BIG T

Defining Testosterone

Once upon a time—okay, until about 50 years ago—scientists thought the male body contained a kind of biological magic. Specifically, they thought that the testes produced a substance that was all masculine and all-powerful.

We know now they were dreaming of testosterone. And some undoubtedly continue to do so, despite the fact that the hormone has turned out to be neither of those things.

Testosterone's reputation stood highest, in a sense, before people actually knew what it was. Biologists of those earlier days, mostly men, imagined a material of pure wonder. And they went to real extremes to find it. They analyzed gallons of urine. They ground up animal parts. One leading French scientist of the nineteenth century sought to prove the existence and potency of this magical male stuff by injecting himself with pureed dog testes. He insisted that the extract boosted his energy and sex drive and enabled him to pee in a higher arc, a major issue for men, obviously, in contrast to women.

In the 1920s, physicians grafted monkey testes onto aging men, trying to restore their virility. They literally had to turn away volunteers. And still other doctors used ground-up goat testes to treat people troubled by everything from epilepsy to depression. Then, in the '30s, a group of German researchers distilled 25,000 liters of policemen's urine, looking for the primary male hormone. How unfair, after such effort, that they didn't find it. They did, however, find another androgen, a related hormone called androsterone. That discovery reassured biologists that the approach itself was solid, that perseverance would bring success.

The German team next mashed up some 2,000 pounds of bull testicles. While they were still analyzing the results, they were beaten to the grail by another team of European scientists. In a classic example of big not always being better, the steroid hormone testosterone was isolated from the testes of mice (although it's not clear how many pounds it took). Dutch scientists published those results in 1935, along with a description of testosterone's crystalline structure. Later that year, German biologist Adolf Butenandt, who had unsuccessfully pursued the hormone through policemen's urine and bull testicles, reported on the successful synthesis of the hormone. There are many scientific discoveries that go unheralded. This was not one of them.

Physicians hailed it as "medical dynamite," the test-tube birth of "sexual TNT." Four years later, Butenandt received the Nobel Prize for his work in demystifying testosterone, especially for showing the world how to make it in the laboratory. Since that time, researchers have become so comfortable with testosterone, they rarely even call it by its full name. Among scientists, testosterone often is simply referred to as the letter T, capitalized of course. The big T.

The discovery stripped away the hormone's mystique; it was no longer an unknown source of unlimited power. As Butenandt and his Nobel cowinner, Leopold Ruzicka, demonstrated, testosterone is nothing extraordinary in terms of life chemistry. It's a cholesterol derivative. The basic structure is a chunky package of carbon rings, four in all, with some tag-along oxygen and hydrogen gripping the edges. Take the same four rings, tack on a little extra oxygen and hydrogen, and you end up with one of the so-called "female hormones"—progesterone. Alter testosterone's oxygen/hydrogen ratio just slightly and it converts into estradiol, the primary estrogen. All the steroid hormones are stepchildren of cholesterol, an indirect reminder that for all we worry about having too much of that stuff, we can't do without it.

Nailing the shape and structure of testosterone has not, however (as researchers once hoped), revolutionized medicine. Butenandt and Ruzicka won the Nobel Prize for basic science: isolating a hormone and showing how to re-create it. Fifty years of work based on those abilities has not uncovered anything as medically beneficial as, say, the smallpox vaccine or the development of open-heart surgery. That's not to say that the synthetic testosterone products, known popularly as anabolic steroids, are a complete disappointment.

Charles Yesalis, of the Pennsylvania State University, a professor of health policy and an expert in anabolic steroids, describes them as valuable in treating children deficient in human growth hormone. Adding synthetic testosterone helps push the youngsters into a more normal growth curve, adding height and weight. If the disease AIDS causes a person's muscles to wither, synthetic testosterone also can help; the compound induces the body to rebuild tissue and blocks the relentless wasting of the disease.

A host of universities are now experimenting with the idea of using testosterone supplements—taken orally or through a skin patch—to counter some of the effects of aging. They are not trying to create 90-year-old studs. In most men, testosterone tends to go into a steady decline after age 40. In the average man, the hormone's

concentration in the blood drops by some 50 percent by the time he reaches age 80. In that same time period, most men lose between 12 and 20 pounds of muscle, 15 percent of bone mass, and nearly two inches of height. Proponents argue that raising testosterone levels back to a "pre-male menopause" high should bring back the strength and energy of youth. "We give eyeglasses to people as they age to maintain visual acuity," says Norm Mazer, of Theratech, a company that developed one of the newest testosterone patches. "'Why not give them testosterone to retain muscle strength and prevent osteoporosis?"

What most of us know best about the anabolic steroids, though, is not their bright health promise but their darker effects. They've gained a shady, black-market reputation as athletic cheats. Athletes—both professional and amateur—use them to pack on muscle bulk, build strength, and outdo competitors. Such usage is based on simple logic: one of the most obvious effects of naturally rising testosterone in puberty is the growth of muscle tissue and associated athletic power. Experts say there may be one million steroid abusers in the United States—bodybuilders, runners, football players, and those in a host of other sports from hockey to swimming, high jumping to weight-lifting. From those steroid-pumped athletes has come the notion of 'roid rages, of people possessed by the demon of a testosterone overdose.

Yesalis believes this is a myth. The athletic world has its share of psychos, he argues, regardless of steroid abuse. What we mostly see is the nasty personality of some athletes reinforced by a sports culture that glorifies the physical response. That's not to say that some people couldn't become twitchy on an overdose of steroids. And several studies indicate that heavy users of steroids are more likely than other athletes to also indulge in tobacco, marijuana, cocaine, and alcohol. "The notion of 'roid rages is blown way out of proportion," Yesalis says. "Let's go to any Penn State versus Ann Arbor [Michigan] football game and I'll show you more cases of alcohol-induced rage."

