also support the hypothesis that the circumcised penis is less sensitive to coitus, leaving circumcised men more likely to seek other forms of stimulation.

The broader sexual practices of circumcised men may help them maintain an active sex life as they age. We discovered that among men aged 45 to 60, circumcised men were about half as likely as uncircumcised men to have recently experienced a cluster of sexual difficulties, including trouble achieving or maintaining an erection, anxiety about sexual performance, and a lack of interest or enjoyment in sex. We speculate that circumcised men, who engage in a wider repertoire of practices than their uncircumcised peers, are more familiar with alternative routes to stimulation and have more options for expressing their sexuality should they encounter difficulties.

Parents thus face a raft of issues when they contemplate circumcision for their sons, from concerns about pain and potential medical benefits and risks to questions about their sons' sex lives. In 1983 at Children's Hospital of Denver Mark S. Brown and Cheryl A. Brown looked at what factors parents actually take into account when they make their decision.

The researchers found that the strongest determinant of whether a boy was circumcised was the circumcision status of his father. Among boys whose fathers were circumcised, 90 percent were circumcised as well, compared with only 23 percent of boys whose fathers were not circumcised. Parents who chose circumcision cited religious, social and aesthetic reasons—such as the desire for the boy to fit in with male relatives or peers—about as frequently as they cited medical reasons.

In the late 1990s arguments about fitting in with peers may lose their sway, as the prevalence of circumcision has fallen from the record highs of the 1950s and 1960s. In 1996 about 60.2 percent of newborns in the U.S. were circumcised; the rates were still high in the Midwest, at 80.9 percent, but had dipped to 36.3 percent in the West. The low numbers for the West may reflect an influx of immigrants from cultures that do not traditionally circumcise, as well as the influence brought to bear by the anticircumcision movement.

Among doctors, the debate continues. Whereas U.S. health insurers continue to provide coverage for routine circumcision, professional medical associations in Canada, Britain and Australia have published position papers in the past three years advising against the practice. And in 1999 the AAP took a step in that direction as well, in concluding that there is insufficient evidence of medical benefit to recommend routine neonatal circumcision. The rest of the medical profession in the U.S., however, still appears sharply divided on this issue.

In the end, parents are left remarkably alone to decide whether neonatal circumcision is right for their sons. Just about the only thing professionals do agree on is that parents' decisions about circumcision should be well informed, as this five-minute procedure at birth may have an effect that lasts throughout their son's life. SA

The Author

EDWARD O. LAUMANN has researched sexual behavior and how the bonds of friendship and marriage help to form communities. He chairs the department of sociology at the University of Chicago, where he has also served as dean and provost. After receiving his doctorate from Harvard University in 1964, Laumann first joined the faculty of the University of Michigan's department of sociology, before moving to Chicago in 1972. He is the principal investigator of the 1992 National Health and Social Life Survey, the results of which have been written up in two books. He is author of 12 books; when not writing, he fanatically plays squash.

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Anticircumcisionists Decry a Male's First Sacrifice

by Mia Schmiedeskamp

JASON GROW *SABA*

***SUPPORT GROUP** for men who feel they have experienced problems resulting from circumcision.*

Men may not long for their tonsils or mourn their lost appendix; they may gladly kiss that extra layer of fat around their midsection good-bye. But their foreskin, harvested so early and so easily, may be sorely missed. In the past three decades, a growing grassroots movement has sung the virtues of remaining "intact." While physicians squabble over surgical risk versus public health, anticircumcision groups have trained their sights on the masses, selling a topic that everyone can readily relate to: sex.

Circumcised men, goes the argument, are missing out. The adult foreskin is rich in nerves; its total length, inside and out, can equal the length of the penis. Ronald Goldman, director of Boston's Circumcision Resource Center, explains that during an erection, the foreskin lies loose along the penis, sliding and providing extra stimulation during intercourse; in contrast, the skin of an erect circumcised penis is tight: "It's like a broomstick—it doesn't have any movable parts."

Furthermore, the foreskin lubricates and protects the glans, which thickens once it is exposed by circumcision. All of this, circumcision opponents say, means that circumcised men cannot experience sex as fully as intact men. In support, they cite anecdotal evidence from men who were circumcised as adults, some of whom assert that sex after circumcision is disappointing.

As with every other aspect of circumcision, disagreements abound about the merits of this argument—many doctors maintain that the circumcised penis offers plenty of sensitivity. In the 1960s Virginia Johnson and William Masters performed neurological tests on circumcised and uncircumcised men and could not discern a difference in response to light touch to the penis, especially the glans. "There really are no other studies that address this issue," says Thomas Wiswell, a physician at Thomas Jefferson University. "All you have are a handful of testimonials and that's it—there is no science."

Wiswell's own history demonstrates the ever changing nature of the circumcision debate. During the 1970s, he actively opposed routine circumcision. "We were zealots—admittedly so," he says. But after he spearheaded research on urinary tract infections in uncircumcised boys, he came to the conclusion that the medical benefits of the procedure outweigh arguments against it. "I was trained as a pediatrician; I am an advocate for the protection of children," Wiswell avers. "I didn't reach this decision lightly."

Neither do anticircumcisionists take their position lightly—they can be vocal and even confrontational in their opposition. Perhaps the one area where their response is clearly tempered, though, is the delicate topic of religious circumcision. Some critics, including Goldman, feel that this question may be best addressed within individual religious groups, because the imperatives for Jewish and Muslim parents are so different from the secular concerns of medicine and sex life.

If opponents are right, and circumcision cuts so close to men's sexuality, why aren't tens of millions of dissatisfied customers storming doctors' offices? Why do so many circumcised men choose to circumcise their sons? Goldman contends that American men don't know much about the role of the foreskin, so they don't know what they have lost. And those who suspect they are lacking something may be in denial. "What man wants to hear that he's missing a normal, natural part of his penis?" Goldman remarks.

Some men, though, are indeed distressed by their lack of foreskin—feeling damaged, betrayed, sexually incomplete. A few even claim that they can recall the traumatic event of circumcision itself. Support groups where these men can express their frustration and rage have sprung up around the country. Some men have even tried to get their lost foreskins back, gradually stretching the penile skin over the course of many months with weights or taut elastic bands. While these men nurse their psychic wounds, opponents of circumcision focus their energy on sparing the next generation. They hope parents will consider the trauma and potential lifelong sexual ramifications of the operation and opt against circumcision. Other activists fight to take the decision away from parents altogether. They argue that until the child is old enough to consent, the practice is simply unethical. Just one more thing for new moms and dads to think about.

MIA SCHMIEDESKAMP received her doctorate in biochemistry from the University of Washington. She received a fellowship in science writing from the American Association for the Advancement of Science and is now a writer in Seattle.

Of Babies and the Barren Man

by Marc Goldstein

Infertility is a medical problem with a long and somewhat ignoble history. In biblical times, a barren marriage was always blamed on the woman, whose womb was said to have been "closed" by God. That chauvinistic attitude toward infertility persisted in the medical community as well as in popular culture until very recently. Only in the past 50 years has research on the male reproductive system revealed the host of troubles that can plague a man's baby-making machinery. Today we know that in about half of all infertile couples, a male factor is a contributing cause, if not the only one.

In fact, about 10 percent of American men who are trying to have a child—about three million men—are infertile, and many others who are not attempting to conceive would not be able to if they tried. These men may have genital abnormalities that were present at birth, or they may be suffering a progressive decline in fertility because of sluggish blood flow from the testes. They may have compromised their fertility by using certain controlled substances or by having a vasectomy. Or their condition may be a result of infection, disease or even medical treatment for other, unrelated conditions.

Whatever the cause, infertility can be a difficult condition for men to accept. It is often mistakenly associated with impotence, or the inability to have an erection. (Impotence does not necessarily impair fertility, nor do most infertile men complain of it.) For many men, being able to impregnate a woman is also an essential part of a macho self-image. Even when these perceptions do not come into play, the failure to father a child can be a profound disappointment. Fortunately, advances in our understanding of the male reproductive system have dramatically improved the ability to diagnose and treat male infertility. Now the vast majority of infertile men have the potential to conceive a genetically related child. All that is required is some time, effort, money—and, of course, a woman.

In the not so distant past, the contribution of the male partner to the act of reproduction was rather obscure. Whereas the mother's role seemed obvious, no one was sure what exactly was required of the would-be father: mere mechanical stimulation, some chemical catalyst or an actual biological donation. When Dutch scientist Antonie van Leeuwenhoek invented the modern microscope in the 17th century, one of the first things he looked at was semen, the fluid that is expelled from the penis during ejaculation. And among the first things he saw were sperm, the whip-tailed cells that carry a man's genes.

It is now clear that conception occurs when a single sperm cell penetrates a woman's egg. The union of these gametes is aided by powerful psychosexual incentives such as arousal and orgasm, and most of the time the system works. About 85 percent of couples regularly having unprotected sex will conceive a child within a year. If a couple still has not conceived after a year of trying, then one or both of the partners may have a fertility problem.

Both partners will need to undergo a fertility evaluation. For women, such evaluations may take a couple of months and require hormone profiles, ultrasound tests, mucus cultures and monitoring of ovulation. The process is usually faster and simpler for men. Although a physical exam and hormone workup will also be performed, the cornerstone of the male fertility evaluation is the semen analysis: an assessment of the shape, number and movement of the sperm cells in a man's ejaculate and of the volume and viscosity of his semen. Abnormalities in any of these factors can cause infertility.

Sperm quantity and quality can be affected by many different factors, including exposure to substances that interfere with the normal functioning of the male reproductive tract [*see box on page 77*]. The inhalation of cigarette smoke, for example, has been shown to impair sperm quality in humans and other animals. Alcohol damages testicular function, lowering sperm counts as well as the male hormone testosterone in heavy drinkers. The active ingredient in mar-

Male infertility can now be treated with advanced surgical and reproductive techniques. Most infertile men can become fathers

ERICA LANSNER

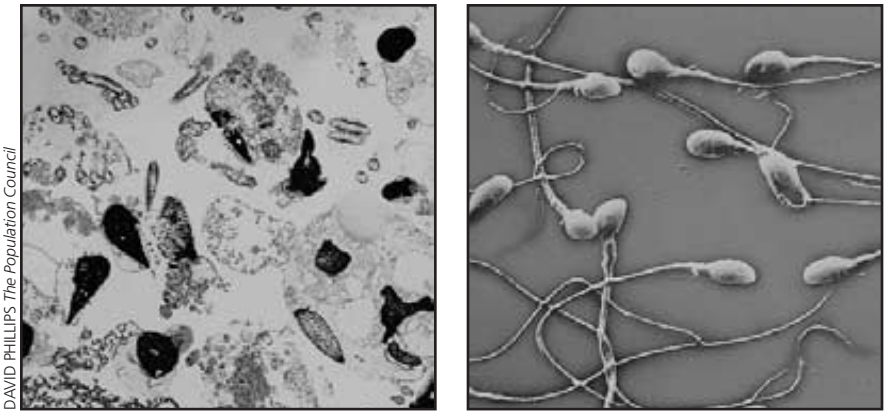
***SEMEN ANALYSIS** assesses the health of sperm placed in the center of the circular Makler chamber. A technician presses one of the buttons to register whether each sperm cell is normal or malformed or lacks mobility.*

ijuana binds to estrogen receptors in the testes and causes abnormally shaped sperm. Studies of cocaine in rats provide incontrovertible evidence that this substance, too, interferes with sperm production.

Some medicines prescribed by doctors for illness can affect fertility as well. A class of medicines for high blood pressure called calcium channel blockers, for example, can inhibit the enzymatic reaction that allows a sperm cell to penetrate the outer membrane of the egg. (Calcium channel blockers have even been contemplated as contraceptives [see "Beyond the Condom: The Future of Male Birth Control," on page 80].) Radiation or chemotherapy treatments for cancer often result in permanent or at least temporary sterility.

Folk wisdom has long acknowledged the vulnerability of sperm cells to a more ubiquitous threat: temperature. More than 2,000 years ago the Japanese used long, hot baths as a contraceptive method. Saunas, whirlpools or steam baths can also temporarily decrease fertility. Even the practice of crossing one's legs may have a detrimental effect: studies by my colleague Michael Bedford of Weill Medical College of Cornell University have shown that sitting with crossed legs elevates testicular temperature enough to influence sperm production. As for jockey shorts versus boxers, the evidence is conflicting. The only thing experts can say for certain is that one should not wear the tight leather pants, favored by some rock singers, that plaster the testes up against the body.

The placement of the testicles outside the body is thus no accident of evolution. The enzymes that regulate production of both sperm and testosterone operate most efficiently at several degrees below body temperature, and the external placement of the testes keeps them cooler than the rest of the body. English author Aldous Huxley made note of this sensitivity in his 1932 novel *Brave New World:* "… male gametes, they have to be kept at 35 instead of 37 degrees centigrade. Full blood heat sterilizes." In fact, if the normal operating temperature of the testicles is elevated by only one to



DAVID PHILLIPS *The Population Council*

***DAMAGED SPERM* (left) *have abnormal shapes and lack well-developed tails compared with their healthy, whip-tailed counterparts* (right).**

two degrees Celsius (two to four degrees Fahrenheit), sperm and testosterone production is adversely affected.

The exquisite temperature sensitivity of the sperm production process probably accounts for the single most common identifiable cause of infertility in men. That cause is varicoceles, a painless condition in which the veins in the scrotum become enlarged just like varicose veins in the legs [*see illustration on page 78*]. The enlarged veins do not drain blood as efficiently as healthy veins, and so the blood pools in the testes, thereby raising the temperature. Studies that I performed more than a decade ago corroborated the findings of the late urologist Adrian Zorgniotti of New York University Medical Center; we found that the temperature inside the testicles of infertile men with varicoceles was 2.5 degrees C higher than the normal testicular temperatures of fertile men without varicoceles—easily warm enough to have a major negative impact on sperm production and quality.

An Insidious Decline

Up to 40 percent of infertile men have varicoceles, and about 15 percent of all men have them. Although the condition may not always result in infertility, there is evidence that it causes a progressive decline in fertility as a man ages. For example, 80 percent of men who were fertile when they were younger and have become infertile later in life—a condition called secondary infertility—suffer from varicoceles. Thus, a fertile man with varicoceles has no guarantee that he will remain fertile as he gets older. This insidious decline in fertility is troubling to specialists as more men and women elect to postpone childbearing until they reach middle age.

The evidence for the adverse effect of varicoceles on testicular function in male infertility is overwhelming. The success of surgeons' attempts to repair varicoceles, however, has been disputed. The idea behind the varicocelectomy is simply to tie off the damaged veins in the scrotum so that blood gets shunted through healthier vessels. Over the past 50 years, studies on the efficacy of a variety of surgical techniques to reverse varicoceles have found conflicting results. Testicular function was not always restored by the repair procedure. The inadvertent cutting off of the main blood supply to the testes that may occur during some types of operations is unlikely to enhance fertility—and serious complications can result from stopping blood flow or tying off the surrounding lymph ducts. For that reason, varicocelectomies were regarded with suspicion by some fertility specialists.

But I have introduced a microsurgical technique that circumvents the problems the earlier repair methods encountered. I developed the technique in the 1980s, while studying the reproductive system of rats at the Population Council's Center for Biomedical Research at the Rockefeller University. My studies required that I transplant testicles from normal rats to previously castrated ones. Rat testicles are quite large in proportion to their bodies; built to the same scale, human testes would weigh about a pound each. Even so, I needed the help of a microscope to sever and carefully reconnect the blood vessels and ducts of my subjects.

When I began my infertility practice years later, I found that it was likewise almost impossible to find the tiny arteries and lymph ducts in human testicles without the aid of a microscope. But by magnifying the area from six to 30 times, I could almost always identify and spare both the testicular arteries and the lymph ducts while ensuring that all the enlarged veins were closed off [*see illustration on page 78*]. Interestingly enough, my friend and colleague Joel L. Marmar of the Robert Wood Johnson Medical School at Camden in New Jersey independently developed the same procedure at nearly the same time I did. Our results have been encouraging: after employing this technique in several thousand patients, Marmar, our colleagues and I have found that the number of healthy, swimming sperm in men with large varicoceles more than doubles and that impregnation rates after one year of trying are 43 percent.

In contrast, men with varicoceles who decline operations achieve successful impregnation only 17 percent of the time. These findings were supported by a 1995 study showing that the impregnation rate for men with varicoceles who underwent varicocele repair was six times higher than the rate for men who did not. The results were especially meaningful because the study, which was sponsored by the World Health Organization, was the first of its kind to compare outcomes between subjects who did and who did not get varicocelectomies. (Previous reports had used before-and-after comparisons of subjects who were operated on.)

Despite these encouraging statistics, varicocelectomy is not appropriate for all men. Those with small varicoceles will have only a 25 percent improvement in the number of healthy, swimming sperm as a result of the operation. The men who will benefit most have varicoceles that are large enough to be felt on physical examination—especially the largest veins that a man can see himself, which look rather like a bag of worms inside the scrotum when he is standing. There are compelling reasons to repair these varicoceles. Because they cause progressive damage to the testicles, they not only decrease sperm count but also lower levels of testosterone, which affects sexual function, the amount of facial hair and muscle strength. We have shown that varicocele surgery raises testosterone levels in infertile men who have low levels to begin with. Thus, men with large varicoceles should consider having them repaired to prevent future impotence resulting from hormone deficiency as well as to prevent further damage to sperm production.

There are alternatives to microsurgery for men with low

sperm counts or poor sperm quality. With in vitro fertilization (IVF)—the technology that gave us the "test-tube baby"—the healthiest sperm can be culled from a man's ejaculate and used to orchestrate conception in the laboratory. With a new technique called intracytoplasmic sperm injection (ICSI), which was pioneered in Belgium by Gianpiero Palermo before he joined our group at New York Hospital–Cornell Medical Center, we can even physically insert a single sperm into an egg cell with a very fine needle. But most couples prefer to do things naturally, and varicocele repair allows conception by way of ordinary sex. It is also much cheaper than IVF. According to calculations published by my urologist partner Peter N. Schlegel, the "per baby" rate—that is, the rate per successful delivery—is less than a third of the per baby rate for IVF, which is about $89,000. The per baby rate includes, in addition to the surgical or fertilization procedures, the costs for the child's delivery, hospital stays and other expenses. For varicocele repair, the surgical fees are $5,000; each in vitro procedure costs about $10,000, and several attempts are usually needed to conceive.

Microsurgery has also greatly aided the repair of blockages or obstructions in the male reproductive tract. Obstructions are suspected if a man with apparently normal testes has no sperm at all in his seminal fluid, a condition called azoospermia. Even though men with varicoceles experience a gradual decline in fertility, their sperm counts rarely drop all the way to zero. But fertility specialists will often see patients who have a zero sperm count—in fact, it is the second most common cause of infertility in men. Before we can treat a man with azoospermia, we need to ascertain whether the condition is caused by a blockage or whether the testes simply are not producing any sperm. To find out, we can measure the blood levels of a hormone called follicle-stimulating hormone, which governs the production of sperm. We also do a testicular biopsy, removing a tiny piece of the testicle and examining it under a microscope for evidence of sperm pro-

Lifestyles of the Infertile




SUBSTANCE OR BEHAVIOR	MECHANISM OF ACTION
ALCOHOL	Decreases sperm production, lowers testosterone levels
ANABOLIC STEROIDS	Disrupts normal hormone activity, lowers sperm count
CALCIUM CHANNEL BLOCKERS	Destroys sperm's ability to penetrate egg
COCAINE	Lowers testosterone levels, sperm production and libido
MARIJUANA	Deforms sperm, impairs sperm movement, decreases sperm production and lowers testosterone activity
NICOTINE	Lowers sperm production, alters sperm shape and impairs sperm movement
RADIATION, CHEMOTHERAPY	Kills sperm cells
WEARING TIGHT PANTS, TAKING SAUNAS, CROSSING LEGS	Raises temperature of testes and reduces sperm production

SOURCE: JON L. PRYOR *University of Minnesota, left to right:* NICK DOLDING *Tony Stone Images;* BERTRAND RIEGER *Tony Stone Images;* LYNN GOLDSMITH *Corbis;* PAUL CHERFILS *Tony Stone Images*

duction. About half the time, the tissue looks like it is functioning normally, and the problem lies elsewhere in the ducts in the scrotum that transport the sperm.

Swimming School for Sperm

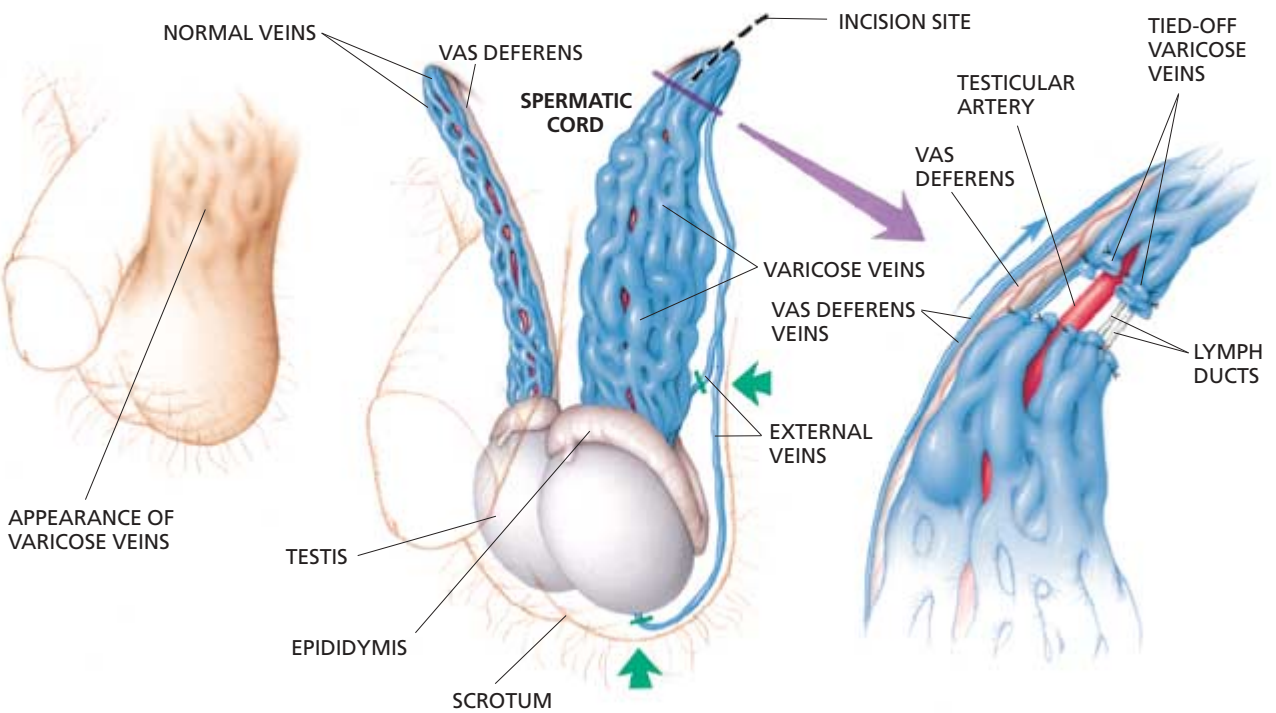
Blockages can result when a urinary tract infection spreads to the reproductive organs, or they can be caused by sexually transmitted diseases, in particular gonorrhea and chlamydia. These infections can scar the epididymis, a narrow, tightly coiled duct that links the testicles to the passages called the vas deferens and serves as a swimming school for sperm. Until the advent of microsurgery, such blockages could rarely be repaired because the epididymis is so small—the duct itself measures just one and a half times the diameter of a human hair. But with magnification and suture materials one seventh the diameter of a hair, the success rates of microsurgical blockage repair are now quite high: sperm return to the semen in more than 75 percent of cases. Much of this success is owed to the efforts of Earl Owen of the Microsearch Foundation of Australia in Surry Hills and his former student, Sherman Silber, a fertility specialist in St. Louis, who together introduced the microsurgical techniques for repairing blockages; the surgery costs about $10,000.

Microsurgery has also helped men who want to reverse a vasectomy, which can be thought of as an elective blockage of the vas deferens. With at least 500,000 men undergoing vasectomies every year and divorce rates topping 50 percent, there is actually quite a demand for such reversals. The procedure is simple in theory: cut out the quarter-inch section of the vas deferens that was closed off and then reattach the free ends. In practice, it is a bit trickier because the part of the vas deferens that was behind the blockage, lacking an outlet, becomes swollen by pressure; meanwhile the part that was on the far end of the obstruction (toward the penis) stays its normal size. Trying to make a leakproof seal between the two is like trying to stitch a garden hose to a fire hose. Again, using magnification, ultrafine sutures and a technique I developed that guides the placement of the sutures, we have had much success in reversing vasectomies. Sperm return in the semen of more than 90 percent of the men on whom we operate, and the average subsequent impregnation rate is 63 percent.

It is true that these blockage repair techniques are of no help to the 5 percent of infertile men who have zero sperm counts because their testes are not producing sperm. In the past, this "nonobstructive" azoospermia resisted treatment altogether. But ICSI, the single-sperm injection procedure, has now made it possible for many of these men to conceive, albeit in the laboratory. In about half of all men with zero sperm counts, a few, rare sperm cells can be found wedged among the other cells of the testes. The hard part is knowing where to look. By avoiding the blood vessels on the surface of the testicles and identifying the tubules that are more likely to contain sperm, New York–Cornell physicians Zev Rosenwaks, Palermo and Schlegel have facilitated impregnation in at least half of these patients. In other words, a quarter of all men with nonobstructive azoospermia, formerly hopeless cases, can now conceive genetically related children.

The recent success stories of infertility treatment are not without their cautionary footnotes. The treatment of nonobstructive azoospermia by way of ICSI is a good case in point.

BAG OF WORMS **(left)** ***is how the scrotum appears with swollen varicose veins that pool blood in the testes, raising their temperature. In a varicocelectomy, a surgeon makes a one-inch incision in the groin area*** **(center)** ***and clips veins*** **(green arrows)** ***external to the spermatic cord, which contains the arteries, vas deferens and other veins. The varicose veins are then tied off, with care taken to avoid the testicular artery and the lymph ducts*** **(right)***. The blood gets routed through healthier veins alongside the vas deferens* **(blue arrow)***.*



JOHN W. KARAPELOU

Genetic testing done by David C. Page and his colleagues at the Whitehead Institute for Biomedical Research and by Schlegel and his associates has revealed that 10 to 15 percent of men with the condition are missing a piece of the Y chromosome, the chromosome that determines the male gender in humans [see "The Key to Masculinity," on page 20]. The genes that control sperm production are also on the Y chromosome, and it is likely that male children born to men with the Y deletions will have the same infertility problem as their fathers. Thus, our treatment for nonobstructive azoospermia may help perpetuate the disease. Fortunately, the chromosomal abnormality does not appear to be associated with any other medical problems.

Another cautionary example is the case of men who are born without a vas deferens. This congenital deformity occurs in about 1 percent of all infertile men, and it can be circumvented by retrieving sperm from the epididymis and injecting them into eggs via ICSI. In fact, most men with the condition can now father children. In collaboration with Rosenwaks, Palermo and Schlegel, our group has attained pregnancy rates of more than 60 percent after just one attempt at sperm retrieval with ICSI.

But it is now known that most men who are missing their vas deferens are also carriers of the gene for cystic fibrosis. Boys with the disease have severe impairments of their respiratory and digestive systems and rarely live to adulthood. Men who carry the gene but do not have the disease risk passing on the gene through IVF techniques, and if the female partner is also a carrier, the test-tube child could end up with the disease itself. Happily, recent advances in IVF technology have allowed fertility specialists to screen embryos for genetic disease before they are returned to the mother's womb, so that they can decide which ones to implant.

Some experts have expressed concern that the techniques of artificial reproduction themselves may be harmful to the children being conceived. Whereas no increase in the incidence of birth defects has been observed with older IVF methods, a doubling in both major and minor defects was recently reported for ICSI births. The resulting rate is still quite low, affecting at most 3 percent of ICSI children. But this troubling statistic is part of a broader good news/bad news scenario that surrounds human reproduction at the close of the 20th century.

ERICA LANSNER

***FROZEN SPERM** for in vitro fertilization are held in a vat cooled by liquid nitrogen at Weill Medical College of Cornell University.*

Mimicking Estrogen

Increasing albeit disputed evidence hints, for example, that chemicals introduced into the environment by industrial processes, by the metabolism of pharmaceutical compounds and by modern changes in diet may be undermining male fertility. These substances, called endocrine disrupters, resemble the female hormone estrogen and have been implicated in genital abnormalities such as undescended testes and hypospadias, an abnormal opening of the urethra (urinary tract) on the underside of the penis rather than at its end. Both these conditions are associated with male infertility, and rates of both abnormalities are escalating throughout the world. In addition, sperm counts in many countries seem to have decreased over the past 50 years, whereas the global incidence of testicular cancer has risen dramatically.

At the same time, our ability to combat male infertility has never been stronger. The same techniques that in the past few years have produced cloned mice and sheep also have tremendous potential for fertility treatments. It is entirely possible that within 10 to 20 years scientists will be able to take cells from any tissue in a man's body and induce the kinds of changes that would enable those cells to fertilize an egg in the laboratory using some future version of ICSI. The steps in such a process are very complex and not clearly understood at present. Once the process is mastered, however, male infertility will become a thing of the past. SA

The Author

MARC GOLDSTEIN pioneered the microsurgical approach to varicocele and blockage repair. Goldstein practices medicine at the New York Hospital–Cornell Medical Center, where he is professor of urology and has been director of the Center for Male Reproductive Medicine and Microsurgery since 1982. He received his medical training at S.U.N.Y.–Downstate Medical Center in Brooklyn and Columbia Presbyterian Medical Center in Manhattan before doing three years' service overseas as a flight surgeon in the U.S. Air Force. On returning, he studied reproductive physiology at the Population Council's Center for Biomedical Research at the Rockefeller University. Goldstein is also a long-distance runner who has finished 14 New York City marathons.

Further Reading

THE COUPLE'S GUIDE TO FERTILITY. Updated edition. Gary S. Berger, Marc Goldstein and Mark Fuerst. Main Street Books, 1995.

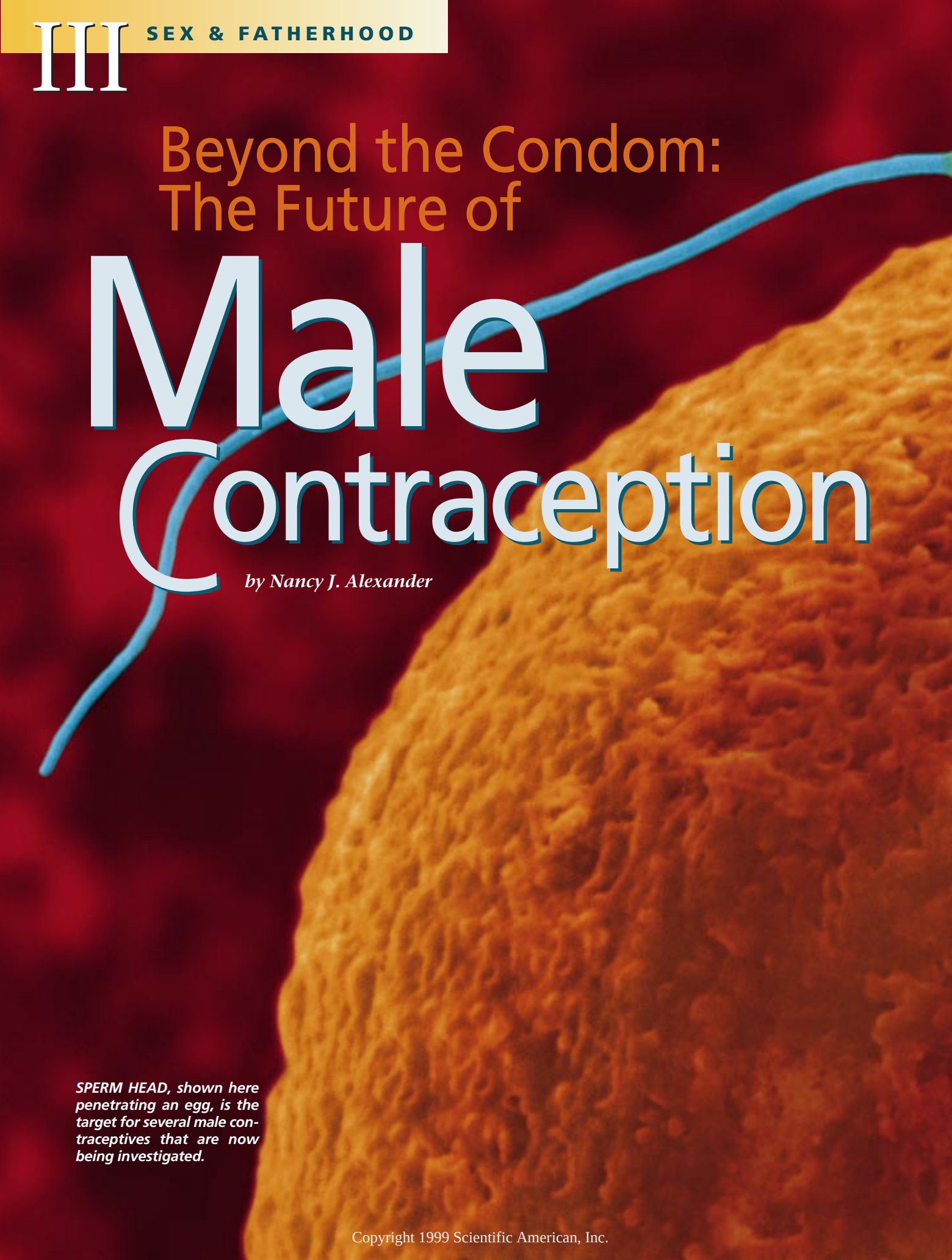
MALE INFERTILITY AND VASECTOMY REVERSAL. American Society for Reproductive Medicine, Birmingham, Ala., 1995. Available from the publisher at 205-978-5000, ext. 127.

TREATMENT OF MALE INFERTILITY. Stuart S. Howards in *New England Journal of Medicine,* Vol. 332, No. 5, pages 312–317; February 2, 1995.

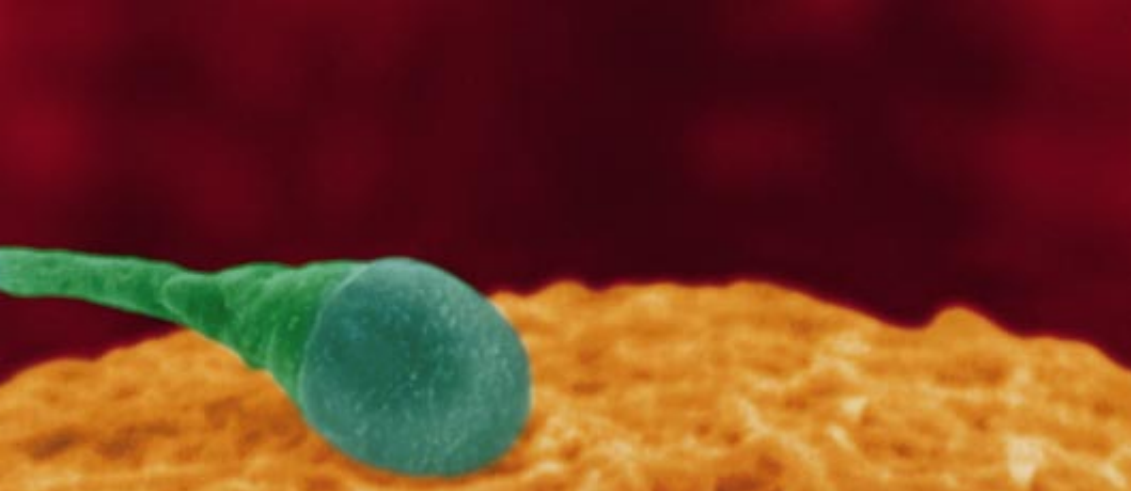
The Center for Male Reproductive Medicine and Microsurgery at New York Hospital–Cornell Medical Center site is at www.maleinfertility.org on the World Wide Web.

Beyond the Condom: The Future of Male Contraception

by Nancy J. Alexander



SPERM HEAD, shown here penetrating an egg, is the target for several male contraceptives that are now being investigated.



DENNIS KUNKEL *Phototake*

The physiology of sperm production complicates development of new forms of men's birth control, but contraceptive researchers continue to explore new leads

Men have long had a limited choice of contraceptive methods: abstinence, withdrawal, condoms and vasectomy. With about three million unplanned or unwanted pregnancies a year in the U.S. alone, however, there is clearly room for more effective methods.

Male contraceptive research today pursues the ideal of birth control that is safe, long-acting but readily reversible, virtually free of side effects and applied sometime other than just before sex. Such a method would also reduce the spread of sexually transmitted diseases and be inexpensive. No product under investigation can meet all these criteria, but several methods could potentially meet many of them.

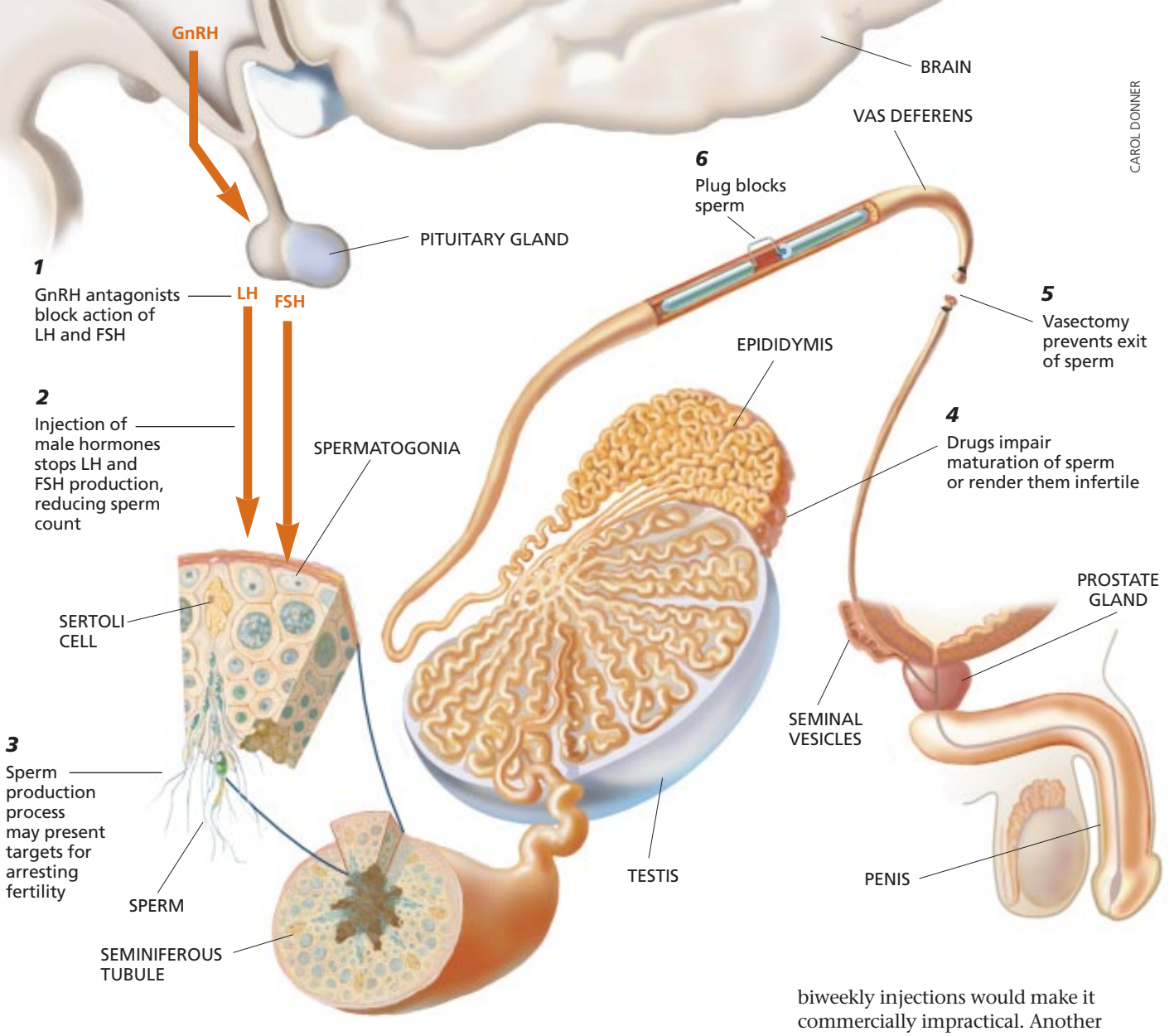
Although research has progressed, male physiology conspires against an easy solution. Every day a man produces tens of millions of sperm, making their elimination or inactivation a daunting task. A woman, in contrast, usually releases only one egg per ovulation cycle. What is more, production of sperm in the testes and their later maturation in the adjoining ducts of the epididymis, where they become capable of fertilizing an egg, take about 75 days. Thus, no intervention in the testes, even if it immediately suppresses the making of sperm, will be contraceptive for almost two and a half months. Conversely, it takes an equal amount of time to return to fertility after stopping use of the contraceptive.