But it's hard to convince people that steroids are not a major source of behavioral problems. After all, they're basically testosterone, right? And today, people don't think of testosterone as the source of sunlike energy. They think of it-—based on several decades of well-publicized research—as a chemical source of violence.

Popular magazines now discuss testosterone as the "hormone from hell," the biological driver behind mindless and criminal behavior. Or as one columnist in a woman's magazine asked plaintively when pondering such masculine chemistry: "Are Men Just Born to be Mean?" It's the surly, muscle-bound image that tends to define testosterone these days, exaggerated to cartoon dimensions—a man with biceps bulging like over inflated balloons, biceps bigger than his brain.

Testosterone is seen as a hormone best suited to our ancestors, befitting the internal chemistry of a club-wielding cave dweller: stupid, mean, and male. Researchers who study violence know the jokes, and they also know they're distortions. Randell Alexander, who specializes in the psychology of child abusers, points out that both mothers and fathers beat up their kids. Alexander, at the University of Iowa, is an expert in shaken-baby syndrome. He's often called to testify at the trials of parents who've killed their children. He's seen both sexes charged with murdering kids. Men do it more often, true, he says, but women are more likely to lie about it. "Women want cover stories," he says. "I think it's cultural. We have much higher standards for what a mother should be than what a father should be. [Mothers] have more to lose. But some of my female colleagues like to say that it's really that men aren't smart enough to think of the cover-up. You know, one of those testosterone-poisoning things."

In other words, now that we have a grip on testosterone and its greasy little cholesterol-based body, we as a society seem not to like it very much. But in our own way, I think we're making a mistake much the same as the one the masculinity worshippers made a century ago. We're underestimating both the hormone and ourselves.

After all, testosterone isn't just a male hormone; it's made by both sexes. Men make it mostly in the testes. Women make it primarily in the adrenal gland and the ovaries. Furthermore, the brain can—and does—convert testosterone into estradiol, so that the so-called "male" hormone easily becomes the so-called "female" hormone. It's those kind of findings that are the real payoff from isolating testosterone. They remind us that biology is slippery. They show that there's nothing simple or straightforward about hormones and behavior. In testosterone, scientists find a sophisticated and remarkably flexible bit of living chemistry.

It's that flexibility, though, that makes understanding the link between testosterone and behavior so tricky. Remember that in the developing human fetus, testosterone seems to provide the early signal, at about six weeks, for a male body. That's different, though, from saying the hormone builds a distinctly male brain, even before birth. If that were proven—which it isn't—we wouldn't spend so much time arguing over whether there's a biology behind gender behaviors. We argue over the uncertainties. What's clear is that steroid hormones, testosterone among them, do interact with the nerve cells, neurons, that make up the brain. They bind to those nerve cells and bring them messages.

Scientists discovered that connection when they found that neurons have receptors for steroid hormones. The receptors are essentially a docking port for the body's messengers. They are very specific; a certain receptor will only recognize and accept a certain substance, be it hormone or immune system agent. In the brain, researchers have found neurons' receptors for androgens, such as testosterone, and also for estrogens.

The brain is thus prepared to listen to what testosterone has to say. And that can be a great deal. Once a hormone locks onto a receptor, it can signal for dramatic changes, from inducing cell division to inducing cell death. Most researchers consider this at least indirect evidence that testosterone is capable of altering the brain and, thus, influencing behavior.

Animal studies began hinting at such influence fairly early. A research group at Stanford University, led by neuroscientist Seymour Levine, found that female rats, given testosterone at birth, not only developed penises, but "knew" how to use them. They could be observed thrusting their bodies, as if ejaculating. The reverse was also true. If they blocked testosterone in newborn males, the penis either shrank to a nub or disappeared entirely. And the males showed no trace of usual sexual behaviors. Often, they wandered over to other males and presented themselves in a receptive, female position.

Levine proposed that the hormone—or lack of it—altered the brain's sexual organization. Later, scientists learned to block androgens very specifically. They could, for instance, create a male rat who had normal testosterone exposure everywhere but in the brain. Those studies tend to support Levine's original idea. Such males had all the right equipment, but were clueless as to how to use it. But further research proved once again that hormonal influences are far from straightforward.

One of the most confusing aspects of testosterone is that, in the brain, it sometimes converts into an estrogen. As I mentioned, men and women both make testosterone; the issue is the different ways we use it. But, as animal studies emphasize, the division between testosterone and estradiol can be very blurred. Many mammals, including humans, make an enzyme, aromatase, that helps convert testosterone to estradiol in the brain. The change is remarkably quick, requiring only one chemical reaction. The reverse, by the way, is not true—estradiol does not easily become testosterone.

In newborn rats, the hypothalamus is apparently geared to such chemical alterations. It is rich with aromatase and packed with estradiol receptors. The latest theory is that rats—and this is rats only—use a testosterone-to-estrogen conversion in masculinizing the brain.

To pursue this idea. Marc Breedlove looked at rats with Testicular Feminization Mutation—the genetic defect, also found in humans, which prevents cell receptors from recognizing androgens. Essentially the hormone is there, but invisible to the cells that normally use it. Breedlove found that male rats with TFM never developed a functional penis. But they acted as if they had. They approached females as if they were fully equipped males. He believes that, in this case, the male rats simply skipped the normal testosterone-to-estrogen reaction in their brains. They used straight estradiol (made in the adrenal glands in males) to carry out masculinization of the brain. Apparently the rats circulated just enough of the estrogen to make that happen.