Given these inherent challenges, wholly new types of male contraceptives may not arrive for at least five to 10 years. This lag may seem surprising, but development of any new contraceptive technology takes 10 to 20 years. In the interim, new approaches to conventional contraceptives, including better condoms, may help meet the demand for improvements in male birth control [*see box on page 84*].

The dream of the male Pill—or its semblance—has not faded, though. Longer-term research is targeted at male contraceptives that function by disrupting hormones, by altering the production and maturation of sperm or by rendering sperm infertile.

Suppressing Hormones

The first truly innovative approach to male contraception will manipulate hormones to stop sperm production. Sperm manufacture is controlled by the secretions of gonadotropin-releasing hormone



***INHIBITION OF MALE FERTILITY** can occur along pathways to sperm production and maturation. Synthetic compounds can impede hormones that eventually trigger sperm production in the testes: gonadotropin-releasing hormone (GnRH) from the hypothalamus and luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary (1, 2). Spermatogonia—precursor cells of sperm—develop in the seminiferous tubules and are nurtured by Sertoli cells; both sites present targets for intervention (3). Drugs might also inhibit sperm maturation in the epididymis (4). Vasectomies cut the vas deferens, preventing the exit of sperm (5). Plugs in the vas deferens would block sperm passage; removal of the plugs would allow the sperm to flow again (6).*

(GnRH) from the brain's hypothalamus, which drives the pituitary to produce luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH stimulates the testes to produce testosterone. This steroid, together with FSH, induces cells called spermatogonia in the testes to divide and ultimately give rise to sperm.

One avenue of hormonal attack would be intramuscular injection of an androgen (testosterone or related male hormones), leading to release of the hormone in the bloodstream. The strategy, which is being studied intensively by the World Health Organization, derives from the finding that circulating androgens instruct the brain to dampen secretion of GnRH and thus of LH and FSH. The reduced production of LH and FSH dramatically decreases sperm production.

This approach has proved highly successful in clinical trials, but the required biweekly injections would make it commercially impractical. Another drawback is that high levels of circulating androgens could produce troubling side effects—notably, increased irritability, acne and lowered levels of high-density lipoproteins (the "good" kind of cholesterol). Fortunately, adding a progestin (a synthetic form of the female steroid progesterone) seems to allow men to take a lower androgen dose, an innovation that should eliminate side effects and be safer than taking an androgen alone. A study in Indonesia that employed both Depo-Provera, a progestin used as a contraceptive in women, and one form of testosterone resulted in zero sperm count. Such a combination treatment will probably offer three months of protection—comparable to what women get from Depo-Provera—and might be marketed by the year 2010.

A similar strategy, adopted by William J. Bremner of the Veterans Administration Medical Center in Seattle, has

explored mixing an androgen with an antiandrogen, a synthetic steroid, which reduces the amount of androgen needed to arrest sperm production.

As an alternative to administering androgens, one could block the activity of GnRH with molecules that do not cause androgen-related side effects. Antagonists consisting of small proteins, or peptides, already exist, but they do not stay in the circulation long enough to be contraceptive unless injected daily. Investigators at Merck have designed a nonpeptide inhibitor, which could lead to a pill. Blockage of GnRH would suppress testosterone production, so that men would have to take replacement androgens to retain muscle mass, male sexual characteristics and libido. Biochemists may also tailor "designer" drugs that mimic the sperm-inhibiting effects of androgens, without accompanying side effects. The Population Council, in fact, has begun testing a testosterone analogue (7-α-methyl-19-nortestosterone). Unlike testosterone, the compound resists degradation into dehydrotestosterone, a metabolite that can trigger acne and swelling of the prostate.

Perhaps in 20 years men will have access to long-acting agents (protective for months) that instead of disturbing natural hormone balances directly interrupt spermatogenesis, the complex process of sperm production. Other agents might also impede subsequent maturation of newly made sperm in the epididymis, one of a pair of four- to six-meter (13- to 20-foot) coiled tubes leading from the testes. Or they may inhibit the fusion of sperm and egg. Contraceptives that act directly on these processes could theoretically overcome two disadvantages of male hormonal methods: their interference with testosterone production and the long delay in both onset of contraceptive action and restoration of fertility.

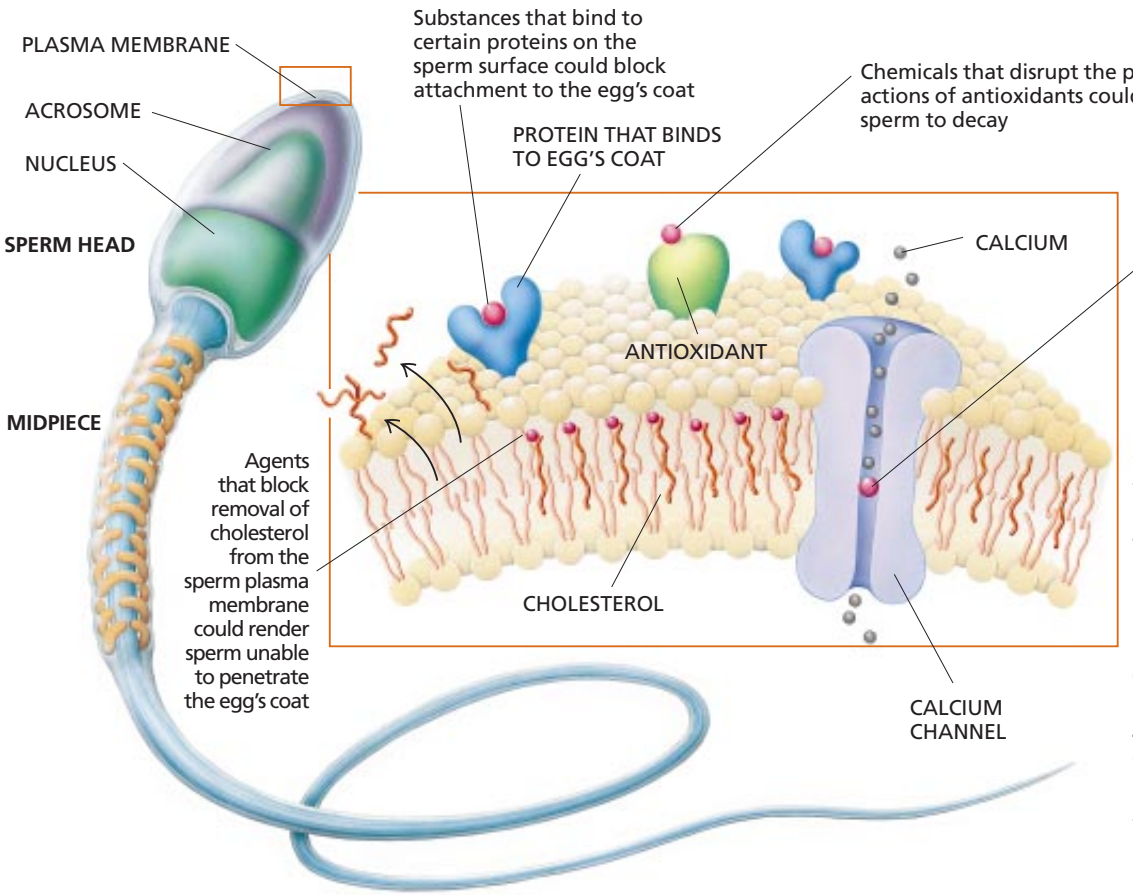
New Strategies

Basic research on sperm formation may lead to an array of new contraceptive strategies. In sperm development the spermatogonia, the cellular precursor of sperm, arise from undifferentiated stem cells found in thin, coiled structures in the testes, the seminiferous tubules. When the stem cells divide, some of their progeny develop into the spermatogonia, which eventually become sperm; the rest remain as stem cells, thereby replenishing the supply of these cells.

Once these events take place, the sperm-cells-to-be move slowly to a central part of the seminiferous tubules, while receiving sustenance from another type of cell, the Sertoli cell. The budding sex cells go through a type of division called meiosis—in which each divides twice, producing four new cells. After meiosis, each new cell contains 23 chromosomes, half the usual number, allowing it to combine with the 23 chromosomes found in the female's egg cell.

Before fertilization can happen, the sperm cells undergo a metamorphosis (spermiogenesis) in which they develop flattened, paddle-shaped heads connected to long tails. At this point, the sperm cells move to the epididymis, the coiled tube that connects a testis with the vas deferens. There maturation continues—sperm become motile, for instance. The young sperm cells remain in the epididymis until they are expelled from the body to become potential fertilizers of an egg.

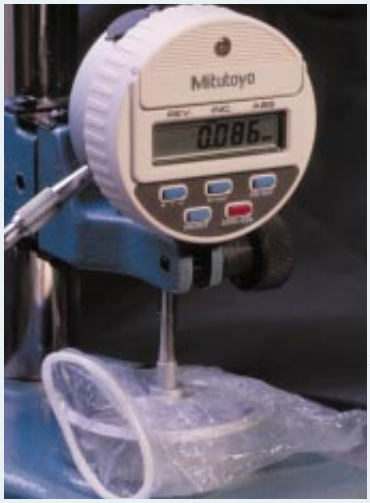
A drug might interfere with almost any stage of this process. It could prevent the stem cells from differentiating into sperm cells, or it might also work



TOMO NARASHIMA

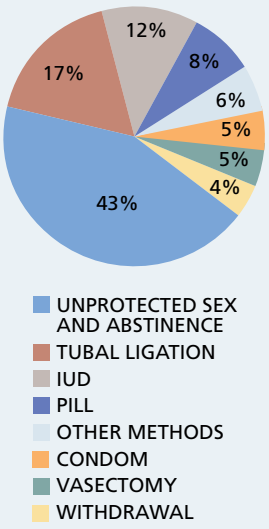
***DEFUSING SPERM** can be accomplished by altering the sperm head. Sperm could be rendered sterile in the epididymis, one of a pair of coiled tubes where the sperm mature. Several approaches* (text blocks at left) *rely on synthetic chemicals* (red dots in detail of plasma membrane) *to alter the head in ways that would prevent sperm from fertilizing an egg.*

Condoms and Abstinence: Current Options for Male Contraception



NATALIE FOBES *Corbis*

***TESTING MACHINE** evaluates the thickness of a condom, still one of the world's most widely used male contraceptive methods.*



LAURIE GRACE

***AVERAGE CONTRACEPTIVE USE** around the world shows that males take less responsibility than their partners do.*

Men who take the responsibility for avoiding their partners' pregnancy can put on a condom, get a vasectomy, practice withdrawal or just say no. The practices of abstinence and withdrawal have not changed much over the centuries, but a few improvements have been forthcoming for condoms and vasectomies.

Abstinence: All adults have periods of abstinence. The definition of abstinence varies, from no genital contact of any kind to not engaging in penetration. Efficacy is virtually 100 percent.

Withdrawal: Coitus interruptus, or withdrawal, has been a major contributor to the diminishing overall birth rate. It is 80 percent or better effective and depends on consistent withdrawal before ejaculation, which may prove difficult for some couples.

Condoms: Properly used, condoms are more than 95 percent effective and are used by an estimated 49 million men. Only latex condoms have been effective against infection by the human immunodeficiency virus (HIV) in clinical trials. Nonlatex condoms, which recently reached the market, have the advantages of longer shelf life and of not being affected by oils and creams that might be used as a lubricant. Some of the new condom designs purportedly provide greater sensitivity because they are of a different material—polyurethane or various copolymers—and may be thinner than latex. Barriers, both physical (condoms) and chemical (spermicides), remain the birth control of choice of 21 percent of women in the U.S.

Vasectomy: This procedure cuts the vas deferens, a muscular tube that connects the epididymis with the urethra. It is an effective method of sterilization used by 45 million men worldwide. Vasectomy prevents the exit of the millions of sperm in the semen and does not affect production of androgens, testosterone and dihydrotestosterone (DHT), which are essential for characteristic male traits, such as facial hair and musculature. In 1985 a new technique was introduced, called no-scalpel vasectomy, that involves teasing the skin apart through a tiny puncture rather than a conventional incision. It speeds healing and reduces fear of surgical mishap.

Although vasectomy can be surgically reversed, it is thought to be a permanent method not appropriate for couples who are considering having children at a later date. A surgical technique, vasovasostomy, can remove the scar tissue where the vas deferens was closed off during the vasectomy and then attach the free ends [see "Of Babies and the Barren Man," on page 74]. The procedure, however, does not always work. It is also expensive and so would be inappropriate for developing countries. Reversible vasectomy methods, which have relied on valves and plugs for the vas deferens, have so far not been sufficiently tested in humans. Ideally, a magnet or electrical impulse would turn off or on the flow of sperm. The strong musculature of the vas deferens, however, usually expels the device.

A newer model, developed by Lourens J. D. Zaneveld of Rush-Presbyterian–St. Luke's Medical Center in Chicago, has circumvented this problem by employing two cylinders of a polyurethane elastomer separated by a thread. Vas deferens contractions during ejaculation move the cylinders within the vas deferens but do not expel it. Studies in Brazil of the reversibility of the procedure have shown promise. But clinical studies have proved difficult to administer: men with successful vas deferens implants seldom want a reversal after only a short period in order to test a scientific concept.

New, nonsurgical methods to block the vas deferens would hold an advantage over a typical vasectomy. Injection of sclerosing agents into the vas deferens, for example, plug the cavity, stopping the advance of sperm. One compound, developed by Sujoy K. Guha of the All India Institute of Medical Sciences in New Delhi, is a liquid plastic that can act as a barrier while only partially blocking the sperm pathway. It generates a positive electrical charge that appears to disarm the acrosome, a bag of enzymes in the sperm head, which fosters sperm-egg binding. A second injection of sodium bicarbonate can reverse the induced infertility. Studies in rats show that fertility was restored 90 days after injection of sodium bicarbonate. Further studies are now ongoing to explore this technique.

In another effort, Chinese investigators have injected a combination of carbolic acid and *n*-butyl cyanoacrylate—the main ingredient in Krazy Glue—as an adhesive to close the tubular passage of the vas deferens. Undoubtedly, finding better ways to turn the vas deferens off and on will continue to preoccupy the research community in the years to come.

—N.J.A.

on the numerous enzymes and other proteins that regulate the function of Sertoli cells, meiosis and spermiogenesis.

In surveying the various stages for intervention, researchers have suggested that disrupting maturation in the epididymis—where the sperm become mobile and achieve the ability to fertilize an egg—might be the most feasible option. Why? Whether delivered by mouth, by injection or by implant, drugs aimed at altering sperm maturation would have to reach the testes or epididymis via the bloodstream; however, blood-borne drugs often cannot pass out of the circulation and into the part of the testes where sperm are manufactured. Further, many drugs that are capable of stalling sperm synthesis have proved toxic to spermatogonia in the testes and would thus lead to irreversible sterility.

The epididymis presents a number of targets for new drug research. Intervention at the level of the epididymis can both affect sperm count and hamper the ability of sperm to fertilize an egg. One set of investigators has found that triptolide, an isolate from a Chinese plant originally used for treatment of skin diseases and rheumatoid arthritis, affects fertility by hindering sperm motility in the epididymis.

Because triptolide disrupted sperm production, researchers worried that it might cause permanent infertility. More recent studies in rats by Amiya Sinha-Hikim and his colleagues at Harbor University of California at Los Angeles Medical Center have shown that at lower doses, triptolide appears to leave sperm production in the testes intact but reduces the number of active sperm in the epididymis by 70 percent.

During sperm maturation in the epididymis, changes in the sperm's outer lipid plasma membrane take place that allow a biochemical reaction that gives sperm the capability of fertilizing an egg. When it encounters an egg cell, a mature sperm's outer membrane merges with a bag of enzymes at its tip (the acrosome). The enzymes then eat through the egg's outer layer to permit fertilization.

Investigators have explored the potential of the antihypertensive drug nifedipine to inhibit fertility, perhaps by preventing the incorporation of a cell receptor into the plasma membrane while a sperm is in the epididymis. This receptor is needed for the plasma membrane–acrosome reaction to allow the sperm and egg to fuse. Susan Benoff and her colleagues at North Shore University Hospital in Manhasset, N.Y., discovered this contraceptive effect when they found that sperm from some men did not fertilize their mates' eggs during in vitro fertilization. Subsequent sleuthing revealed that the men were taking nifedipine, a calcium channel blocker. Stopping the medication reversed the effect.

Benoff suggests that the drug interferes with the discharge of enzymes from the head of the sperm that are essential for fertilization of the egg. Current studies are attempting to determine whether a calcium channel blocker similar to nifedipine can be designed so that it would affect sperm function but would not decrease blood pressure and heart rate, as nifedipine does.

Study of the epididymis may also suggest other ways to inhibit fertility. During the 10 to 14 days that they develop in the epididymis, sperm acquire cholesterol that prevents them from undergoing prematurely the biochemical reaction between the plasma membrane and the acrosome. Chemicals that disrupt the uptake of cholesterol by sperm in the epididymis—either by starving or by overloading them with the substance—might yield contraceptives that would either block the plasma membrane–acrosome reaction or cause it to take place in the epididymis before it can occur between the sperm and egg. Another strategy for a new contraceptive would hinder the action of antioxidants in the epididymis that protect the plasma membrane from free radical chemicals that could damage it.

Selling the Male Pill

In the near term, the challenges may lie as much in the marketing as in the science. Some companies hesitate to develop male contraceptives because of the difficulty of marketing to men. Unlike women, who typically see a gynecologist once a year, men often do not have any relationship with a family physician or urologist, who would alert them to the availability of new drugs.

As with any drug, moreover, potential side effects could lead to a liability quagmire for manufacturers. But perhaps the biggest worry is that a male contraceptive may introduce a new set of tensions between sexual partners. Women must trust the partner—who does not risk pregnancy—to ingest a pill faithfully or to self-administer an injection. To gain acceptance for a male contraceptive, drug companies may have to market accompanying test kits that a woman could use to ascertain a man's sperm levels, an assurance that the man meant what he said.

Regardless of which approach clears the science, marketing, legal and social hurdles, researchers will press on in their pursuit of new male contraceptives to address the important issues of population growth and unintended births. World population currently stands at 5.8 billion and is still increasing rapidly. In the U.S., of the nearly three million unwanted or unintended pregnancies, according to the most recent (1994) statistics, about half ended by elective abortion. Male contraceptives that are more convenient, reliable and accessible can play a role in controlling a burgeoning population and in making more births those of choice. SA

The Author

NANCY J. ALEXANDER has directed contraceptive research programs for many years. She recently joined Organon, Inc., a pharmaceutical company in West Orange, N.J., as an associate director, focusing on current and new methods of contraception. Alexander is also a professor of obstetrics and gynecology at the University of Medicine and Dentistry of New Jersey. She was previously chief of the contraceptive development branch at the National Institute of Child Health and Human Development. In that role, she had responsibility for directing a broad research and development program aimed at new fertility regulation methods for both women and men.

Further Reading

ANTIHYPERTENSION DRUG MAY DOUBLE AS MALE CONTRACEPTIVE. Rachel Nowak in *Journal of NIH Research*, Vol. 6, No. 1, pages 27–30; January 1994.

MALE CONTRACEPTION: IDEAS FOR THE FUTURE. David E. Cummings and William J. Bremner in *Current Therapy in Endocrinology and Metabolism*, Vol. 6, pages 300–304; 1997.

Information on male contraceptives is available at the Population Council site at http://www.popcouncil.org on the World Wide Web.

Teenage American Males:

Growing Up with Risks

Compared with adolescent girls, boys face more danger from alcohol and drugs, auto accidents, HIV, homicide and suicide

by Freya Lund Sonenstein

JUSTINE PARSONS

During their teenage years, most American boys develop into vigorous, healthy young men with few physical conditions requiring medical attention. Nevertheless, many of them engage in behaviors that may compromise their health, either during adolescence or later in life. Young men are much more likely than young women to have several sexual partners, to drink, to use marijuana, to drive recklessly and to engage in physically violent behavior—and they experience correspondingly higher death rates. As higher mortality and health problems have become more widely recognized, a growing number of health promotion initiatives have focused on male teenagers and the special risks they face, with the aim of guiding them toward changing the behaviors that make them vulnerable.

Death rates are low among both male and female teenagers, which attests to their general good health. Accidents and unintentional injuries, followed by homicides and suicides, account for the greatest number of deaths among all teens. This means that most deaths among teenagers are the result of their behavior rather than of disease or other natural causes.

Although deaths among teenage boys are rare in absolute terms, Elizabeth M. Ozer and her colleagues at the National Adolescent Health Information Center at the University of California at San Francisco report that across all races, teenage boys die more frequently than female teens because of accidents, injuries, homicides and suicides. In 1996, for example, according to the U.S. Department of Health and Human Services (DHHS), the death rate among all males 15 to 19 years old was 112 per 100,000, more than 2.5 times the rate among all females in that same age group. In 1996, for 15- to 19-year-olds, motor vehicle crashes accounted for 40 deaths per 100,000 among white male teens (versus 21 among white female teens) and 29 deaths per 100,000 among black male teens (as compared with 13 among black fe-

male teens). Homicides accounted for 12 deaths per 100,000 among white male teens (against fewer than three for white adolescent girls) and a stunning figure of 100 deaths per 100,000 among black male teens (versus 13 for black adolescent girls). Suicides resulted in the occurrence of 16 deaths per 100,000 among white male teens (versus fewer than four for white female teens) and 11 deaths per 100,000 among black male teens (against two for black female teens).

Over the past three decades, overall death rates among all teenagers have fallen, primarily from decreases in deaths related to illness and motor vehicle accidents. Unfortunately, against this declining death rate several disturbing countertrends are clearly visible among adolescent boys. For example, between 1970 and 1993 homicide rates more than doubled among males 15 to 19 years old—increasing from eight to 21 per 100,000. (These rates have recently started to fall.) Among black male teenagers, the rate rocketed from about 50 per 100,000 in 1985 to a chilling 141 per 100,000 teens in 1993. Suicide rates have also increased among male teenagers. From 1970 to 1996, the rate has almost doubled for white male teens, from nine to 16 per 100,000, and more than doubled for black male teens, from five to 11 per 100,000, according to a 1998 report from the DHHS. It is clear from these statistics that young American boys are increasingly falling victim to violence inflicted by others or by themselves.

The dramatic spike in the murder rate took place between 1985 and 1993. Although there is no conclusive proof of the causes of this tremendous rise over so short a period, this time frame does coincide with the appearance of crack cocaine on the streets of some large cities, the dramatic rise in male teenage involvement in drug dealing and its attendant violent disputes, and the spread of handguns among urban male teenagers.

ANDREW LICHTENSTEIN *Impact Visuals*

A Violent World

Indeed, many more male teenagers than in the past apparently engage in behaviors that carry the threat of physical harm. For example, alarmingly high numbers of male teenagers appear to be carrying weapons and engaging in violent behavior. In the 1995 National Survey of Adolescent Males (NSAM), Charles F. Turner, currently at Queens College of the City University of New York, and his colleagues working on the NSAM found that 12 percent of 15- to 19-year-old boys reported carrying a gun in the past month, and 27 percent indicated that they carried a knife or razor. Nearly 9 percent had pulled a knife or gun on someone else in the past year, and more than twice as many (21 percent) had someone pull a knife or gun on them. Approximately one quarter (26 percent) had threatened to hurt someone within the past year, more than one third (34 percent) had experienced such threats, and 44 percent had been in a physical fight. Significantly more than half (58 percent) of adolescent boys had engaged in one or more of these behaviors, and most who did engaged in more than one.

For female teenagers, life is very different. For example, the 1995 Youth Risk Behavior Surveillance Survey, conducted in classrooms around the country by the U.S. Centers for Disease Control and Prevention, shows that 8 percent of high school females reported carrying a weapon on one or more days during the month surveyed.

DONNA BINDER *Impact Visuals*

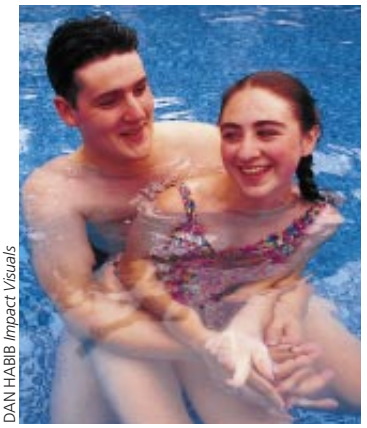
Alcohol, Drugs and Tobacco

Teen use of alcohol and illicit drugs also threatens their health. Alcohol is associated with higher rates of motor vehicle accidents, school problems and delinquency. Again, boys are more at risk than girls are. In 1997 the Monitoring the Future study conducted by the University of Michigan found that 38 percent of male 12th graders reported binge drinking—that is, having five or more drinks in a row—within the two-week period surveyed. The comparable—and substantially lower—proportion for females was 24 percent.

In contrast, the same survey indicates that marijuana use among male and female 12th graders has risen since 1992, after declining during the 1980s. In 1997, 26 percent of males versus 20 percent of females surveyed had used marijuana in the previous 30 days. Rates of reported use of other drugs such as inhalants, hallucinogens and cocaine are lower, ranging from 8 to 12 percent for male 12th graders. Intravenous drug use, with its very high immediate health risks, is lower still, at 1 percent of males 15 to 19 years old in the past year. The 1998 National Survey of Adolescent Males shows, however, that a worrisome 5 percent of male teens have engaged in intravenous drug use at some time.

Adolescence is also the time when many people begin to smoke cigarettes or use tobacco in other forms, a behavior that carries long-term health risks and costs. Rates of smok-

ing among male and female teenagers are comparable and relatively high: in 1997, 24 percent of female 12th graders and 25 percent of male 12th graders smoked daily. Whereas boys are not at higher risk from cigarette smoking, they do use much more smokeless tobacco (19 percent of boys as compared with 1 percent of girls), which carries higher risks of oral cancer and other health problems.



DAN HABIB *Impact Visuals*

More Partners and Rising STDs

Many people have sex for the first time during their teenage years, the health consequences of which vary considerably depending on how young the teenager is, whether contraception is used, and the number and types of sexual partners the person has over time. The health risks of early sexual activity for girls, especially unprotected sex, are widely recognized as unintended pregnancies or births. Less attention has been paid to the health risks sexual activity poses for male teenagers, probably because it is expected that "boys will be boys." Nevertheless, unprotected sexual intercourse for male teenagers can result in sexually transmitted diseases (STDs), including HIV.

Boys are at higher risk from sexual activity because more of them are active. In 1995 just over one half (55 percent) of males and almost half (49 percent) of females 15 to 19 years old reported that they had had sex at least once.

Although in 1995 most teenagers at 15 to 19 were sexually experienced, only a small fraction of them were very sexually active, having multiple partners in a given year. Males are more likely to engage in multiple relationships than females are and to be exposed to risks, such as increased exposure to HIV and STDs. Among sexually experienced 15- to 19-year-olds, 62 percent of females and 44 percent of males have had only one partner in the past year, and 8 percent of females and 10 percent of males have had no partners. Relatively few teenagers—13 percent of girls and 20 percent of boys—report more than three partners in the past 12 months.

Some teenage boys also initiate homosexual contacts. In the 1995 NSAM, 5.5 percent of 15- to 19-year-olds reported that they had sexual contact with another male (including mutual masturbation, oral sex or anal sex). This study also demonstrated that teen reports of same-sex contacts are strongly influenced by the way the questions are posed: boys were much more likely to report same-sex contacts in a computer-administered format than in a self-administered paper-and-pencil questionnaire—the 5.5 percent statistic comes from computer-administered data.

It may seem anomalous that within the same age group, 55 percent of boys are sexually active, whereas only 49 percent of girls are. Yet this discrepancy may be accounted for in several ways: the boys may be having sex with girls younger than 15 and older than 19; the boys may be having sex with multiple girls in this age group, whereas the girls with whom a given boy has sex have him as their only partner. Moreover, because the data are self-reported, some may respond dishonestly in order to give more socially desirable answers.

Of course, when teens initiate sexual intercourse early, they have the opportunity to accumulate several partners through their teenage years, even at the rate of only one a year. By age 19 the average unmarried, sexually experienced male teenager has had nine partners, whereas his female counterpart has had only three partners.

The number of sexual partners that an individual has had and the number of liaisons those partners have had are critical indicators of risk for STD transmission: the more partners, the higher the risk, which places the more sexually active boys at greater risk than the girls.

Many teenagers, however, report using condoms or other forms of contraceptive protection when they have sex, and over the past decade the substantial rise in condom use among teenagers has been one of the major public health success stories. It is believed that much of this rise is the result of education programs and the recognition of the threat of AIDS. Between 1979 and 1988, condom use reported by sexually experienced male teenagers ages 17 to 19 living in metropolitan areas more than doubled from 21 to 58 percent who used a condom during their last sexual episode. By 1995 the rate had increased again to 67 percent for all those boys between ages 15 and 19.

Still, the risk remains very great: in 1995 more than one quarter (27 percent) of male teenagers in the NSAM reported having had unprotected sex in the past year. The risks were substantially higher among African-American and Hispanic male teenagers, of whom 39 and 37 percent, respectively, said they had had unprotected sex in the past year.

The Institute of Medicine (chartered by the National Academy of Sciences) has characterized sexually transmitted diseases as a "hidden epidemic" because most people do not know that of the top 10 most frequently reported diseases in 1995 in the U.S., five were STDs. In fact, Ozer and her colleagues have stated that STDs are the most common and destructive infections among adolescents. In a recent report from the Institute of Medicine, Thomas R. Eng and William T. Butler have estimated that 25 percent of new cases of STDs are among 15- to 19-year-olds, possibly because teenagers still show an abysmal lack of knowledge about the risks and dangers involved. For example, in 1995 only 1 percent of teenage males in the NSAM thought that their last partner probably or definitely had an STD, a proportion well below actual prevalence rates. In 1997 in the 15- to 19-year-old group, nearly twice as many girls than boys had gonorrhea, and nearly eight times as many girls had chlamydia.

Teenagers are much more familiar with the dangers of HIV infection and AIDS. The actual number of AIDS cases among teenagers is quite small (less than 1 percent), but the high rate of STDs among teens indicates how vulnerable teens are. (In 1997 the highest age-specific gonorrhea and chlamydia rates among females and the second highest rates among males were in the 15- to 19-year-old group.) Indeed, in 1996 AIDS was the sixth leading cause of death among males ages 15 to 24 and the second leading cause of death among 25- to 44-year-old men in the U.S. This second statistic is significant regarding AIDS risks for teenage boys: currently the number of deaths caused by AIDS is substantially higher among men than among women. Because of the long incubation period, it is believed that for many of the AIDS cases diagnosed among adults, the actual transmission of the virus occurred during the patients' teenage years.

JUSTINE PARSONS

Multiplying the Risks

Even though teenage boys engage in more risky behavior than girls, the greatest danger to male teenagers seems to be that a significant percentage of them multiply their risk even further by engaging in more than one risky behavior. Studies have shown that teenagers who become involved at early ages in one risky behavior—violence, substance use or sex—are highly likely to be involved in others. For example, the 1995 NSAM reveals that male teenagers who use drugs or have school problems or past criminal involvement are more likely to be sexually active. Research has also shown that psychological factors—including personality traits such as unconventionality, low levels of self-control and an apparently inborn "sensation seeking" trait that may be rooted in (or expressed through) the chemistry of the central nervous system—may all be precursors of multiple-risk behavior. Different degrees of these traits can be identified in children as young as age five, which suggests that they are influenced by both inheritance and early family life.

Multiple-problem behavior is more common among boys than girls, and a disturbingly large fraction of teenagers engage in many risky behaviors simultaneously. In 1995 among males aged 15 to 19, 55 percent were sexually experienced, 37 percent had some involvement with criminal behavior (they were picked up by the police, arrested or jailed), and 37 percent had used marijuana, cocaine or other illegal drugs in the past year. The statistics in the NSAM show that 29 percent of teenage males exhibited none of these risks, 54 percent exhibited one or two of these risks, and 16 percent engaged in all three.

The higher occurrence of problem behaviors among teenage males suggests that the origin of these behaviors rests in biogenetic differences between boys and girls and in differences in social expectations about gender behavior. Some studies have uncovered interesting evidence linking testosterone levels with risk-taking behavior. Reid J. Daitzman, a psychologist and independent researcher in Stamford, Conn., and Marvin Zuckerman of the University of Delaware, for example, showed that higher testosterone levels were related to sensation seeking in college males. J. Richard Udry of the Carolina Population Center at the University of North Carolina at Chapel Hill conducted a longitudinal study of 13-year-old boys in a North Carolina school district and found that testosterone levels measured at the start of the yearlong study predicted the number of problem behaviors that the boys would—and later did—engage in.

Yet this association between hormone levels and behavior did not persist over the study's second and third years. Udry speculates that hormonal changes in early adolescence may be critical for the initial development of problem behavior at that time: afterward the behavior is self-perpetuating, independent of subsequent testosterone levels. This study also examined the effect of social and psychological measures on risk

taking and found, for example, that low levels of religious participation and high levels of autonomy consistently and independently predicted higher rates of problem behaviors.

There is also evidence that social pressures play a role as well. For example, teenage males who strongly endorse a traditional view of masculinity are more likely to engage in risky behaviors. Joseph H. Pleck of the University of Illinois and his colleagues found that boys in the 1988 NSAM who scored higher on a scale of traditional male-role ideology—which measures how teens think males should behave—were more likely to engage in problem behaviors such as getting suspended from school, drinking, using drugs, being picked up by the police, taking multiple sexual partners, tricking or forcing someone to have sex, and using condoms inconsistently.

Pleck's eight-item scale measuring beliefs about male roles includes both positive and negative items that are not intuitively linked to most of the problem behaviors:

1. It is essential for a guy to get respect from others.
2. A man deserves the respect of his wife and children.
3. I admire a guy who is totally sure of himself.
4. A young man should be physically tough, even if he is not big.
5. A guy will lose respect if he talks about his problems.
6. It bothers me when a guy acts like a girl.
7. I don't think a husband should have to do housework.
8. Men are always ready for sex.

Teen males scoring highest on this scale are more likely to engage in risky behaviors, and this correlation holds across racial-ethnic groups and other subgroups defined by age or educational expectations. This study literally indicates that endorsing beliefs about being tough and getting respect—traditionally part of the core of what it means to be a man in the U.S.—may lead young men to engage in behaviors that endanger their health.

Programs to Change Risky Behavior

On the positive side, evidence shows that if teenage boys can avoid risky behaviors, they can improve their chances of better health in adolescence and later life. Fewer motor vehicle deaths and increased use of condoms among young men over the past decade demonstrate that risky behaviors can be altered. These changes may be coming about at least in part because of education and prevention programs.

As a result, many health prevention initiatives have sprung up around the country to help teenagers avoid and overcome risky behaviors. They have typically focused on single behaviors or problems: smoking, drinking, drug use, careful driving or safe sex. Increasingly, however, as it has been recognized that young people face multiple risks, it has become clear that prevention efforts should be more wide-ranging and should deal with the varied risks teens face and with the overall family and neighborhood context in which risky behaviors arise.

For me, this message was underlined by a review I recently conducted, which examined programs working with teenage boys to reduce sexual risk taking. I found that programs that successfully attract young men and promote responsible sexual behavior appear to share two philosophical principles. The first is that they must respond to the social environments and pressures faced by the young males in their communities. They must focus on concrete life issues—increasing self-esteem, building relationship skills, improving academics and creating a positive outlook for the future—to give young men the tools they will need to take control of all the areas of their lives.

The second principle is that the programs need to focus on redefining what it means to be a man. We found this theme reiterated in a range of programs targeted to male teenagers across cultural settings. In Hombres Jóvenes con Palabra ("Young Men with Integrity"), Jerry Tello has developed a rites-of-passage initiative for Latino youth, in which the concept of *machismo* is reclaimed and redefined to reflect the traditional concept of *el hombre noble* ("the noble man"): a man of his word who takes care of his girlfriend, family and community. In the Youth Education and Development Program run by the Urban League of Eastern Massachusetts, young men in Roxbury explore the difference between biologically fathering a child and being a caring, committed "dad." In Des Moines, in the It Takes Two curriculum developed by Tom Klaus of the Legacy Resources Group in Carlisle, Iowa, participants dismantle conventional gender stereotypes such as G.I. Joe and Barbie and learn how to build mutual respect and shared responsibility into relationships between men and women. Across these programs, staff work to redefine "manly" as taking responsibility and having positive values and goals.

Both research and the results of these programs indicate that broad-based approaches are needed to address these behavior-related health risks and to help teenage boys avoid drugs or alcohol, risky sexual behavior and violent relationships. Successful programs respond to the multiple risks teenagers face, as well as to the family, peer and neighborhood conditions that predispose teens to risky behaviors. There is also promising evidence that changing male teenagers' ideas about what it takes to be a man could curb some of the risky behaviors that young men believe attest to virility but that actually threaten their health. SA

The Author

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Further Reading

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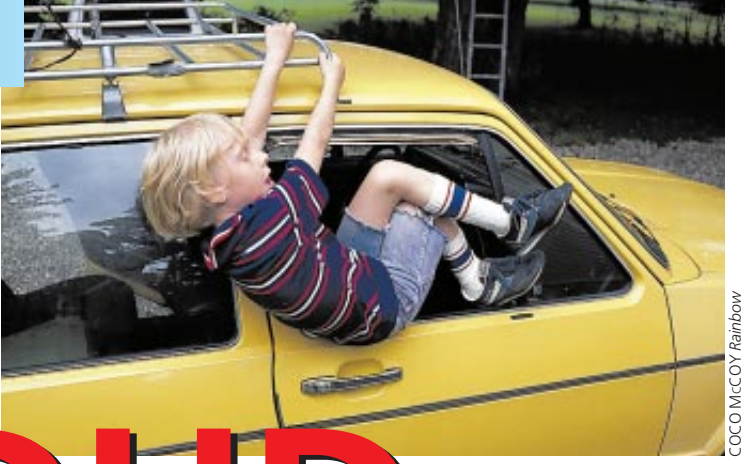


COCO McCOY *Rainbow*

Grappling with ADHD

by Tim Beardsley,
staff writer

Ritalin seems to help affected children in more

More than 1.5 million children in the U.S., 80 percent of them boys, are now medicated to treat attention-deficit hyperactivity disorder (ADHD). The number is growing rapidly. Girls account for about one third of all cases but are less likely to be treated, probably because they are less disruptive.

The alarm that many physicians and parent-advocacy groups feel about this mass medication is not hard to understand. The ultimate cause of the syndrome, which leads to distractibility and impulsivity, is entirely obscure. A prominent researcher, Russell A. Barkley of the University of Massachusetts Medical Center in Worcester, has identified the condition as a developmental failure in brain circuitry that governs inhibition and self-control [see his article "Attention-Deficit Hyperactivity Disorder," SCIENTIFIC AMERICAN, September 1998]. And ADHD often persists into adulthood. Yet although the affliction can be inherited, genetic studies suggest that it is an extreme form of common types of behavior rather than a clear-cut pathology. Rules for diagnosis exist, but physicians probably both overdiagnose and underdiagnose it because of differences in methods of evaluating patients.

The preferred treatment for ADHD has prompted particular anxiety. The drug most commonly used, Ritalin, is a mild stimulant, but others, such as Adderall and dextroamphetamine, are versions of amphetamine, a well-known drug of abuse. Use of stimulants to treat ADHD has increased eightfold in the past decade, and the drugs may be continued for as long as a patient shows symptoms, often for years. The trend has dismayed critics, such as Steven P. R. Rose of the Open University in the U.K.: he describes it as the "medicalization of everyday life." Between 3 and 13 percent of children in the U.S., who in times past would simply have been called ill behaved, inattentive or impulsive, are now diagnosed as victims of ADHD.

The scenario could look like mass child abuse: adults, confounded by the overexuberant behavior of some of their charges, medicate them to boost their academic performance and to make them easier to live with. Most parents initially show reluctance to ply their children with a psychoactive drug, and the raging public controversy has probably deterred many from resorting to Ritalin. A clutch of recent books may fan their fears by airing worries about the long-term effects of the drugs, which have not been thoroughly studied.