It may be that male brains use estrogens very differently from female brains. There's no indication of the reverse, nothing to suggest that estradiol makes female rats act like males. But the point is, Breedlove emphasizes, that we have arbitrarily labeled things as male or female when they really belong to the whole species. Through evolution, hormones would have been adapted in either sex in whatever way worked best. Conservation is a basic principle of evolution; nothing that works is thrown away. "Natural selection shows no concern for our labels of what is masculine and what is feminine," Breedlove says.

He's careful to add that estradiol appears unusually potent in rats. Humans also convert testosterone to estradiol in the brain, but it doesn't seem to carry the same punch. TFM boys do behave a lot like girls. Obviously, their background estrogens are not driving masculine behaviors in a way comparable to rats. There are some studies that suggest that in humans, the testosterone-to-estradiol conversion may play a role in irritable reactions. But it's important to be cautious with such results; scientists are still trying to understand when the brain converts testosterone—and why.

What we know for sure is that even in adults, testosterone can alter body shape and look. "It's the primary difference in appearance between men and women," Yesalis says. "If a woman receives a lot of testosterone, on a prolonged basis, you will see pronounced changes. The clitoris will get bigger. She will often develop a deeper voice, male pattern hair growth, and male pattern baldness too. Have you ever noticed how many women bodybuilders have that high teased-up hair? That's to cover the bald spots. Give a female enough testosterone and you will virilize her."

He and other experts agree that high doses of anabolic steroids are most potent and produce the most visible effect in young females, whose bodies are still forming. The compounds are least effective in young males,

already nearly topped out on testosterone. "Males have to accept the fact that they are what they are and they can't alter it chemically," says Neil Carolan, who counsels young steroid users in Syracuse, New York.

That sharp alteration in female appearance, though, reminds us again that testosterone is not purely male in its effects. If females lacked receptors for testosterone, it wouldn't affect them. It might just float aimlessly and uselessly. Both sexes make testosterone and use it; the really dramatic difference is that men make so much more of it. On average, ten times as much circulates in their blood. As Yesalis suggests, the male system is naturally loaded with testosterone. An anabolic steroid boost, therefore, is less transforming. Extra testosterone can make women look a lot like men—a pretty extreme change—while in men it merely exaggerates what they already have.

Interestingly, scientists suspect that because females are less routinely exposed to high levels of testosterone, they're more sensitive to its effects. Perhaps males get used to the hormone and it takes a lot to push them into response. The kind of testosterone levels that normally circulate in a woman's body would be almost meaningless in a man's body, far below any effect level. In either sex, though, testosterone looks extremely potent. The average man has only about sixty millionths of an ounce of testosterone circulating in his body at any given time. But women have only an average six millionths of an ounce, a bare hormonal quiver in a man's blood.

The background body chemistry—whatever internal settings say how high testosterone will run in our blood—is called baseline. Most researchers believe genetics determine the baseline. Genes, they say, provide the settings, the code for hormonal construction to keep male testosterone levels generally higher than women's. The obvious result is our differing body shapes. But what seems to have captured both the popular and the scientific imagination recently is the idea of a direct link between testosterone and behavior. That's what gives us jokes about hormone-poisoned male brains, about the caveman persona. Although research has not directly connected testosterone to the way men act, it has offered a strong circumstantial case.

Many researchers do see a sometimes unpleasant correlation between testosterone and personality. As the argument goes, if the baseline is high, a man is likely to exhibit a classic T-type attitude toward life—edgy, assertive, in-your-face. There is very good and very provocative science behind that idea. In a curious way, the notion is both complicated and supported by the fact that **T levels are rarely stable. They appear to respond positively or negatively to almost every challenge—and not always in the way we might predict.**

Think for a minute of an athlete—say a wrestler—in training. Every day he heads for the gym, pumps those muscles. He lifts weights, does push-ups, lifts weights again. You might imagine that such a superjock would be a testosterone-stud, practically oozing the big T out of his ears. The effect of intensive training, though, turns out to be exactly the opposite. In wrestlers who drive themselves to their physical limit, testosterone levels drop so hard they become comparable to the baseline of men who've been castrated—a bare trickle of hormone. Testosterone, in a sense, seems to take overexertion and stress to the point of exhaustion as a signal for retreat. The same phenomenon shows up in new soldiers in boot camp. In that stage of army life where the military traditionally treats new recruits like dirt, trying to wear them down so they can be rebuilt into good soldiers, testosterone plummets like a falling stone. This turns out to be really bad news for anyone trying to get in shape, self-defeating for both army and athlete. As T-levels drop, so does the hormone's powerful influence on building up muscles. An overworked athlete starts losing muscle mass and strength.

It was out of that dilemma that athletes first began turning to anabolic steroids for recovery of lost testosterone and muscle maintenance. The idea, before it went too far, was simply to be able to train like hell, and benefit from it rather than losing. Of course, that missed the point that testosterone doesn't stay depressed forever.

Once the soldier marches off to battle, once the wrestler steps onto the competitive mat, testosterone rises again in response to challenge. We see obvious parallels to this in monkeys, who have had their testosterone levels analyzed even more than humans have. If a male monkey sees an attractive and available female, his T-level spikes up. If another monkey—say a male of higher rank—covets the same female, he may muscle right into the pair, pushing the would-be lover away, displaying the long, wicked canines of a fighting male. At this point, as a fight approaches, the T-level rises in both monkeys—as if driving an internal readiness for battle. After the fight, testosterone stays high or even climbs a little more, maybe 20 percent higher, in the winner. In the loser, it falls by as much as 90 percent.

If you believe that testosterone is linked to behavior, then this pattern actually makes a lot of sense. High testosterone is the hormonal equivalent of cockiness. "The winner is still primed to take on all comers; it may suit him to be balanced right on the edge of aggression. The loser? The last thing he wants is some pushy little hormone shoving him into battle again when he's had no time to recover. Low testosterone is the hormonal equivalent of licking one's wounds. It's that very loss mode that seems to operate in exhausted athletes and soldiers, a hormonal signal that they've pushed too far.

"In monkeys, the finding is quite striking," says Kim Wallen, at Emory University's Yerkes Regional Primate Research Center. "Winning a contest increases T in the winner for about twenty-four hours; in the loser, it

stays lower for an even longer time. However, if the loser simply sees a sexually receptive female—especially if the winner has moved away—that boosts the loser's testosterone back up. So now you know [what accounts for] the popularity of strip bars: they're where male losers go to get their T back up." The testosterone numbers from monkeys do show that a little sexual voyeurism is a wonderful antidote for fallen testosterone. Watching other monkeys have sex—at some level, comparable to strip bars or porno flicks, I suppose—boosts male monkeys' T-levels up some 400 percent.

Wallen's colleagues Tom Gordon, an associate director of the Yerkes center, and Irving Bernstein, a psychologist at the University of Georgia, have done some remarkable studies of testosterone flexibility working with rhesus macaques. Rhesus macaques maintain a certain status as the bad boys of the monkey world. They are big, hardy monkeys from Asia, quick to react and quick to take offense. Their canine teeth are daggerlike and they use them that way. They fight with passion. They bite, they scratch, and they've been known to yank each others tails so hard that they pull the skin right off. Veterinarians, rather graphically, call this a degloving injury.

Rhesus macaques are also very smart monkeys. In laboratories, they've been taught to play simple computer games. They can use a joystick to shoot down targets. And they are intensely social animals, accustomed to companionship and miserable in isolation. They normally live in a steady ordered society, dominated by strong-willed and bossy females. As with chimpanzees, rhesus females build a supportive social network, with daughters baby-sitting for mothers and mothers carrying their infants with them during the day. They do not, however, have female-female consorts as Japanese macaques do; rhesus macaques are unfaithfully polygamous and consistently attracted to the opposite sex.

And, as with the equally polygamous chimpanzees, in rhesus macaque society, there's always an alpha, who's climbed atop the male hierarchy. Back in the late 1960s, Yerkes researchers thought that Mr. Alpha would also be Mr. T, brought to power by his supermacho testosterone levels. Gordon and Bernstein began a series of tests, expecting straightforward proof of that idea. The first set of blood draws, in several different groups, seemed to reinforce the idea. The alpha males did have a higher testosterone baseline.

But then the scientists discovered that these levels stayed high only as long as the male was in alpha position. If he lost a fight, they fell dramatically. If the boss monkey was put into an awkward situation, say, caged with a group of strange and unfriendly females, his T levels plummeted. To understand that drop, you first have to realize that a rhesus male, surrounded by a group of females, is almost never in the position of a star surrounded by fans.

Rhesus macaque females are tolerant of males only when they want to be; that's usually in the mating season. They are otherwise easily annoyed by the male presence, and irritated rhesus females formidable. Because they are so tightly networked, they can easily gang up on a perceived adversary. They fight viciously, too. "Among rhesus macaques, you don't worry about just the males hurting you," Gordon says. "They're all dangerous. Of the severe injuries we see here at the primate center, of those bad enough to treat, many more of them are caused by female aggression than male."

In terms of a survival strategy, then, there's good reason for an alpha male, surrounded by hostile females, to adopt a nonthreatening, good-guy approach. It wouldn't be particularly helpful to strut around in challenge, or to display a testosterone-induced take-all-comers attitude. For monkeys and for us, Gordon points out, it would be a major liability to be trapped by a hormone into an eternal fighting position. We all need the ability to retreat gracefully—or even just quickly. The rhesus macaque studies of testosterone's response to status were so compelling that when Richard Nixon was forced to resign as president in 1972, Gordon got calls from newspaper reporters asking him whether he thought Nixon's T-levels were dropping. (In a noncommittal kind of way, he said he thought it possible.)

Since then, researchers such as Alan Booth of the Pennsylvania State University, Allan Mazur at Syracuse University, James Dabbs at Georgia Stale University, and Richard Udry at the University of North Carolina at Chapel Hill have compiled a vivid portrait of testosterone rise-and-fall in humans. They've demonstrated again and again that this is a hormone acutely tuned to where—and who—a person is on a given day, week, or year. Each of us may inherit certain baseline T-levels, but they were never meant to lock in place. They fluctuate on a daily cycle and according to daily events; if there was ever a hormone designed to blow-hot-blow-cold, it seems to be testosterone.

Human studies are often done simply by asking people to spit into vials; it turns out that the testosterone level in saliva is an accurate reflection of the hormone's concentration in blood. That discovery, more than a decade ago, caused a major leap in the number of testosterone studies—people being far more willing to spit than to have blood drawn.