Yet spending time with an ADHD-affected child can leave a powerful impression that the youngster, not just the caregiver, carries a burden of troubles. Children with ADHD perform poorly in the classroom and have difficulty making friends. And those whose condition persists into the teen years seem to be at increased risk of abusing drugs and having automobile accidents, according to Rosemary Tannock of the Hospital for Sick Children in Toronto. (Children diagnosed with ADHD are also more likely than others to drop out of high school and to get into trouble with the law, but, Tannock notes, these consequences seem to stem from separate conduct disorders that are often, confusingly, present in children with ADHD.)

The known problems associated with ADHD start to make treatment sound more reasonable. Many conditions besides ADHD that are medically treated are just extreme forms of a common abnormality; hypertension is an example. And a range of studies leaves no doubt that at least in the short term, stimulants work. Medication allows the majority of ADHD children to complete tasks more effectively and to relate better with teachers, parents and other kids. It apparently does not boost long-term academic achievement, however.

Behavior management techniques, such as "time out" for everyone to cool down when things get heated and earning privileges for good behavior, may help somewhat at the time they are used. But a new study of the effects of 14 months of treatment, conducted under the auspices of the National Institute of Mental Health (NIMH), strongly supports drug therapy in conjunction with regular visits to a doctor as the therapy of choice, finding little benefit from behavioral techniques either alone or in combination with medication. Peter S. Jensen of the NIMH and others conducted the study at multiple sites. Other forms of treatment, including dietary supplements, restricted diets, psychotherapy, biofeedback and play therapy, have not shown any beneficial effect.

Stimulants also appear to be remarkably safe. At the therapeutic dosage, they rarely cause dependence, nor do they cause euphoria. Sixty years of experience with prescribing the drugs have revealed no obvious long-term side effects, points out Alan J. Zametkin of the NIMH. Moreover, a study by Jan Loney of the State University of New York at Stony Brook seems to quash a long-standing worry that Ritalin could push kids toward subsequent abuse of illegal drugs. An

earlier study had raised that alarming possibility, but its design was not able to distinguish adequately the effect of treatment with stimulants on illegal drug abuse from the effect of ADHD itself, according to Loney. Her study, in contrast, constituted a "natural experiment" that made the distinction clear. Boys in Iowa with behavior problems had been assigned, effectively at random, to see one of three physicians. Two prescribed stimulants for most cases of ADHD; the other almost never did. Loney's data indicate that treatment with prescription stimulants seems to reduce by a third the risk of drug abuse years after treatment has ended: 58 percent of those with ADHD who had not received stimulant treatment had some experience with illegal drugs, as compared with only 38 percent of those who had been treated. Timothy E. Wilens of Harvard Medical School likewise finds that treating childhood ADHD with stimulants reduces (by an impressive 68 percent) the subsequent risk of drug or alcohol dependence in adolescents. Wilens says he does not know whether the protective effect will persist.

ways than one, but doubts still persist about long-term effects

In essence, the controversy over short-term effectiveness and safety of drug therapy for ADHD has drawn to a close. Drugs have won the day over any of the myriad alternatives proposed. Yet other controversies surrounding the condition and its treatment are unlikely to dissipate soon. Multiyear studies on the safety of stimulants are needed, notes John Heavener of Children and Adults with Attention Deficit/Hyperactivity Disorder, a patient-advocacy organization. And some doubters, such as Donald A. Berry of Duke University Medical Center, are still troubled by the possibility of unrecognized long-term side effects. Berry, who participated last year in a 13-member panel organized by the National Institutes of Health that issued a consensus statement on ADHD, says he was the lone member who resisted recommending the use of stimulants. Still, the lack of formal evaluations on long-term side effects is hardly unique to Ritalin and other stimulants.

The inconsistencies in ADHD diagnosis and treatment remain a problem, according to the draft report of the NIH consensus panel. Some practitioners do not use structured questionnaires that would provide a more definitive diagnosis but instead rely on parents' assessments to guide their decisions. Moreover, family practitioners are more likely to prescribe medication than psychiatrists or pediatricians are. "People have been slipshod sometimes about diagnosis," comments Virginia Douglas, a pioneer researcher at McGill University. "There is a tendency to start using [stimulants] whenever people have difficulties with a child." Drug therapy succeeds in inhibiting behavior but at the cost of sapping natural spontaneity. "It makes for a more regulatory style," Douglas says, "and makes carefree kids cautious." But she does endorse stimulant treatment with appropriate monitoring. And most physicians, parents and teachers contend that the opponents of stimulant treatment have no good arguments left. The drugs' clear benefits, Zametkin asserts, make hypothetical fears nothing more than "inflammatory" rhetoric.

Another priority, the NIH consensus panel reports, is sorting out the links between ADHD and other coexisting conditions, including depression and oppositional-defiant disorder (basically, chronic disobedience). And there remains the possibility that as prescription stimulants are more widely used, more of them may be abused. But many families who confront the dilemmas of ADHD-induced unruliness and worry about possible consequences should take comfort that current therapies appear to be safe and to control symptoms. For some children, they may spell the difference between a measure of calm at school and at home and an existence of unrelenting chaos. SA

Diagnosing ADHD

Psychiatrists suspect attention-deficit hyperactivity disorder (ADHD) if the individual persistently displays six or more of the following symptoms of inattention or six or more symptoms of hyperactivity and impulsivity. The signs must occur often. (Adapted with permission from the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders.* ©1994 American Psychiatric Association.)

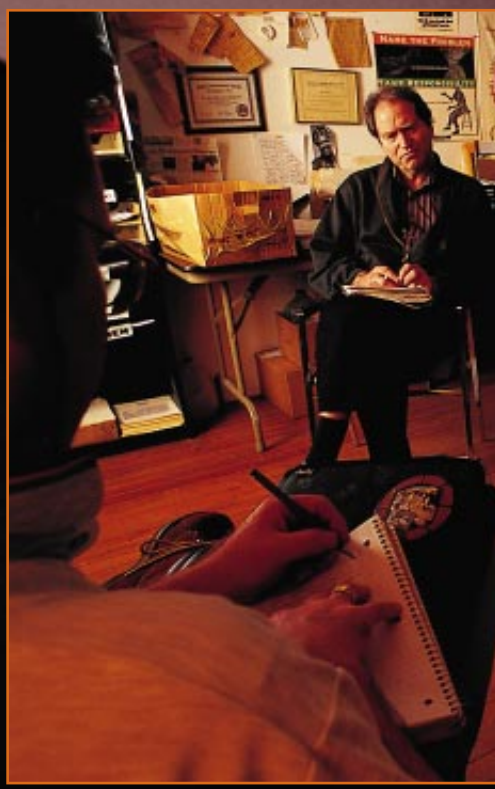
INATTENTION

- Fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities
- Has difficulty sustaining attention in tasks or play activities
- Does not seem to listen when spoken to directly
- Does not follow through on instructions and fails to finish schoolwork, chores or duties in the workplace
- Has difficulty organizing tasks and activities
- Avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork)
- Loses things necessary for tasks or activities (such as toys, school assignments, pencils, books or tools)
- Is easily distracted by extraneous stimuli
- Is forgetful in daily activities

HYPERACTIVITY AND IMPULSIVITY

- Fidgets with hands or feet or squirms in seat
- Leaves seat in classroom or in other situations in which remaining seated is expected
- Runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, subjective feelings of restlessness)
- Has difficulty playing or engaging in leisure activities quietly
- Is "on the go" or acts as if "driven by a motor"
- Talks excessively
- Blurts out answers before questions have been completed
- Has difficulty awaiting turns
- Interrupts or intrudes on others

Treating Men Who



J. D. TALASEK *Phototake*

Batter Women

ANN STATES *SABA*

TREATMENT PROGRAMS for men who batter generally follow one of three principal approaches. This group session conducted by Men Stopping Violence, a program in Atlanta, uses the feminist model: it aims to change men's attitudes toward women by undoing their sexist socialization.

Treatment programs for men who abuse their partners are proliferating, but their effectiveness remains unclear. A growing body of research about the types of men who batter may help experts tailor treatment more precisely

by Marguerite Holloway, **staff writer**

The scene is a football field. Three-hundred-pound bodies are preparing for the all-American pastime: bone-crunching battering. A player on the field turns to the camera: "There was a woman who walked into doors and one who frequently tripped on smooth floors." Other football players pick up the story: "A mother of three broke her arm on the stairs; another simply stumbled over a chair. There was a woman who hid scars under her hair, and for some reason, she's no longer there." It is a bone-chilling poem, part of a public-service campaign against domestic violence sponsored by the Liz Claiborne Foundation and one of the first to speak directly to men. The advertisement took its cue from real life. The years following the O. J. Simpson trial have seen an ominous rise in reports of sports figures assaulting women—with little repercussion for many of the athletes. Christian Peter of the New York Giants has been convicted twice for assaulting women, and he continues to play. Darryl Strawberry of the New York Yankees was arrested for threatening his then wife with a gun. The list goes on, running through the ranks of other football teams and a host of baseball and basketball lineups.

Although Northwestern University researcher Jeffrey Benedict—author of *Public Heroes, Private Felons*—has found athletes disproportionately violent toward women, they are

ANN STATES *SABA*

TERRENCE "RED" CROWLEY of Men Stopping Violence says the goal of the treatment program is not only to change men's attitudes of superiority toward women—"an attitude that encourages domestic violence"—but also to engage the entire community so that violence against women is not tolerated.

hardly the exception. According to the most recent figures from the National Institute of Justice, approximately 1.5 million American women are raped or physically assaulted, or both, by an intimate partner every year. Despite three decades of awareness about domestic violence—including efforts to identify, treat and protect battered women and, more recently, to arrest consistently men who batter—the practice appears tragically entrenched.

As the recent advertisement indicates, however, men are increasingly being targeted in public-awareness campaigns and in intervention programs. Since the mid-1980s, many states have mandated arrest for incidents of domestic violence, and consequently the judicial system has been swamped with cases of men who batter. In many instances, courts have been requiring that offenders attend treatment programs or receive counseling. This demand has led to a proliferation of programs for batterers, but it has also led to controversy. Many people who treat battered women and children are concerned that money will be redirected from shelters or from women's services. Furthermore, there have been few data to show that treatment programs are effective.

Nevertheless, many experts who have been treating men who batter say methodologically sound studies are beginning to show the programs do have an impact. In addition, some studies of men who batter suggest that there are very different kinds of abusers. Rather than lumping all men into one category, as was generally done in the 1970s, researchers are defining batterer types. These findings could have implications for refining treatment programs, and accordingly they are being championed by therapists and experts who have argued that a tailored, integrated approach would be most effective in treating men who batter.

"I am relieved to see this kind of thing emerging. We need to lend a scientific lens to this, as we do to any other psychological phenomena," comments Janet A. Geller, director of the Family Violence Prevention Center at the Jewish Board of Family and Children's Services in New York City. "Because at one time, men were being objectified as well: they were all batterers because of power and control. That is partially true, but it is too linear an explanation. Human beings are much more complicated than that."

Feminist Legacy

Treatment programs for men who batter originated in the late 1970s, growing directly—and, initially, tentatively—out of the battered women's movement. Women's activism drew attention to the horrors of domestic violence, bringing hidden abuse into public view and establishing shelters (a solution that began in England in 1971). After a few years, though, people who worked with the victims of violence began to turn their attention to men, who would often just move on to another relationship in which they would batter again. And they started to see different women coming in who had been abused by the same man, recalls Richard M. Tolman, professor of social work at the University of Michigan, who began working in 1980 with men who batter in Anchorage, Alaska. "People began to ask, 'What about men? Can we help them? Can they be stopped?' "

The first programs for men were built around what is called the pro-feminist model. Counselors view violence as an extension of patriarchy, as a way of men maintaining power. Men enrolled in these programs go through resocialization. They examine how men and women are socialized by looking at magazine advertisements, films and other cultural forces that shape how men's and women's roles are defined. And they learn new skills for dealing with their relationships: how to express frustration or anger without becoming violent. This is the approach taken, for instance, by Men Stopping Violence, a program begun in Atlanta in 1982. "Historically, there has been a presumption of male su-

periority in the world," explains Terrence "Red" Crowley, director of the program's community intervention evaluation project. Men Stopping Violence places emphasis on social change rather than on simply treating individual men. "We figure out how to challenge and deconstruct their thoughts and beliefs about women that encourage violence against women," Crowley elaborates. "We want to be a visible presence in the community to indicate to the community that violence against women is a problem and that it exists."

The pro-feminist model is the most popular and widespread method of batterer treatment. The other two methods emphasize either family interaction counseling or psychotherapy. The family interaction approach, which examines the couple's relationship, is the least common because it has been criticized for being potentially dangerous to the woman: if she complains during a session, she may end up being beaten to a pulp at home. Indeed, 20 states actively prohibit couples counseling for this reason. The psychodynamic model focuses on the batterer's history and psychological problems and aims to work them out during therapy. Some of the most well-known and long-standing batterer treatment programs—such as EMERGE in Boston—combine elements of the pro-feminist approach with cognitive behavioral techniques, examining gender roles but also examining past and current relationships with women as a forum for self-exploration and change.

Despite the fact that programs for men who batter have been around for two decades, it has been hard to assess whether the programs are successful. In many instances, the question is moot: 30 percent of the men referred to programs do not show up, and about half those who do drop out. For those who stay, success seems to range from 53 to 85 percent—when success is defined as the cessation of beating according to reports by the woman. But some studies have found that abuse sometimes ceases on its own after the batterer is arrested, without the need for further intervention. And one study found that men who went through treatment became even more physically aggressive.

"I don't think the data are clear-cut," says Tolman, who has co-authored a review of programs with Jeffrey L. Edleson of the University of Minnesota. "We just don't know at this point which [programs] are most effective." Tolman compares batterer treatment services to services for psychological problems: "We just haven't had any stunning success in any realm of psychotherapy. People need to keep that in mind."

Assessing efficacy has been very difficult for many reasons, explains Edward W. Gondolf, professor of sociology at Indiana University of Pennsylvania and research director at the Mid-Atlantic Addiction Training Institute. First, the study methods have often been very different, making it difficult to compare studies: some have relied on subsequent arrest records to check success, some on the victims' reports of recurring violence, and others on a combination of both; some have described only the absence of physical abuse, not the presence of verbal and emotional abuse. Second, the programs all run for different periods, and there is no agreement on what length of follow-up is sufficient. Third, few studies have had control groups because it would be unethical: an untreated batterer in a control group might kill his wife during the course of the study. Fourth, response rates are often very low. The enormous costs of longitudinal research limit how well treatments can be monitored. Gondolf notes that the study he is currently conducting costs $1 million to track about 840 people in four cities for 15 months. The study, which is funded by the Centers for Disease Control and Prevention, was recently extended to 48 months—for another $1 million.

Costly as it may be, the careful methodology seems to be paying off. Gondolf is finding that treatment makes a difference. Just over a year after starting treatment (which lasts three to nine months), a third of the men were still violent with their partners. But two and a half years after the programs ended, less than 20 percent of the men were violent, suggesting that the treatment sinks in gradually. Gondolf notes that the four programs being evaluated are long-standing, behaviorally focused ones that are closely connected both to the courts and to community and victim services. In these cases "there seems to be a program effect," Gondolf says. "The vast majority of men are not reassaulting. And considering this crew, that is pretty good: over half have alcohol problems, lower income and lower education. This doesn't mean that the programs are responsible for all that or that [the abusers] are wonderful people. It does mean that

RICHARD M. TOLMAN, a professor of social work at the University of Michigan, notes that the data are largely unclear about whether treatment programs for men who batter are effective. But longer-term studies and more consistent methodologies may resolve this problem.

PETER YATES

The Hidden Violence against Men

In the field of family violence, nothing is more contentious than studying women who are violent toward men. To many researchers who have devoted themselves to helping women escape domestic abuse, it feels taboo even to consider the possibility. Yet a series of studies suggests that men are occasionally victims of domestic violence as well.

"We have to take seriously the fact that there are women out there who are using violence," notes Richard M. Tolman of the University of Michigan. But he and other researchers point out that the consequences of violence against men are rarely as serious as those against women are. The greater physical strength of men makes a difference: for instance, a man slapped by his wife could end up with a red welt across his cheek, whereas a wife slapped by her husband may end up in an intensive care unit.

JEAN-MARC GIBOUX *Gamma Liaison*

DAVID M. NEVERS of Clarendon Hills, Ill., is one of the few men willing to claim publicly that he has been physically abused by a woman. Nevers says his ex-wife slapped him, kicked him in the groin and pushed him down a flight of stairs.

The controversy about female violence first erupted in 1975, when Murray A. Straus of the Family Research Laboratory at the University of New Hampshire and his colleagues reported that men and women were equally aggressive. The researchers questioned people from 2,000 households and found that 11.6 percent of men and 12.1 percent of women were violent toward their intimate partner. The study was immediately criticized for its use of the Conflict Tactic Scales, a sampling method that does not examine the extent or consequence of the injury or the context in which the violence occurred. "The Conflict Tactic Scales equates a slap across the face with a life of terror," explains Terrence "Red" Crowley of Men Stopping Violence, a treatment program in Atlanta for men who batter. "It doesn't deal with the severity of the injury or the mortality. Or the systematic nature of it. Clearly, women make violent choices. But by and large, men are not terrified of women."

In later studies, Straus and his collaborators continued to find almost identical rates of violence, but they also reported differences in the types of violence used. The researchers reported that men were much more likely than women to use the most dangerous and damaging forms of aggression: beating up a partner, wielding a knife or using a gun. These findings are supported by those of a 1992 report in the *Archives of Internal Medicine,* which examined 93 couples seeking counseling for marital problems. Fifty-six of the 65 couples who reported violence said it was reciprocal. But we have interrupted the violence." His research also suggests that programs make a difference over and above the effect of arrest: rates of recurring violence by men who were arrested but dropped out of treatment are much higher than those of the men who were arrested and treated.

Court Involvement

Assessing efficacy is increasingly important as more and more states mandate standards for treatment. After a 1984 study done in Minneapolis found that arresting batterers appeared to be a powerful deterrent, police all over the country began to increase arrests in domestic violence cases. The courts have been overwhelmed with men who abuse, and treatment programs are seen as part of the solution—in many cases, notes David Adams of EMERGE, because "batterers come across as well spoken and respectable," judges and lawyers still don't viscerally think of these men as criminals. (The Minneapolis study has been replicated several times, and the results have been conflicting. Other researchers reached the conclusion that arrest was not a barrier; in one study, arrest actually appeared to increase recidivism. The controversy continues even now, with the two authors of the original paper arguing different sides.)

To impose some quality control on the burgeoning programs, many states have established standards for treatment. Yet the standards vary widely, Gondolf notes. In Maryland, for instance, the state devised a very general guideline, urging the incorporation of new scientific research and allowing flexibility in approaches. In some other states, however, the standards specify exactly what form of treatment should be used. For instance, Tolman points out that some states mandate the use of group treatment—even though, he notes, it is possible that in some cases individual therapy could be more effective. Many researchers remain wary about the trend toward standards in the face of unproved treatment models. "People are just supposed to follow a curriculum," says Geller of the Jewish Board on Family and Children's Services. "But some programs take whoever comes into them without ruling out the inappropriate ones. Sometimes they don't use trained clinicians," she adds. "This is serious. Somebody could kill somebody."

Despite concerns about the state standards, many experts laud recent moves to integrate all elements of the domestic violence and criminal justice system. Unifying the response of the police, the courts, the shelters, women's services, batterer programs, hospitals, the medical community, and mental health and substance abuse services offers the best hope, according to Tolman. "When the messages are similar, there is a much greater chance of behavior being influenced," he says. Crowley of Men Stopping Violence echoes this view: "We change the culture, and men will change."

Another trend that many researchers are glad to see is the growing body of work on the types of men who batter. Rather

only the women suffered broken bones, broken teeth or injury to their organs.

The most recent National Institute of Justice data do not support Straus's finding of equal rates of domestic violence. In 1998 the National Violence against Women Survey found that 1.5 million women are raped or physically assaulted, or both, by an intimate partner every year, compared with 834,700 male victims of domestic abuse. But even if fewer men than women are attacked by intimates, some researchers note that they still need to be helped—without draining resources from services for women and children. Irene Hanson Frieze, a professor of psychology at the University of Pittsburgh who has studied female victims of domestic violence, says she increasingly feels that violence against men needs to be addressed as well. A few years ago Frieze conducted a study on violence in dating relationships. Two thirds of the 305 students between the ages of 18 and 22 that she talked with reported some form of violence, and for the most part, according to all parties, women were more violent. "This is typically mild violence," Frieze explains. "Like he flirts with somebody and she slaps him, and neither takes it very seriously." But she notes that the ongoing violence could eventually catalyze a violent counterattack.