Human research suggests that testosterone is responsive not only to physical challenge but also to mental or intellectual competition. First, a few more examples of physical response: By following testosterone in male tennis

players, scientists can basically follow the match itself and even, without watching the game, tell who won. (They take saliva samples before the game, during scheduled breaks, and afterwards.) In both competitors, T-levels rise before the match. As the game continues and as the players settle into the match, testosterone begins to drop in both. If a player loses, testosterone falls even harder. In the winner, just as with the monkeys, it rises again—according to theory, preparing him for the next comer. But men don't have to be dashing about a court hitting balls to display that competitive pattern. It's identical in chess players: the same Jagged upward streak of hormone before the game; the steady leveling during competition; the sudden jolt of victory and the T-drop of defeat. In fact, it's enough just to watch a sporting event. Researchers found a comparable rise or fall among spectators at a soccer match, depending on whether their chosen team won. (This was an Italy versus Brazil match. "The scientists tracked the soccer fans down in bars afterwards. One unhappy Italian became so upset discussing the match, he screamed so loudly that his throat tore. Surveying the bloody saliva sample, he announced to the researcher: "It's my heart that's bleeding, saliva girl.")

There's a definite link, for men, between testosterone and anticipation of conflict. But we don't know this: Does testosterone sharpen that sense of anticipation? Or does anticipation itself cue a rise in testosterone? The tennis and chess competitions clearly raise that question. In both cases, if a winner regarded his victory as mere luck, if he didn't believe that he triumphed through skill, strength, or both, then testosterone did not rise. It didn't drop like a loser, but there was no triumphant leap to it. And this would make sense, too. If you were an early human, battling it out in some ancient forest, and you won, say, because your opponent fell over a rock, you might not want to challenge the rest of the tribe.

This flexibility, let's emphasize, doesn't mean that baseline testosterone is irrelevant. If it was, the baseline male-female difference wouldn't be so dramatic. But it certainly makes the science both more interesting and more complicated. Putting baseline testosterone into perspective is extraordinarily difficult because it flickers up and down so much. If you didn't understand that, and you took a random blood analysis on the day that a tennis player had just lost a championship match, would you get an accurate background measurement? One of the complaints about testosterone studies, in fact, is that they are often based on only a few measurements. That may be too simple a way to accurately measure a complex compound.

We do know, mostly from work in other species, that consistently high T-levels can be linked to chronic impatience and even aggression. Some of the best work on this line comes from John Wingfield, the avian biologist at the University of Washington in Seattle, who has done detailed testosterone comparisons of bird species.

Remember Wingfield's studies of monogamous bird species, such as sparrows, who normally form a dedicated partnership? Those male birds tended to be lower in testosterone overall than their counterparts among polygamous species. The sparrow males' T-levels drop even further as soon as they become parents. Wingfield found he could change the male's attitude toward monogamy by altering testosterone. If he implanted a testosterone pump in a male sparrow, pushing up the bird's T-levels, then all notions of fidelity vanished. The longtime companion was airborne, out of the nest, chasing the available females. The dedicated father, normally so reliable about bringing home dinner, suddenly lost all interest in the squawky little things in the nest. And, by the way, that indifference brought on a precipitous drop in survival of the baby sparrows.

Not surprisingly, then, the males of polygamous species—flashy cardinals, pushy blue jays—tend to have higher baseline T-levels. But what is especially interesting is that those T-levels seem relatively constant, less responsive to the vagaries of life. The polygamous birds stayed cranked, more wired, more aggressive. In fact, knowing the connection between hormone and behavior, anyone who observed blue jays and sparrows could make a strong guess as to which species was running on high-octane testosterone. Wingfield wonders whether there's an evolutionary feedback loop wherein the responsive father bird develops a flexible hormonal chemistry, and more flexibility in his response to the world around him allows him to be a more responsive father.

He theorizes that parental care played a role in natural selection: "If expression of parental care is high, then T must be held in check." A male bird that takes no role in raising young can be more consistently aggressive. But a dad that is crucial to the survival of his offspring can't be so edgy that he's dangerous to them; neither can he afford to risk them becoming fatherless chicks because he constantly rushes off to fight. What he needs is a system that will tend toward calm, except in times of danger or instability. Then a jolt of testosterone could be very useful. Say that an invading male is entering the territory, one who might even attack the nest. "Then the ability to increase T secretion to combat the intruder is crucial," Wingfield notes. The same quick response might be helpful if the intruder seemed interested in seduction. "T secretion *appeals* to be *most* flexible in species in which males show parental care. How this relates to mammals and humans. I'm not sure. This needs careful thought, because mammal and bird parental care systems are so different."

If you were to carry over Wingfield's bird observations into the realm of human behavior, it would suggest that high-testosterone men should be, basically, birds-on-the-wing, prone to promiscuity, indifferent to their children, and quick to perceive insult and take offense. Wingfield cautions against approaching this too literally or assuming that we understand how the hormone works: "Testosterone is certainly very well studied, perhaps the best-studied steroid hormone. However, it is also tainted by urban legend and popular literature, which can surest facts that are actually untrue, such as the idea of testosterone-poisoning." It may be, he says, that testosterone's real influence is in the realm of sexual behavior, including mating and establishing pair bonds. Those behaviors might result in aggression—for instance, guarding a mate—but the influence would be very indirect.

It's worth noting, I think, that humans do have a highly responsive testosterone system, more like the monogamous birds' than like that of the polygamous ones. And if you look at marriage and testosterone directly, you do find some interesting analogies to birds. In a 1993 study, Alan Booth and James Dabbs looked at T-levels across a range of relationships, from dating to marriage to divorce. High-testosterone men seemed more likely to make a mess of marriage. They were less likely to marry at all and if they did, they were far more likely to divorce, often because they were unfaithful or physically abusive.

But it also seemed that testosterone levels didn't merely predict the relationship—they responded to it. Single men tended to be higher in testosterone than married men. This makes sense if you consider a single man somewhat comparable to a mate-seeking male in other species—out there in the competitive fray. Along that line, you might predict the next finding, this time from Allan Mazur: once married, once settled into a comfortable and stable relationship, men's T-levels dropped. (Again, as mentioned earlier, there's some indication that men's testosterone levels, as in birds and mice, drop again as they become parents.) Also, in our species, instability changes that. Booth and Dabbs found that testosterone levels rose steadily if the marriage began to falter, and rose higher if it moved to anger and argument. T-levels also rose if the marriage broke up and the man moved back into competitive daring. As Wingfield does with birds, we can speculate here about the existence of a feedback loop: Do men with high T-levels tend to have bad marriages? Or does a bad marriage push testosterone levels up? And if so, do those higher levels produce edgier behaviors in a husband, making the marriage worse?

This leads us to the chicken-or-egg dilemma of linking testosterone to violence. Dabbs points out, for instance, that despite more than 20 years of searching, no one has been able to identify criminals and noncriminals by their testosterone levels. You can find high testosterone levels among prisoners, but you can also find them in successful and law-abiding men. Given that, Dabbs has tried narrowing the focus, comparing prisoner to prisoner. Among criminals, there appears to be an association between higher testosterone levels and more vicious crimes. Along with his Georgia colleagues, Dabbs recently surveyed almost 700 inmates in a state prison. They found that car thieves and burglars tended to have lower T-levels than armed robbers and killers. Even more consistent, though, was that higher-testosterone inmates, no matter what their crime, tended to be those in constant trouble, the in-prison rule breakers. Most particularly, they seemed to enjoy rule-breaking if it involved confrontation. They liked facing someone else down.

Dabbs began to suspect that the hormone could be better linked to attitude than to violent behavior. Men with high circulating testosterone simply tended to be more edgy, more in-your-face, more take-no-shit-from-nobody. It's a theory only, but he thinks it could help explain the difference in violent behavior among criminals, and perhaps some of the gender difference in aggression as well. Again, this would be indirect. If testosterone helps make a person more quick to challenge or snap back, then those reactions could produce violent results. In an evolutionary context, the hormone might have become part of a competitive response, even an ingredient in success. It might be a real advantage for a male seeking alpha position to be primed for confrontation—as long as he could also drop back with failure.

Robert Prentky, who studies violent rape, arrived at similar conclusions. Prentky, based at the private Joseph J. Peters Institute in Philadelphia, spent some time in a frustrating search for a connection between high testosterone and tendency to rape. He didn't find it. He found differences within the community of sexual abusers, but it wasn't clear what they meant. For instance, rapists of adult women tended to have higher testosterone levels than child molesters. There was a slight connection between violent rape and higher testosterone. The highest reading came from the only rapist who also murdered his victim; his testosterone levels were nearly twice as high as the average rapist and about two and a half times higher than any of the child molesters. Prentky noted, as Dabbs had, that none of the readings were out of the normal range of testosterone baseline in the overall male population. Instead, Prentky said the most consistent finding was that higher T-levels correlated with anger and with a desire to strike out physically in response to it.

One point stressed by scientists who study testosterone is that if the hormone pushes an aggressive response, that doesn't inevitably mean violence. It doesn't have to result in criminal behavior or murderous anger. There are many ways to channel a pushy and competitive personality. Aggressive hockey players tend to be high in

testosterone; so do virtuoso criminal lawyers. Ministers, interestingly, tend to have fairly low levels. One carefully crafted, but very small, study looked at testosterone levels among four young physicians on a boat together during a two-week holiday cruise. Each man brought a woman as a companion. The researchers had the doctors provide a series of saliva samples from the trip. After making the testosterone measurements, the scientists interviewed the women, asking them to rate the men according to how much each physician wanted to be dominant—the alpha male—and how aggressively he pursued it. Although they were not told the results, the women's answers accurately predicted the man with the highest testosterone levels. In this case, the link between high testosterone and the quest for dominance looks fairly real.

Obviously, there are abundant theories on the connection between testosterone and aggressive behavior, meaning that no one has the answer. "It plays a role, but we don't know how much of one," Dabbs says. There's evidence, again from monkeys, that the hormone responds not only to challenge but to the individual's very specific social status at any given time.

Thomas Insel, the director of the Yerkes primate center, and a colleague from the National Institute of Mental Health, James Winslow, once explored some of those complexities in squirrel monkeys, a species of tiny South American tree dwellers. These animals were housed in a laboratory, caged in pairs. The male-male pairs quickly established a dominant-submissive relationship. Overall, perhaps because of winning boss status, the dominant males were higher in testosterone. And, when both monkeys were placed with a familiar female, the high-status males were much more sexually aggressive.

Insel and Winslow did not try to alter testosterone levels. They were interested, rather, in whether testosterone interacted with another hormone, oxytocin, the one so often linked to bonding and social connection. Although oxytocin's role in males is still somewhat mysterious, Insel and Winslow decided to explore whether, if they injected it into the squirrel monkeys, they could see a behavior change. They also wanted to find out if that behavior would be different depending on the monkey's status.

It turned out that status was the key. The scientists found that after oxytocin injections, the dominant monkeys became more aggressive and more sexually assertive. That didn't happen in the subordinate monkeys. Their speculation was that while oxytocin, as expected, stimulated the males' interest in females, it was status that seemed important in how that interest was demonstrated. Dominant males became much more insistent about it; subordinate males remained tentative.

Insel and Winslow speculated that testosterone might be part of the chemistry behind those differing reactions. Studies in rodents had shown that steroid hormones such as testosterone can induce the brain to create oxytocin receptors. (The same is true with another hormone associated with bonding, vasopressin. If testosterone is suppressed in monogamous prairie voles, the males tend to lose interest in relationships. Scientists think that this is because the brain receptors for vasopressin don't get made in sufficient numbers.)