The findings were surprising to Frieze but not as surprising as what happened when she was interviewed about her work on several call-in radio talk shows. Frieze recalls that she was astounded by the number of men calling in to say that their wife or girlfriend had hit them and to ask where they could go for help. "There is no place for them to go," Frieze says. "The people at the shelters would laugh at them." —*M.H.*

than follow the purely cultural explanation that men batter because they can and because they need to maintain hegemony, these findings suggest that men batter for very different reasons—and that they can be treated accordingly.

The types generally fall into three main camps, although some finer subdivisions and other categories can be found in the literature as well. The first is referred to as family-only, meaning that these men are primarily violent toward intimates. This group is not well understood, notes Amy Holtzworth-Munroe of the University of Indiana, who has helped define these types. "We don't know why they cross the line," she says. "They do not hate women, and they do not think violence is good." In contrast, the other types are less remorseful. The second type is described as generally violent and antisocial. Holtzworth-Munroe says these men are very violent both in and outside the family and are often involved in criminal activity. Men in the third group are called dysphoric or borderline. They are most violent in the family setting, are often very depressed, and can be quite needy and dependent on their wives or partners.

"One of the important things about these typologies is that we get some clues that will help us predict who will be the most dangerous type during a relationship," says Daniel G. Saunders of the University of Michigan. For instance, "the most severely physically abused men in childhood develop antisocial traits, abuse alcohol and have a criminal lifestyle." They do not show high levels of anger or jealousy, he says, but they become the most severely abusive with their partners. Many of these men were intensely beaten, often by their fathers, Saunders notes, "and they often justify what their fathers did: 'He had to do that to raise me right,' or 'He made me into a man.' "

Saunders has found that for men with antisocial traits, the pro-feminist structured treatment groups have the most success. In contrast, men who are in the other two categories—that is, family-only and dysphorics—do better in less structured psychotherapy groups.

This kind of flexibility in treatment is crucial, says Geller, who has been treating men who batter since 1977. "I believe everything about the feminist perspective, and I subscribe to it," she notes. "But we need a combination." By doing a careful assessment of the men, Geller says, she is able to design appropriate treatment: "Regardless of the modality, an abuser can change." And she also does what many consider taboo: she works with couples—once she has determined that the counseling is safe for the woman. "Women who are abused need different interventions. Some are prepared to leave the relationship," Geller describes. "Then there are women who are staying in the relationship."

Some researchers are concerned that the focus on types is going to play out badly, prompting courts to give differential treatment to men who batter. "Perhaps judges are inclined to think that maybe [certain types] don't need as long a program or no program at all," argues Adams of EMERGE. "I am not disputing that batterers come in different types, but frankly I don't trust court personnel or psychologists to do those kinds of typologies without imposing their own biases." Adams gives a recent example of a psychologist who, during a court evaluation of an offender, concluded that the man was not a batterer—the physical abuse his wife has suffered wasn't battering, because she had been drunk when she was bound and dragged around the house.

Given that violence between intimate partners shows no sign of abating, Adams's concerns need to be reckoned with. Courts, hospitals and communities need more well-trained staff. Adams and others describe what is commonly a whirlwind assessment and a judicial system stretched to the limit. "There are huge numbers of batterers, and judges don't want to have all these hearings," he says. "So batterers are shopping around. They give guilty pleas [in exchange] for private therapy or a short 10-week anger program as opposed to 40 sessions, and the judges are going for it." The consequences show up every day in the newspaper. SA

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Recent advances in diagnosis and treatment promise to extend survival time and improve the quality of life for many patients

by Marc B. Garnick and William R. Fair

The death rate from prostate cancer in the U.S. has declined for several of the last few years, but the disease still claims too many lives. It will strike an estimated 179,300 men this year and prove fatal in 37,000, making it the second leading cancer killer of men, behind lung cancer. For such reasons, we and others continue to seek ever better ways to manage this disorder, which is especially prevalent in those older than 65 years. We cannot claim that the ideal solution for every patient is at hand, but a spate of exciting recent discoveries deserves notice.

Some of the newer findings address a vexing flaw in the sole noninvasive screening test for detecting microscopic prostate cancer, the form most amenable to a cure. The test measures the level in the blood of prostate-specific antigen (PSA), a protein released by prostate cells. Both normal and malignant prostate cells secrete this substance, but when cancer is present, the levels in the circulation often rise. Elevated PSA levels can thus warn that the prostate gland harbors cancer even if the tumor is too minute for a doctor to feel. The other main screening test, the digital rectal exam, can identify only tumors that are no longer microscopic. In that procedure, a doctor inserts a finger into the rectum and, through its wall, feels the prostate for hardness or lumps.

Unfortunately, the PSA test is not particularly specific. As many as 25 percent of men with cancer will have normal PSA levels—usually defined as those equal to or below four nanograms per milliliter (ng/mL) of blood. At the same time, more than half of men with higher PSA levels are, in reality, cancer-free.

Before discussing the leading ideas for minimizing that error rate, we should acknowledge that use of PSA testing for mass screening has long been, and remains, controversial. In essence, some physicians, especially in Europe, doubt the need for identifying microscopic prostate cancers, which develop after a once normal prostate cell becomes unresponsive to the usual controls on proliferation and migration. Microscopic tumors, they point out, often grow too slowly to cause symptoms in a man's lifetime or to affect how long he lives. Consequently, doctors may do more harm than good by exposing large numbers of men to PSA testing, to follow-up tests (such as ultrasound imaging and biopsy) in response to elevated scores and then, if a hidden spot of cancer is found, to the side effects of therapy.

Other physicians, we among them, counter that the PSA test generally finds malignancies that will, in fact, affect survival time (become "clinically significant"). Moreover, scientists cannot yet distinguish conclusively between microscopic tumors that will become lethal and those that will not; hence, denying treatment to men with such cancers would certainly doom an unpredictable group of them to a premature death.

Improving Detection

Even investigators who favor PSA screening are unhappy about its lack of specificity. One scheme that may better distinguish patients who have cancer from those who do not relies on a sliding scale of acceptable PSA levels, with the top limits for normal starting low and rising with age. The approach is based on the observation that as men grow older their PSA concentrations tend to climb, even if the prostate contains no cancer. Ideally, such sliding scales should lower the threshold of suspicion for men in their 40s and 50s, in whom prostate cancer tends to be most aggressive. And they should spare more men in their 60s and 70s from unnecessary follow-up tests. Some doctors worry, however, that age-adjusted scales will miss malignancies in the older groups.

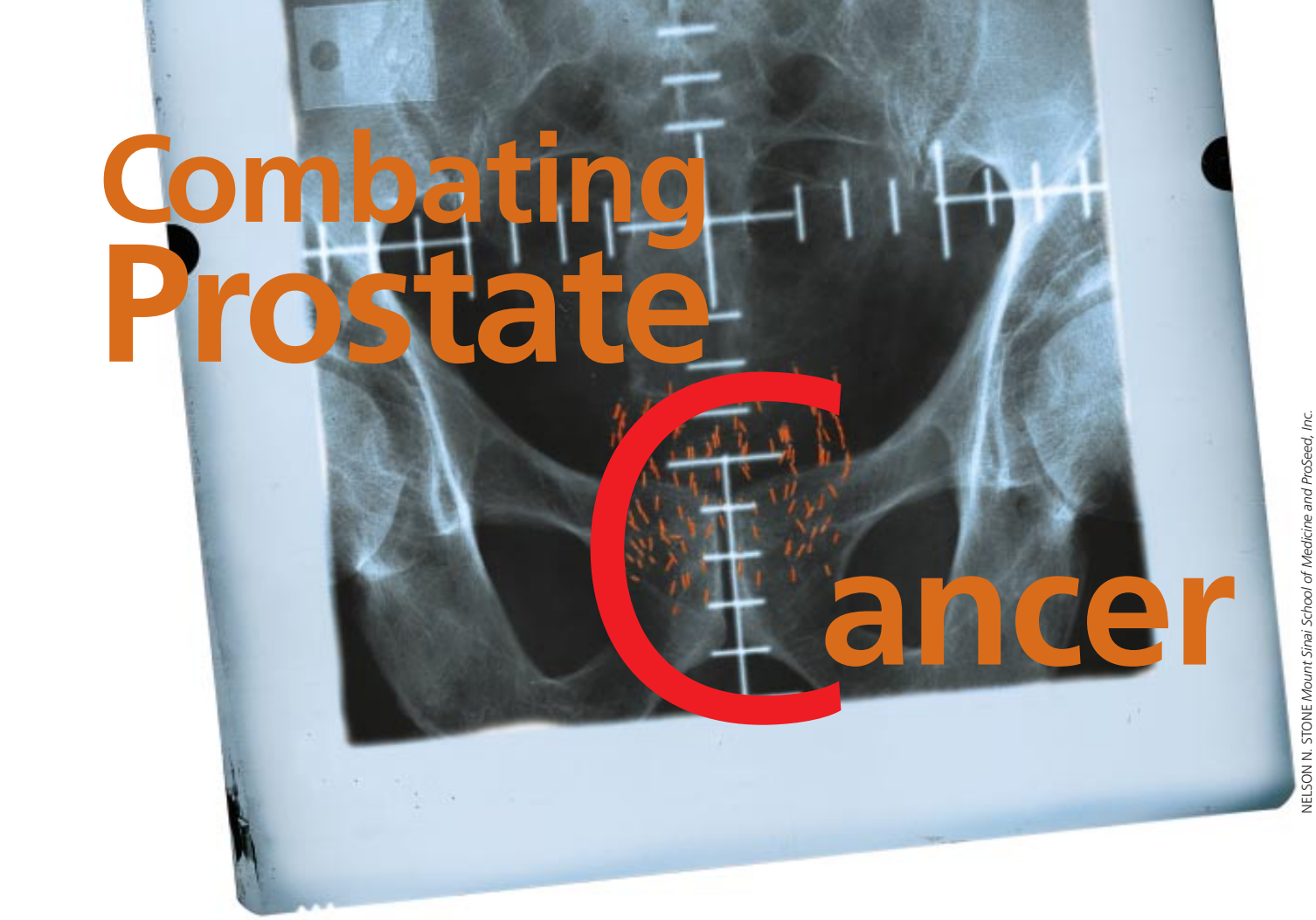
When two or more consecutive PSA results are available, the rate of change from one year to the next, otherwise known as PSA velocity, can help single out patients who have cancer, regardless of whether their raw PSA scores are in the normal range. Increases of greater than 0.75 ng/mL may signify that a biopsy is warranted.

A third manipulation can be especially helpful when a PSA score falls in the gray zone between clearly normal and clearly abnormal, such as between 4 and 10 ng/mL. Along with considering age to decide whether a given patient probably has cancer, physicians can take a blood sample and look at the relative levels of free PSA molecules (those not complexed to other proteins) and protein-bound versions. Men with prostate cancer tend to have an abnormally low ratio of free to bound PSA.

Aside from PSA, other molecules released into the circulation may undergo changes in structure or amount when cancer arises. Scientists are attempting to develop screening tools based on such changes. Certain tests may even identify men who do not yet have prostate cancer but are likely to acquire it; such individuals need extra monitoring and may benefit from promising ideas for prevention. Researchers, for instance, are investigating whether high levels in the blood of a molecule called insulinlike growth factor-1 can serve as a warning that a man has prostate cancer or is at increased risk for its development.

Geneticists, too, are searching for indicators of an increased propensity for prostate cancer. Brothers and sons of women who have breast cancer or who carry a mutant form of genes

Combating Prostate Cancer



NELSON N. STONE *Mount Sinai School of Medicine and ProSeed, Inc.*

RADIOACTIVE PELLETS **(red), *or "seeds," have been inserted into the prostate gland in an attempt to destroy a cancer within it. At one time, seed implantation, also known as brachytherapy, produced disappointing results. The seeds were often distributed unevenly, leaving some parts of the gland untreated. Today templates placed on the patient, combined with real-time ultrasound imaging of the prostate, enable physicians to achieve a uniform distribution and a much improved success rate.***

linked to breast cancer and prostate cancer have a somewhat elevated risk. Genetic screening tests for susceptibility to prostate cancer have not yet been perfected, however.

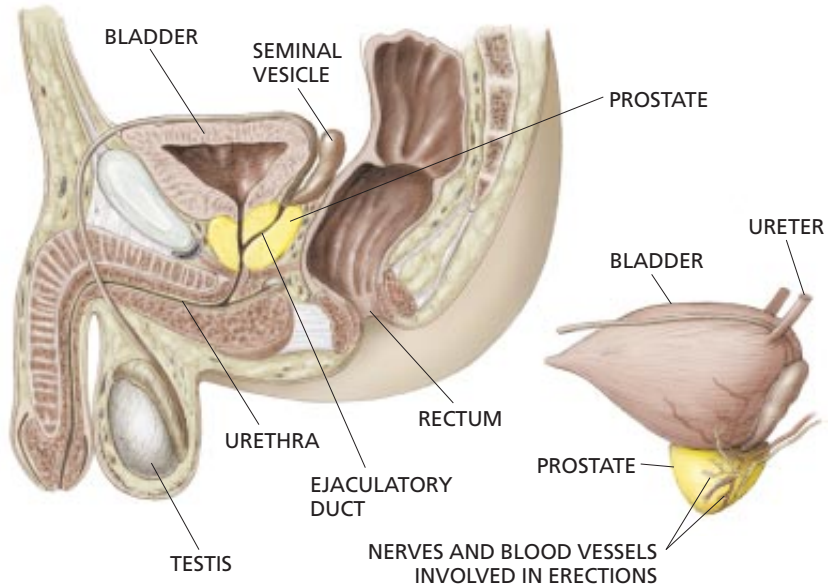
Who Can Be Cured?

If a man is ultimately found to have prostate cancer, doctors will assess its stage, or extent of spread. Accurate evaluations are critical, because the stage determines the type of therapy a patient should receive. Risks of intensive, curative therapies include impotence, incontinence and feminization, among other effects. Unfortunately, existing diagnostic methods often produce an inaccurate picture of tumor stage, but new tools are helping to remedy this serious problem.

Regardless of doctors' best efforts, men are understaged—initially deemed to have less advanced cancer than they actually harbor—with astonishing frequency. This misassessment is true of so-called clinical staging, which is based on tests, such as analysis of prostate tissue, before a patient has therapy. To a lesser extent, it also plagues "surgical," or "pathological," staging, which usually provides a truer picture of a patient's status. In surgical staging, pathologists examine any tissue removed during a prostatectomy, including a margin around the prostate, some lymph nodes and the seminal vesicles. Malignant cells in the margin or in other extraprostatic tissue indicate that a tumor presumed to be confined to the prostate is more extensive than was thought and has a good chance of having spawned undetected metastases (cells proliferating at distant sites).

Tools able to provide more informative images of the primary tumor are beginning to improve the accuracy of clinical diagnosis. In most patients, neither computed tomographic (CT) scanning nor standard ultrasound procedures can provide a clear picture of a tumor or its spread beyond the prostate gland. An experimental ultrasound technique now showing promise applies a signal-processing technology known as spectrum analysis. Sound waves are bounced off the prostate as usual, but the machinery analyzes all the information in the sound echoes instead of the much smaller fraction used by more ordinary ultrasound devices. Then a sophisticated computer program translates the full set of data into a three-dimensional view of the gland.

New approaches to magnetic resonance imaging (MRI) are under study in parallel. MRI devices emit magnetic fields around a patient to produce cross-sectional images of the body. Typical systems do not yield high-resolution maps of a prostate tumor. But when a patient also has a small emitter of electromagnetic waves inserted into his rectum (an "endorectal coil"), the resulting views can often show whether,



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PROSTATE GLAND **(yellow), *which helps to maintain the viability of sperm and participates in semen production, lies close to several structures involved in bladder, bowel and sexual function. As prostate tumors grow, they often impinge on the bladder or urethra, causing such urinary problems as frequency and urgency. Treatments deployed for prostate cancer can likewise affect the surrounding tissues, causing incontinence, rectal inflammation, impotence or other effects.***

and how far, the tumor has grown past the prostate gland. Magnetic resonance spectroscopy, which measures metabolic activity in a viewed area, may further help distinguish between normal and cancerous tissue.

A more mathematical strategy for gauging a cancer's true stage has recently begun to serve as an aid for deciding on a course of treatment. It relies on tabulations of the probability that a patient clinically determined to have organ-confined prostate cancer actually has a more extensive primary mass or metastatic disease.

Other novel approaches to clarifying a tumor's true stage concentrate specifically on assessing signs of aggressiveness—that is, they look for new clues to the growth rate and metastatic potential of the cancer. Before treatment, these tests can help determine which patients need prompt, and possibly systemic, therapy. They might also provide some guidance for deciding which technically curable tumors do not, in fact, need to be cured—because they are so slow-growing that they are unlikely to cause symptoms and turn lethal in a patient's lifetime. Assessments of tumor aggressiveness can also help indicate whether follow-up systemic treatment is advisable for patients who have already undergone surgery or radiation.

Several emerging or experimental approaches to predicting tumor behavior fall under the heading of "molecular" staging tools. They look at genetic alterations or at changes in protein structure or concentration that are more characteristic of metastatic prostate cancer than of localized tumors or normal prostate tissue. If those features appear in biopsied tissue, they suggest the cancer can be fast-growing and prone to metastasizing.

The study of cancer-related molecules is also generating fresh ideas for pinpointing metastases. A promising avenue of research involves molecular "highlighters" (usually radioactively tagged antibodies) that circulate in the body, finding and marking prostate cells in nonprostatic tissues. Normal prostate cells cannot survive outside their original milieu. The presence of prostate cells far from the gland indicates that the wayward cells are cancerous and may well have succeeded in establishing metastases in new sites. A test deploying an antibody able to recognize a protein called prostate-specific membrane antigen is already in clinical use, and others are being investigated.

Making Therapy More Effective

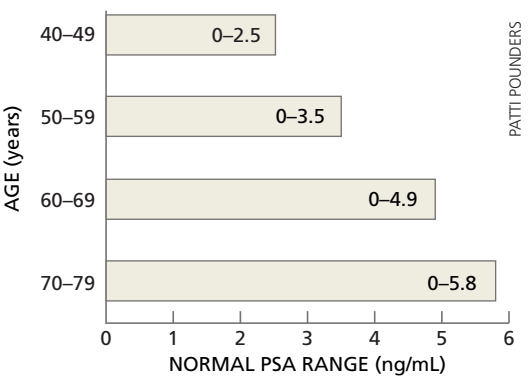
Just as detection and staging methods are undergoing change, so, too, are treatments. Surgery is still considered the "gold standard" for treating organ-confined disease, because it has produced the best survival times in long-term studies. But enhanced approaches to radiation therapy and new applications of hormonal therapy are improving survival prospects.

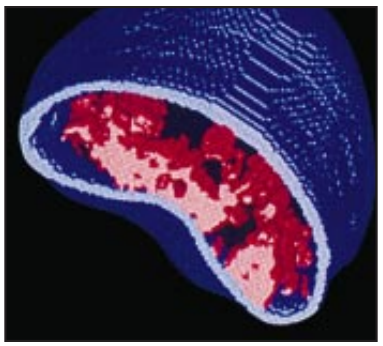
Classical radiation therapy takes the form of external-beam radiation, in which a linear accelerator moves around a patient, shooting intense x-rays or gamma rays at the prostate from several different angles. This rotation aims to limit the radiation hitting healthy tissue in the "line of fire" while still providing a high aggregate dose to the tumor (although normal tissue close to the prostate still receives potentially damaging doses).

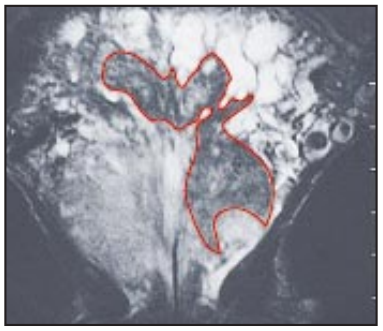
In a recent study that followed patients for five years, this approach appeared to be as successful as prostatectomy in curing relatively small tumors confined to the prostate gland. When a mass in the prostate is large, standard doses of radiation may be too low to erase all cancer cells. And the higher doses that are needed may be too toxic to structures close to the prostate.