Perhaps, then, a squirrel monkey with high testosterone levels has an extra-large number of oxytocin receptors. And perhaps, again, a charged-up brain response stimulates the animal to act like a bossy and confident alpha male. The subordinate animal doesn't get that extra kick. And perhaps he never will. Perhaps being the low monkey in the relationship keeps his testosterone levels down, his oxytocin receptors confined. It's purely speculative, but it emphasizes the idea that testosterone does not act in isolation. It responds to status, desire, competitiveness. We actually don't know all the conditions to which it might respond. We know just that testosterone does rise and fall to the situation. The hormone's very unpredictability can produce all kinds of behavioral fallout.

It's relatively easy, though, to talk about testosterone, dominance, and aggression in monkeys and rodents. The biology of violence in humans, though, is extraordinarily difficult, partly because it tends to be judged by political standards as well as scientific ones. Behavioral geneticist Greg Carey, of the University of Colorado in Boulder, points out that we already have a simple genetic screen of an unborn fetus that measures risk of violent behavior as an adult. Doctors simply have to check for the Y chromosome; men are seven times as likely as women to be arrested for a violent crime. And so, does that fairly label all boys as potential thugs? The same dilemma exists when you focus on a specific biological factor, such as testosterone. The high-hormone sex (male) is more aggressive, but an individual high-T man may be a decent and law-abiding member of society. An individual woman may be a murderer. Neither the chromosomes nor the hormones provide an obvious explanation for the difference.

Evolutionary psychology offers some reasonable speculation as to why males, in general, seem so much more aggressive than females. The theory is not so different from those which explain risk-taking or emotional differences. It hinges on the fact that we descend from a mating system in which males must compete hard in order to become fathers, and in which females work hard to raise and support the young. That male reality demanded aggression and rules with which to contain it—hierarchy, competition, dominance. The testosterone drive is part of

that, a source or a result. While females also had to compete, sometimes for mates and sometimes for food, their primary goals were social support, child care, and child protection. Their reality didn't stand on quite so sharp an edge.

What I'm describing, of course, is a polygamous social system. In monogamy, life is different. John Wingfield emphasizes that monogamous bird species not only tend to be monomorphic (the sexes look the same), but females usually have the same testosterone levels as males. Wingfield suspects that stems partly from the fact that they share in defense duties, such as protecting the property boundaries. This seems to me to be once again a reminder of our ambiguously monogamous nature. Men have the flexible T-levels that characterize monogamy and parenting. But the fact that testosterone varies so widely between men and women hints, once again, that we spring from a polygamous past.

It also needs to be emphasized that testosterone is only one part of the biology-and-aggression question. It interacts with other hormones in a complicated balance of power. There are certainly other strong biological influences on aggressive response. As an example, there's the brain's acutely sensitive use of the neurotransmitters noradrenaline and serotonin in regulating the flight-or-fight response. This combination is not only potent in all of us, male and female, it's extremely responsive, like testosterone, to the pressures of the world around us.

Noradrenaline and serotonin are an incredible balancing act. Serotonin is essentially the soft voice of reason: calming, controlling impulses, regulating against aggression. In an argument with a child, however irritating (and they can be extremely so), most of us do not resort to fists. That is, in part, due to the pull-back effect of serotonin, the introduction of a cooling system. Noradrenaline, by contrast, is the primal scream, all reaction and action. Have you ever been in a near-miss car accident and felt your heart speed up, and had your foot on the brake before you consciously thought of doing so? That's noradrenaline, blowing spark into fire.

The two neurotransmitters ebb and flow in the brain, in rough synchrony, so that a person with higher serotonin will tend to be lower in noradrenaline, and vice versa. Again, there appears to be a genetic baseline for these neurotransmitters. Women, in general, are about 30 percent higher in serotonin than men, reinforcing the notion that females are less reliant on a fight response. Unusually high noradrenaline has been found in a series of violent men, such as Finnish men imprisoned for assaults, and U.S. Marines discharged for abusive behavior. Very high levels of noradrenaline are also found in people who attempt suicide in the bloodiest possible ways.

However, neuroscientist Bruce Perry, of the Baylor School of Medicine in Houston, points out that—as with testosterone—the balance of these neurotransmitters is acutely responsive. Contact with kindness can be physically calming it can raise serotonin levels. University of Minnesota studies show that as jittery infants, born with high noradrenaline levels, relax into the security of a loving home, their noradrenaline levels case down too. By contrast, Perry says, vicious and violent experience sends noradrenaline screaming upward. He's found this pattern particularly in stressed-out children of the inner does. In an environment where last reactions can save your life, the slow-down, think-about-it influence of serotonin can be a foolish response.

And studies of inner-city residents, interestingly, find a very comparable pattern with testosterone. Allan Mazur and Alan Booth did a detailed analysis in which they found that young men living in dangerous urban environments tended to maintain—almost to an individual—unusually high testosterone levels. "After a while, we began to suspect that what we were seeing was pure response to stress," Mazur said. "These men were living in an atmosphere where they were constantly being challenged. It was survival. I don't think it's surprising to find that they had elevated testosterone."

As my own appreciation for the complexity of testosterone began to grow, I began to wonder how the hormone affected women. After all, we women make testosterone too. Is a woman with a higher baseline of testosterone more aggressive or competitive? If a woman chooses a challenging profession—my own field of journalism, for instance—does that drive her biology into a more combative state?