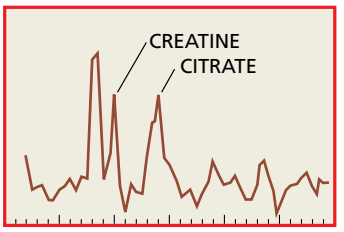
A relatively new technique, known

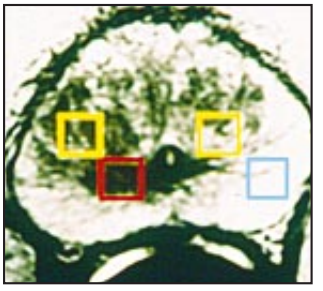
LEVELS OF PSA (prostate-specific antigen) in the blood can indicate whether a man is likely to have prostate cancer and thus needs diagnostic testing. One scale adjusts the definition of an acceptable PSA value as a man ages, instead of using four nanograms per milliliter of blood (ng/mL) as the top normal level for everyone. Doctors are still debating the best cutoffs, however.

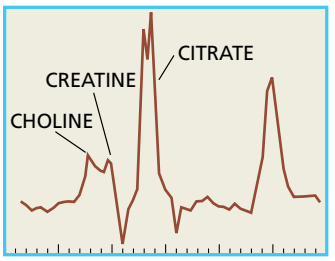












***NEW IMAGING APPROACHES** may help reveal the full extent of a tumor before treatment is attempted. A technique that extracts extra information from ultrasound echoes can generate a three-dimensional picture* (top left) *that distinguishes normal tissue from a tumor* (red). *Combining an "endorectal coil" with standard magnetic resonance imaging (MRI) can also delineate a tumor* (bottom left, outline added). *And MR spectroscopy can add an extra dimension to such results* (below). *By assessing differences in metabolic activity across an imaged gland* (graphs), *it distinguishes cancerous tissue* (red box) *from normal tissue* (blue box). *The yellow boxes highlight noncancerous abnormalities.*

as three-dimensional conformal radiation therapy (3-D CRT), makes it possible to deliver once unheard-of doses to organ-confined tumors without increasing the risk of damage to nearby tissues. In this method, now available at most major medical centers, radiation physicists produce cross-sectional CT scans of the prostate. Then a computer combines the information into three-dimensional images of the gland as it will be "seen" by the rotating accelerator. The computer also directs the accelerator to shape and reshape the radiation beam so that at all times it matches the precise dimensions of the individual's prostate and thus minimizes the amount of radiation striking outside the gland's boundaries.

Although 3-D CRT has not yet been shown conclusively to produce higher cure rates, it appears to be promising and does seem to limit side effects. Proof of greater effectiveness might be needed before the technique, which is more expensive than standard radiation therapy, becomes accepted universally.

Many men choose a rather different form of radiation therapy: brachytherapy. A surgeon puts radioactive, rice-size pellets directly into the prostate, where they emit radiation from within the gland. The seed procedure often proves appealing to patients because implantation is relatively simple, requires minimal hospitalization (lasting perhaps a day or two) and leaves no surgical wound. If a tumor extends past the prostate, brachytherapy may be combined with external-beam radiation to attack the outer reaches of the mass.

When brachytherapy first became available decades ago, it seemed promising, but its long-term results were unsettling. The pellets had to be placed without the aid of imaging technology, and parts of the prostate often ended up with few or no radioactive seeds. These days many brachytherapists perform the procedure with the help of a template placed between the scrotum and rectum. The approach now appears to be about as effective as external-beam radiation or surgery for treating men who have low-stage tumors that seem relatively unaggressive.

A number of medical centers offer another fairly simple way to attack tumors in the prostate: cryosurgery, or freezing the gland with probes containing liquid nitrogen or argon gas. Cryosurgery comes with a high risk of side effects, and its ability to eliminate tumors is not known.

We are impressed by recent findings supporting the value of hormonal therapy as a supplement to classical "definitive" therapies (those intended to achieve a cure). Preliminary reports suggest that such combination therapy often works better than the standard therapy alone. When hormonal therapy is delivered before radiation or surgery, it is known as neoadjuvant hormonal therapy. When it is given with or after those treatments, it is known as adjuvant hormonal therapy.

The idea behind combination treatment is simple. Neoadjuvant therapy aims to shrink bulky tumors so that radiation or surgery can eliminate them more readily. In the case of brachytherapy, for instance, physicians have a hard time inserting the radioactive seeds into glands containing large tumors. Reducing the tumor before insertion can ease the procedure and potentially increase the chance of success; it may also reduce side effects. Adjuvant therapy aims to mop up stray cells left behind at the tumor site after primary treatment and also to destroy cells elsewhere that have broken free and could pose a metastatic threat. Animal studies suggest that hormonal therapy delivered before or with radiotherapy may, in addition, increase the sensitivity of prostate cancers to radiation.

Hormonal therapy usually consists of a combination of two drug classes. One such class includes so-called superagonists of gonadotropin-releasing hormone (GnRH), a substance that is released by the brain and that leads ultimately to testicular secretion of testosterone, the major male hormone that promotes the growth of prostate tumors. GnRH superagonists initially result in increased testosterone secretion, but after a few weeks they inhibit testosterone manufacture and cause prostate tumors to shrink. The other drug class is made up of antiandrogens, which block testosterone from inducing the proliferation of cancerous prostate cells. A permanent means of halting testosterone production—surgical removal of the testes (bilateral orchiechtomy)—is also available.

The most impressive results have

top left: ERNEST J. FELEPPA *Riverside Research Institute, New York City; bottom left:* CLARE TEMPANY *Brigham and Women's Hospital, Boston; right:* HEDVIG HRICAK *University of California, San Francisco*

come from clinical trials of hormonal therapy combined with radiation. For example, in a study of 415 patients treated in Europe, those receiving three years of adjuvant therapy plus radiation survived longer than those who received radiation alone. Estimates projected that 79 percent of the first group but only 62 percent of the second group would still be alive five years after treatment. The study did not include a "hormonal-therapy-only" arm, however, so it cannot address whether combination therapy is superior to hormonal treatment alone.

Long-term investigations of neoadjuvant therapy have yet to be completed, but some studies strongly suggest a benefit from this approach as well. At the Memorial Sloan-Kettering Cancer Center in New York City, one of us (Fair) and his colleagues evaluated the ability of this treatment to ensure that tumors initially believed to be organ-confined were indeed fully within the prostate at the time patients underwent a prostatectomy. They found that three months of presurgical treatment increased the incidence of organ-confined disease at surgery and markedly lowered the frequency of worrisome tumor cells in the outer edges of the excised tissue. Yet to be determined is whether the tumor control achieved in the study will translate into a lower incidence of local recurrence or metastasis in the subjects and, hence, into enhanced survival rates.

Sadly, we have no dramatic news for men who already have metastatic cancer. Hormone therapy usually extends life, but tumors eventually become resistant to the treatment. Investigators are attempting to uncover the molecular basis of this resistance, in the hope of designing drugs able to overcome it.

Scientists are, however, closing in on a way to eliminate a major drawback of hormonal therapy in those with metastatic prostate cancer. Recall that the GnRH superagonists usually prescribed as part of hormonal therapy initially stimulate testosterone production before shutting it down. In that early phase the drugs thereby promote tumor growth and so can exacerbate symptoms. An agent that blocks GnRH activity directly, an antagonist called Abarelix, is being developed by one of us (Garnick) and colleagues at Praecis Pharmaceuticals in Cambridge, Mass., in collaboration with other companies.

As many researchers struggle to improve existing tools for detecting and managing prostate cancer, others are attempting to develop entirely new kinds of therapies. Most of these future treatments would work systemically, preventing cancer cells that escaped first-line attack from establishing metastases. If metastasis could be prevented, death rates from prostate cancer would surely plummet.

Promise of Dietary Intervention

One idea being evaluated is decidedly low-tech: nutritional intervention, especially adoption of a low-fat diet. Conceivably, nutritional interventions might also prevent the development of symptomatic primary tumors.

A suggestive epidemiological finding comes from placing countries on a grid according to death rate from prostate cancer and average fat consumption per person. The U.S. and western European nations, which ingest the most fat, also have the highest prostate cancer mortality rates. Conversely, men in the Pacific Rim nations, who consume the least fat, have a much lower death

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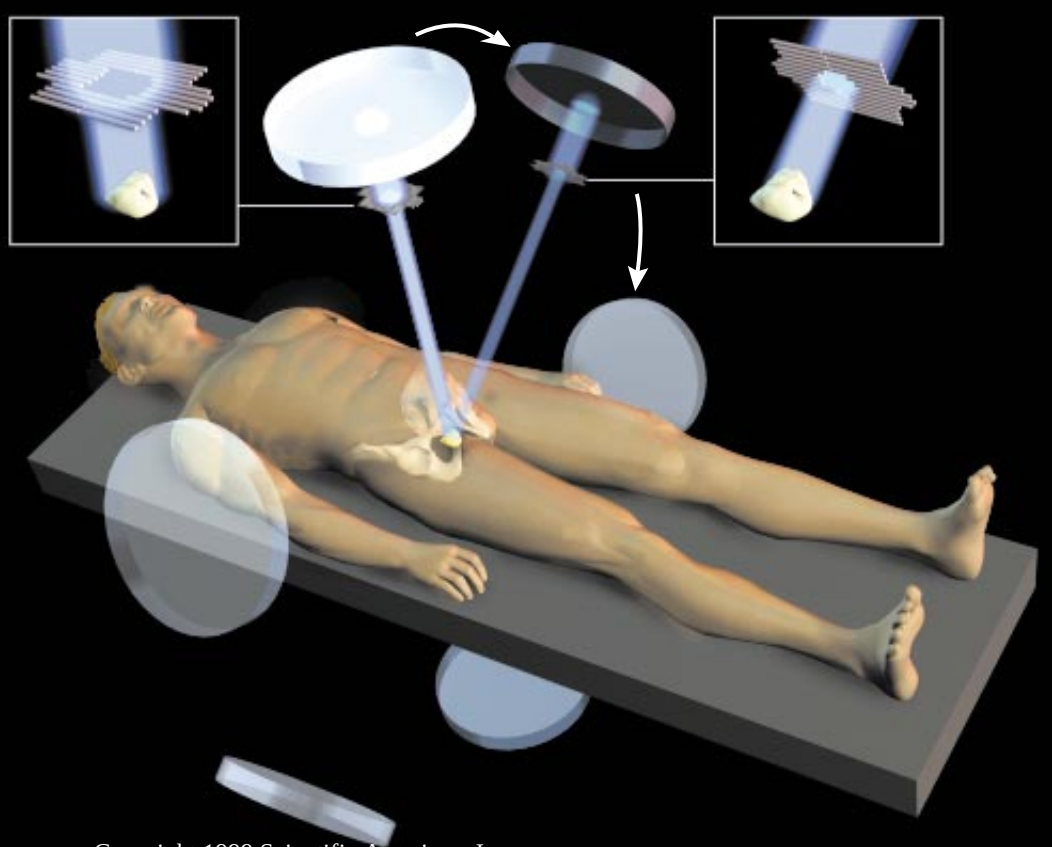
A Radiotherapy Advance

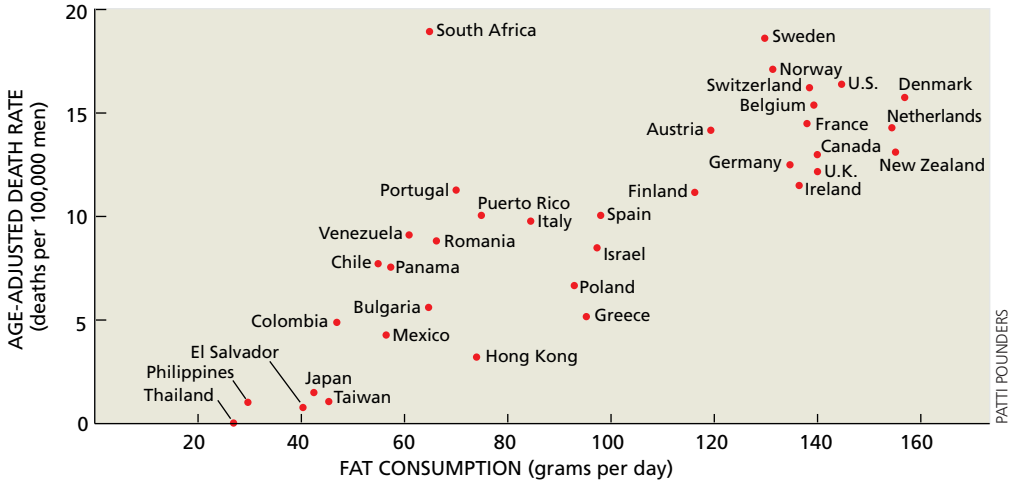
Three-dimensional conformal radiation therapy (3-D CRT) allows doctors to increase the doses of radiation delivered to the prostate gland without increasing damage to nearby tissues. As is true of standard radiation therapy, a linear accelerator rotates around a patient, pointing x-rays or gamma rays toward the prostate. But the conformal technique adds an important twist.

Before treatment is begun, digital images of the individual's prostate are prepared and compiled into virtual 3-D models of how the gland will "look" to the accelerator from all angles. Then the accelerator shapes the beam to match those "beam's-eye views" (*insets*), thus reducing the amount of radiation hitting the bladder, rectum or other unintended targets.

—M.B.G. and W.R.F.



A Link between Diet and Prostate Cancer



SOURCE: K. K. Carroll and H. T. Khor in Progress in Biochemical Pharmacology, *Vol. 10, 1975*

MORTALITY from prostate cancer tends to be highest in those countries that register the most fat consumption. This finding, from 1975, is one of many indicating that consuming fats can serve to promote prostate tumor growth and that a low-fat diet might limit such growth.

rate from prostate cancer. Moreover, a laboratory experiment conducted by Fair and his co-workers at Sloan-Kettering found that human tumors transplanted into mice grew fastest in groups of mice that had diets highest in fat.

Another dietary component that seems to influence prostate cancer—this time as an inhibitor of growth—is soy protein, a substance consumed in abundance in Japan. Soy reduces the amount of testosterone circulating in the blood and also inhibits an enzyme that converts testosterone to its more potent form in prostate cells. Some evidence implies that tomato products, vitamin E and the mineral selenium can inhibit tumor growth as well. Other components of food are also being explored as potential contributors to, or shields against, prostate cancer. Needed now are more human studies assessing the protective value of diet.

Interestingly, animal studies indicate that dietary components can increase or decrease the tendency of a microscopic cancer to grow into a dangerous mass but do not affect the processes that originally cause a normal cell to become malignant. This insight may help explain why the incidence of silent microscopic cancer (as measured by autopsies of men who die from causes unrelated to prostate cancer) is essentially the same worldwide, whereas that of palpable prostate cancers (ones that have managed to grow) varies with geography.

Tomorrow's Therapies

Several other intriguing ideas for systemic therapy derive from an emerging understanding of how prostate cancer develops and becomes increasingly aggressive. These ideas are in very early stages of exploration.

A number of the genes and proteins being evaluated as markers of virulence seem to participate in tumor progression. Some of those substances, therefore, may eventually serve as useful targets of therapy. Similarly, workers are trying to identify agents that will stop fats from stimulating molecular pathways that facilitate tumor growth.

In recent years, scientists have shown that few, if any, cancers can reach large sizes unless they sprout new blood vessels. Drugs that block such tumor blood vessels from arising are already being studied in many cancer patients, including those with prostate cancer.

Gene therapy is another possibility, although scientists will probably need many years to perfect this approach. A particularly intriguing idea would be to deliver genes coding for substances that are toxic to cells. If those genes were engineered to switch on only in prostate cells, they would give rise to the toxin in the prostate and in metastatic deposits but would have no effect on and do no damage to other kinds of cells.

Also in its infancy, but quite tantalizing, is research into vaccines: substances that would incite the immune system to attack cancerous prostate cells anywhere in the body without hurting nonprostatic cells. The immune system is capable of attacking malignant cells but often fails to recognize them on its own. Vaccines could potentially be administered both to prevent prostate cancer in men at high risk and to prevent recurrence in those who have already been treated for the disease.

Such targeted therapies will undoubtedly take many years to develop and evaluate. In the interim, research into improving detection, staging, treatment and prevention is intensifying. Certainly, much work remains to be done before the challenges of combating prostate cancer can be overcome, but we are heartened to see the pace of research quickening. SA

The Authors

MARC B. GARNICK and WILLIAM R. FAIR co-direct a yearly international conference on emerging treatments for prostate cancer. Garnick is clinical professor of medicine at Harvard Medical School and a physician at Beth Israel Deaconess Medical Center. He also serves as the chief medical officer at Praecis Pharmaceuticals in Cambridge, Mass., where he is developing a new hormonal therapy for prostate cancer. Fair is Florence and Theodore Baumritter and Enid Ancell Chair of Urologic Oncology and director of the John and Robert Bendheim Prostate Cancer Research Center at Memorial Sloan-Kettering Cancer Center in New York City. He is also professor of urology at Cornell University Medical Center.

Further Reading

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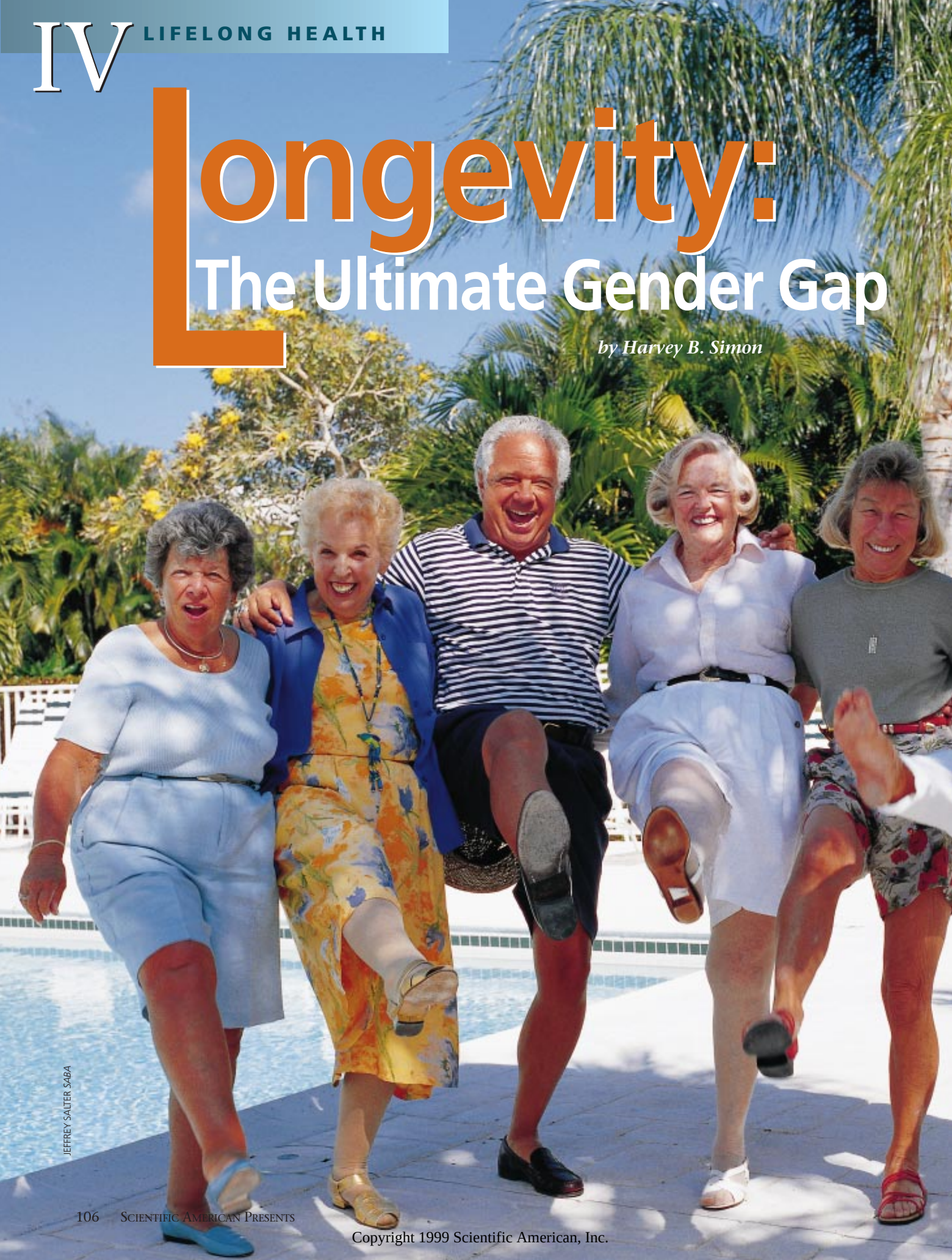
Longevity: The Ultimate Gender Gap

by Harvey B. Simon



JEFFREY SALTER *SABA*

An American man's average life span is nearly six years shorter than a woman's. Differing hormone levels and lifestyle choices may help explain the disparity

ELDERLY MEN are greatly outnumbered by elderly women in most retirement communities in the U.S. Women are about 40 percent more likely than men to live to the age of 65 and almost three times more likely to reach 85.

Why can't a woman be more like a man?" It's a humorous question asked by Professor Henry Higgins in a show-stopping song from the Broadway musical *My Fair Lady*. But Higgins would sing quite a different tune if the subject was longevity. When it comes to life span, Why can't a man be more like a woman? Women do indeed live longer than men. But why? And can men do anything to catch up?

Over the past half a century, life expectancy in the U.S. has risen slowly but steadily year after year. The main reasons for this trend are the dramatic advances in medical diagnosis and treatment as well as the changing American lifestyle, with its new emphasis on healthier diets and regular exercise and its declining dependence on tobacco. One thing, though, has not changed: the gender gap in life expectancy. People of both sexes are living longer, but the gains in women's life expectancies have outpaced those of men. In 1930 the average life span for American women was 61.6 years, and the average for men was 58.1 years; by 1997 the average female and male life spans had risen to 79.2 and 73.6 years, respectively. In other words, the gender gap is now 60 percent greater than it was 70 years ago [*see chart on page 109*].

It is an impressive difference, and it is responsible for the striking demographic characteristics of older Americans. Half of all women older than 65 are widows, and widows outnumber widowers three to one. At age 65, for every 100 American women, there are only 70 men. At age 85, the disparity is even greater: only 38 men for every 100 women. And the longevity gap persists even into very old age; even beyond age 85, the average woman will outlive the average man by 1.2 years. That is why female centenarians outnumber their male counterparts nine to one.

The gender gap is not unique to America. In fact, every country with reliable health statistics reports that women live longer than men; the observation is at least as old as health statistics themselves, because women outlived men by nearly three years when such data were first recorded in Europe more than 200 years ago. The longevity gap is present both in industrial societies (79 versus 73 years in western Europe and Australia) and in developing countries (54 versus 51 years in sub-Saharan Africa). It is a universal phenomenon that suggests a basic biological difference between the aging processes in males and in females.

Doctors are not sure why women live longer, but it is likely that many factors contribute to the gender gap. Males differ from females from the very moment of conception. It's all in the genes: females have two X chromosomes, whereas males have one X and one Y. The Y chromosome begins the process of sexual differentiation in the second trimester of pregnancy, when the fetal testicles secrete the male hormone testosterone. The importance of fetal hormones in determining sex characteristics is obvious, but their role in influencing longevity is far from clear. Still, new research suggests that events during fetal life can affect health in adulthood. For example, studies have shown that a low weight at birth—often caused by poor nutrition during pregnancy—increases a man's risk of heart attack and stroke in adulthood. So it is conceivable that the levels of sex hormones at the very beginning of life also might influence events at the very end of life.

Estrogen and Testosterone

Indeed, the longevity gap makes its first appearance in embryonic life itself. Sperm cells that contain a Y chromosome can outswim sperm bearing an X; as a result, 115 males are conceived for every 100 females. But for reasons that are not entirely understood, male embryos are more likely to miscarry than females, so boys outnumber girls by only 104 to 100 at the time of birth. The excess of male deaths continues in infancy and early childhood, but the difference is small until adolescence, when testosterone kicks in and boys start behaving like men. The results: motor vehicle accidents, homicides and other violent deaths that send the male death rate soaring to three times the female rate between ages 15 and 24. By age 25, females outnumber males, and the gender gap keeps widening with each subsequent decade of life.

The difference in estrogen and testosterone levels between men and women is the simplest way to account for the gender gap, although it does not fully explain the variance in life expectancies. During their reproductive years,

GLENN HUNT *Liaison International*

"APPLE SHAPE" is a common manifestation of abdominal obesity in men. In contrast, obese women typically carry their weight on their hips and thighs, leading to the "pear shape." Researchers believe that abdominal obesity is riskier than lower-body obesity.

women are much less likely than men to suffer from heart disease. Estrogen makes the difference: the female hormone lowers LDL ("bad") cholesterol and raises HDL ("good") cholesterol. After menopause, estrogen levels plummet, LDL rises and HDL falls; it's no wonder, then, that heart disease is the leading cause of death in older women as well as in older men. But women who take estrogen after menopause have about 50 percent fewer heart attacks. They benefit, too, from a similar decrease in strokes as well as a reduced risk of colon cancer and possibly Alzheimer's disease. Even without postmenopausal hormone replacement, women have high estrogen levels for the three to four decades between puberty and menopause; that's up to 40 years more than men, and it helps to explain the gender gap.

Estrogen protects women, enhancing their longevity by reducing the risk of heart attack and stroke. Although men have much less estrogen, they have much more testosterone. Produced by the Leydig cells in the testicles, testosterone rises to high levels during fetal life, when it plays a crucial role in the development of the male genital organs. That work done, the hormone falls to low levels by one year of age; it remains low until puberty, when it surges up to the adult range. Testosterone levels remain steady until about age 40, when they begin to drift down. But it is a slow decline that averages only about 1 percent a year, and most men continue to produce sperm cells even when their testosterone levels drop well below their peak.

Testosterone makes the man: the hormone is responsible for the large muscles, strong bones, deep voices and receding hairlines that characterize the gender. It is essential for sperm production and fertility, and it has an important, if not completely understood, role in libido and potency. Testosterone also contributes to the aggressive behavior patterns that typically distinguish men from women. But can testosterone also make men ill? The very large doses of androgens (male hormones) that are used illicitly by some athletes certainly are hazardous, frequently causing aberrant behavior, liver tumors, sterility and heart disease. Drug abuse is one thing, natural testosterone another—but new evidence suggests that even the normal levels of testosterone produced by a man's body may increase his risk of suffering a life-shortening disease.

The prostate is an obvious example. In the prostate, testosterone is converted to dihydrotestosterone (DHT), the hormone that causes up to 80 percent of men to develop benign prostatic hyperplasia (BPH) as they advance in years. BPH is well named; it is a benign enlargement that does not usually shorten life, although it often lengthens one's time in the bathroom. (The enlarged prostate squeezes the urethra, which slows the urine stream.) But DHT is also the hormone that drives prostate cancer, the disease that kills about 3 percent of American men [see "Combating Prostate Cancer," on page 100].

Testosterone may also raise a man's risk of heart disease and stroke, the first and fourth leading killers of American men. Five mechanisms have been postulated: adverse effects on cholesterol metabolism, including a rise in LDL cholesterol and a fall in HDL cholesterol; accumulation of abdominal fat, which may lead to high triglyceride levels and insulin resistance; activation of the blood-clotting system and increased red blood cell mass; spasm of blood vessels; and direct effects on heart muscle cells, causing enlargement and possibly injury. Some of these effects can be produced with testosterone administration in experimental animals, and some have been observed in men who abuse androgens. But more study will be needed to find out if a man's normal testosterone can cause similar abnormalities in his cardiovascular system.

Men cannot change their chromosomes, and very few would change their hormones, even in quest of longevity. But men can catch up with women by refraining from some of the lifestyle choices that add to the gender gap.

Smoking and Alcohol

Before 1960 smoking was far more prevalent among men than women. In 1955, for example, 56.9 percent of adult men were smokers, compared with only 28.4 percent of adult women. Since then, however, the smoking rates have converged: the prevalence among women peaked at 33.9 percent in 1965 and then slowly declined to 23.1 percent by 1994, but over the same period the prevalence among men plummeted to 28.2 percent.

If smoking is one of the causes of the longevity gap, why is the gap getting larger even as smoking rates have equalized? It is because smoking kills slowly. People who start smoking today will pay a steep price for their habit, but the payment won't come due for many years. Unfortunately, women are now suffering from a generation of tobacco abuse; as recently as 1960, lung cancer was rare in American women, but it is now their leading cancer killer, claiming 66,000 lives annually. In the 1990s, at least, smoking is one longevity factor that won't make men envy women. It is an area with plenty of room for improvement by both sexes.

Like smoking, alcoholism is traditionally a male problem that is increasingly shared by women. Small to modest amounts of alcohol protect a man's health, reducing his risk of heart disease. But larger amounts shorten life, increasing the incidence of hypertension, stroke, liver disease, accidents and various cancers. Heavy drinking has certainly shortened the life spans of many American men.

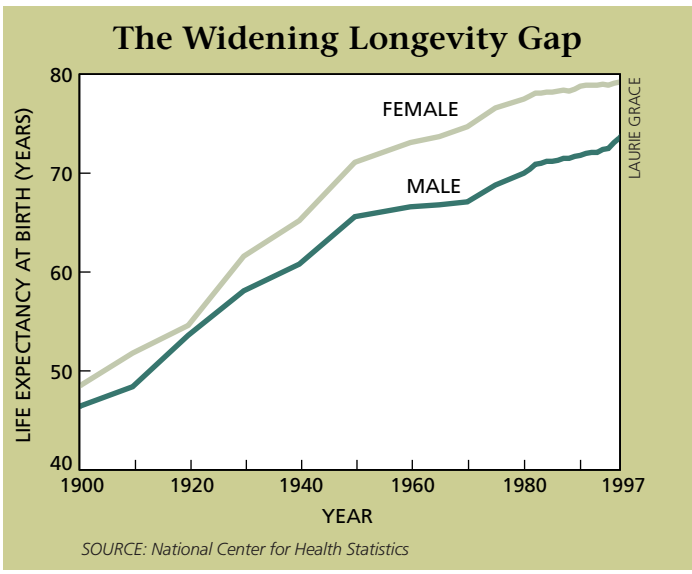
Diet and Health Care

The differing diets of men and women may also help explain why women live longer. In most cases, women have a healthier diet than men, eating a greater proportion of vegetables and a lower proportion of meat. A 1997 survey conducted by the U.S. Department of Agriculture found that men consume an average of 96 grams of fat a day, which accounts for about 44 percent of their daily caloric intake. Women, in contrast, get just 32 percent of their calories from fat. In America, "real men" don't eat broccoli—but they should. The masculine ideal of meat and potatoes should give way to potatoes and vegetables, fruits, grains and fish. Diet really does make a difference.

In 1992 Finnish scientists shocked the cardiological world when they published a report linking high levels of iron with a greatly increased risk of coronary artery disease. Because women lose iron with each menstrual period, the research fueled speculation that lower iron levels in the blood might partially account for the protection against heart attacks that is enjoyed by premenopausal women. A 1997 Finnish study seemed to corroborate the findings when it reported that men who donate blood have a lower risk of heart disease than men who do not donate.

Does iron explain the male vulnerability to heart disease? Probably not. Five American studies have examined the question, and each failed to corroborate an association between iron and heart disease. More studies will be needed to resolve the conflicting data; at present, although there are many good reasons for a man to donate blood, longevity does not appear to be one of them.

A more significant factor contributing to longevity is that women take care of their own health better than men do. Women are more diligent about checkups and preventive care. They are better at listening to their bodies and reporting discordant signals to their doctors. They even spend more time reading health publications. A walk down the health aisle of your local bookstore tells the tale: books on women's health greatly outnumber books on men's health, because publishers respond to consumer demand. It's true, too, of periodicals. *Scientific American Presents* published its issue on women's health a year before its issue on men's health. Harvard Medical School launched its *Women's Health Watch* in 1993, but the *Harvard Men's Health Watch* did not make its debut until 1996—and whereas at least three other health letters for women have been introduced by other publishers, *Harvard Men's Health Watch* remains the only one of its kind.



LIFE SPANS of American men and women have been diverging for most of this century. The average life expectancy for women is now 5.6 years greater than the life expectancy for men.

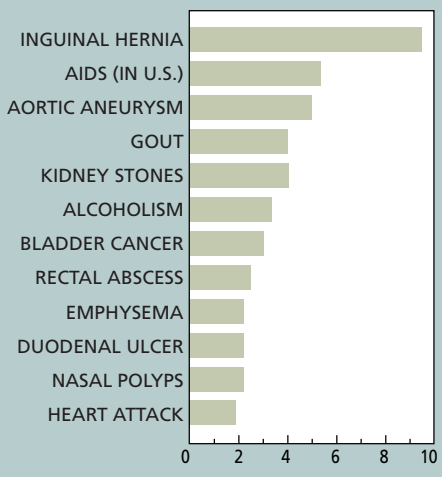
If you look around a primary care physician's waiting room on an average day, you might think you were in a gynecologist's office. That is because women visit doctors much more often than men; a 1998 survey conducted by CNN and *Men's Health* magazine found that 76 percent of the female respondents had been tested for health problems in the past year, compared with only 64 percent of the men. The disparity is particularly pronounced between the ages of 15 and 44. Even when men

Male and Female Illnesses

Men and women each have medical problems that are unique to their sex; only men get prostate disease or testicular cancer, and only women face the risk of childbirth and diseases of the female reproductive organs. Although breast cancer is usually considered a female disease, men are not immune. In fact, about 1,400 American men are diagnosed with the disease every year—a small number compared with the 180,000 cases in American women but far from trivial.

Though not unique to either gender, other diseases have a marked predilection for men or women. For example, lupus and other autoimmune diseases that cause vascular inflammation are much more common in women than in men. But men have problems of their own; the accompanying tables list the diseases that disproportionately strike males (*right*) and the 10 leading causes of death for American men and women (*below*). —*H.B.S.*

Illnesses That Strike More Men than Women



Leading Causes of Death

	U.S. MEN	U.S. WOMEN
1	HEART DISEASE	HEART DISEASE
2	CANCER	CANCER
3	ACCIDENTS	STROKE
4	STROKE	CHRONIC OBSTRUCTIVE LUNG DISEASES
5	CHRONIC OBSTRUCTIVE LUNG DISEASES	PNEUMONIA AND INFLUENZA
6	PNEUMONIA AND INFLUENZA	ACCIDENTS
7	HIV INFECTION	DIABETES
8	SUICIDE	KIDNEY DISEASE
9	DIABETES	BLOOD INFECTIONS
10	HOMICIDE	ATHEROSCLEROSIS

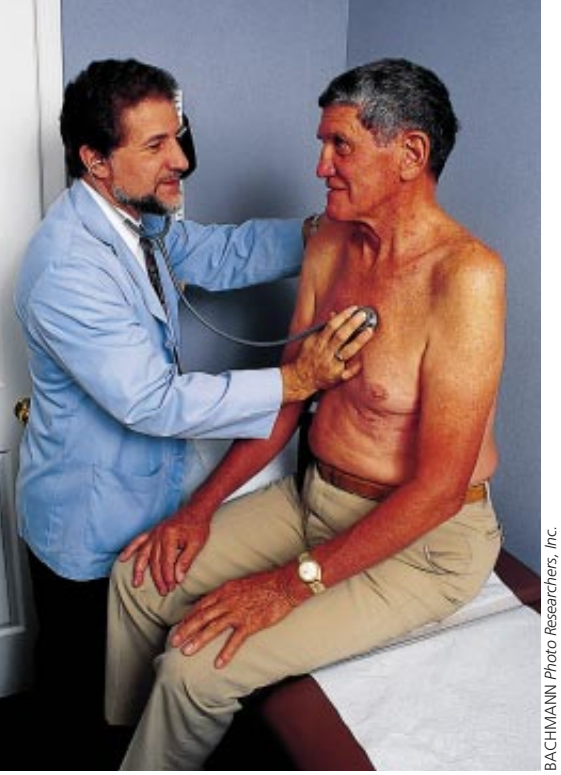
LAURIE GRACE

do visit their doctors, they tend to minimize symptoms, gloss over concerns and even disregard medical advice. It is hard to know why men make such poor patients; busy work schedules and competing responsibilities and interests may play a role, but the macho mentality appears to be the chief culprit. Who can blame men for wanting to be John Wayne? But by following the example of that quintessential American he-man, men fail to take the simple steps that can protect them from heart disease and lung cancer—the very same illnesses that struck down Wayne at the age of 72.

Obesity and Stress

Another way that men can protect themselves from heart disease is through regular exercise. American men are slightly more likely to exercise than women, but about two thirds of men are not regularly active, and about one quarter do not participate in any physical activity at all. Largely because of lack of exercise and poor diet, an astounding 59 percent of American men are overweight (defined as having a body mass index of more than 25). About half of American women are overweight, too, but there is a difference. Women tend to carry their weight on their hips and thighs (the "pear shape"), whereas men add it to their waistlines (the "apple shape"). Scientists do not know the reason for the difference, but it may have something to do with the fact that abdominal fat is more responsive to adrenaline, the hormone produced in response to stress. When adrenaline is secreted into the bloodstream, fat cells in the abdomen tend to release larger amounts of free fatty acids. The resulting burst of energy was quite useful for prehistoric men in "fight or flight" situations—which may be why the apple shape evolved in men. But over time, free fatty acids can impair the normal functioning of the liver and increase the risk of diabetes, hypertension, heart attack and stroke. So abdominal obesity in men is much riskier than lower-body obesity in women. Aesthetics aside, most women are shaped better than men.

Stress itself may also be a factor that increases the chances of coronary disease. The stereotype of the hard-driving American male—succeeding at business but raising his blood pressure and clogging his coronary arteries in the process—contains more than a grain of truth. So-called Type A behavior—with its concomitant anxiety, stress and hostility—has been implicated as a heart disease risk factor, and this trait tends to be more prevalent in men than in women. Men who are feeling stress over their shorter life expectancy might be able to narrow the gap a bit by learning to relax.



BACHMANN *Photo Researchers, Inc.*

***PHYSICAL CHECKUPS** are anathema to many men. They visit doctors much less frequently than women do. And men often minimize their symptoms and disregard medical advice.*

How to Age Successfully

Every man," wrote Jonathan Swift, "desires to live long, but no man would be old." Faced with the ever present tick of the clock, can a healthy middle-aged man tell if he is likely to remain free of the disabling diseases that often tarnish the golden years?

To find out, scientists evaluated 6,505 men between the ages of 45 and 68 who were in good health when the study began in the mid-1960s. As part of the famed Honolulu Heart Program, researchers tracked the men for nearly three decades. Of the men who survived to reach ages between 71 and 95, 40 percent remained free of both physical and cognitive impairment. The best predictors of successful aging were low blood pressure, low blood sugar, abstinence from tobacco and not being obese. It's a short and simple list—and it presents a set of goals that most middle-aged men can achieve with measures as simple as a proper diet and regular exercise. *—H.B.S.*

Blame it on genes and hormones or on societal expectations, but men are typically more aggressive than women. Even in primitive societies, males assume the risk of hunting while women take on the safer task of gathering. In industrial societies, too, men pursue more dangerous occupations and hobbies. Violent encounters between men pose the greatest danger of all; even discounting wars, violence and trauma kill far more men than women. Men younger than 25 years are eight times more likely than women to fall victim to homicide. Among young African-American men, homicide is the leading cause of death. Women, it's true, face the unique challenge of childbirth, but maternal mortality is low in the modern world and does not begin to offset the male penchant for risk and violence.

What is more, men often fail to take advantage of social supports—the assistance provided by networks of friends and family members. The adage "people are good medicine" is true: support networks reduce the risks of many illnesses, ranging from the common cold to heart attacks. In some studies, at least, support groups even improve the outlook of cancer patients. In contrast, social isolation has been identified as a heart disease risk factor. Time and again, studies have shown that women are more aware of their own feelings—and the feelings of other women—than men are. Women are not really from Venus, any more than men are from Mars, but good interpersonal communication may help explain why women live longer on Earth.

Furthermore, in most human societies, women nearly always assume the responsibility of child-rearing. In some other species, though, males and females divide the chores more evenly. Could parental chores pay off in longevity? To find out, scientists at the California Institute of Technology examined the life expectancy of male and female monkeys, apes and humans. They found that in the species where males and females assume similar responsibilities for raising their young, the males and females have similar life expectancies. In the species where males do not participate in child-rearing, however, the males do not live as long as the females. Of course, this does not necessarily mean that the act of parenting can add years to a man's life span; it is possible that the child-rearing males have greater longevity encoded in their genes because of natural selection. But young fathers might be wise not to dismiss it as monkey business when it's time to change a diaper or warm a bottle.

Why do women live longer than men? The explanation is complex, depending on both biological and behavioral differences between the sexes. In today's changing world, women seem to be acting more like men. When it comes to health, at least, it's a step in the wrong direction. With apologies to Professor Higgins, it's men who should be more like women. SA

The Author

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Further Reading

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Information on men's health and longevity is available at http://www.harvardhealthpubs.org/Harvard_Search on the World Wide Web.