I put this question to Kim Wallen, at Emory. It turned out that he doesn't think testosterone operates in women as it does in men. I still liked what he had to say: "What I find intriguing," he replied, "is the possibility that a woman's testosterone is not affected by environment in the same way as a male's testosterone. This would mean that she would never have the increase from winning, but also never have the decrease from losing. In other words, she would be buffered from the fluctuations that males have to deal with due to the [extreme responsiveness] of their testosterone system."

Wallen continued: "This is actually a more reasonable scenario since it seems to follow the sort of differential selection that has acted on males and females. The male pattern of live fast and die young' can take *advantage* of the momentary burst of testosterone to push a momentary advantage. Females, on the other hand—I'm talking about primate females—have a vested interest in long-term stability. This comes from nurturing their slow-growing offspring to independence. No short-term bursts of testosterone are going to facilitate that. Thus, I would think less about how women might be changed by a competitive environment and more about how they might

change such an environment by a less-mercurial (my wife's favorite description of me, that and a Ping-Pong ball) response."

The idea that women would be naturally steadier in a high-stakes situation also appeals to me (although I will also confess that I'm the Ping-Pong ball in my marriage). Wallen is correct in that if you consider our evolutionary history, at least what we understand of it, there are good reasons why hormonal influences might be different. That doesn't mean that testosterone might not also be influential in the way women behave. Assuming that women manufacture the hormone for some reason, then it's still worth exploring what little we do know. The preliminary results are downright provocative.

There's some suggestion that if you pump women full of synthetic testosterone—as in steroid-sculpted bodybuilders—they develop a progressive nastiness. A 1994 study by Dutch scientists found that female athletes who boosted their training with the use of anabolic steroids became rapidly angrier and more easily irritated by the people around them. But that did not translate to aggressive behavior. They didn't start shoving people around. They just became grouchy and obnoxious.

My favorite woman-on-testosterone story comes from James Dabbs, of Georgia State, who studied testosterone in female prisoners. This is a single case, meaning that it's statistically meaningless. But it's a great, if gruesome, story. The woman was in jail, indirectly because her husband had been on the telephone. That is, he had been talking on the phone for a long time and that annoyed her. She ripped the phone out of his hand and started beating him on the head with it. When he fled and locked himself in a bathroom, she got their rifle from under the bed. She beat a hole through the door with the gun, fatally shot him through that hole, and then smashed the gun apart on the floor.

The cautionary point is that while the story certainly reminds us that women can be violent—in this case, spectacularly so—it's not proven that high testosterone turned this woman into a gun-smashing lunatic. There's more of that story, a lot more, than a single hormone. If the correlation were that simple, after all, you'd expect all those steroid-pumped female athletes to be literally murderous on the track. Since we can't argue that high-testosterone men are exceptionally dangerous, we can hardly make that case for women.

In the past couple of decades, there have been a few studies linking testosterone with women's behavior. The first notable one was published in 1980. It compared two androgens, testosterone and androstenedione (a chemical that sets up the production of testosterone), in women across a spectrum of careers and lifestyles, from executives to homemakers. The researchers found, in general, that women who occupied "traditional" roles—housewife, clerical worker, salesclerk—had lower androgen levels than those in professional careers or pursuing such careers through college. One widely cited interpretation of the study was that, in this case, the androgens might serve as status indicators. That is, women were more stressed as homemakers or in low-level jobs. Such subordinate positions were depressing their androgen production, something comparable to the beaten-down soldiers. The more "successful" women pursuing traditionally male occupations, apparently, felt like winners and had higher androgen levels.

Of course, there are other ways to read the study. Speaking as a working parent. I'm not convinced that mastering office politics confers greater status—or offers greater rewards—than raising children. But patenting does not require the competitive one-upmanship that corporate life often does. So the androgen results make me wonder, instead, about competitive natures. Might the women who pursued high-end professional careers bring with them a higher-testosterone background?

Richard Udry, from North Carolina, investigated that kind of question in a study tided "Androgen Effects on Women's Gendered Behavior." The study was built on a resource of unusual depth: The Kaiser-Permanente health maintenance organization, based in northern California, has been conducting a study of child development for more than 30 years. As part of that study, Kaiser researchers collected blood samples from pregnant women in the 1960s and froze them. They then continued to follow the health of the women's children.

When Udry learned of the program, he saw a rare opportunity to look at testosterone in two generations of women. He could look at the mothers, going back to their pregnancies through the frozen blood samples. He could test the now-adult daughters. He and his colleagues traced some 350 daughters of the women in the Kaiser study. The women agreed both to give blood samples and to extensive interviews.

Superficially, the results of the study closely resembled the 1980 findings: Women who choose a professional career tended to be higher in testosterone than those who stayed at home. Udry extended the analysis further, though. His survey team interviewed all the daughters in depth, asking a broad range of behavior and lifestyle questions. The questionnaires ranked the daughters on a scale of masculine- to feminine-style behavior. It's important to note that these were traditional American definitions; they weren't meant to define who or what men and women should be. The scientists based them on the country's culture during most of the century. For example,

ranking marriage as very important put women high on the feminine end of the scale. So did having children; the larger the family the stronger the score. Putting career emphatically first was masculine, as was refusal to do all the housework and a tendency to thank God for child care. The scientists later correlated the answers with the testosterone readings.

High-testosterone women tended to be less likely to have children, less enthralled by the whole notion of parenting. Lower-testosterone women usually had a great deal more interest in children and in dressing up. They liked makeup; they liked jewelry. They liked cooking better than the high-testosterone women did. They enjoyed interior decorating more. Overall, the high-T daughters tended to be children of high-T mothers. That raises a familiar question of feedback between biology and behavior. Is this a genetic predisposition of some kind, passed along from mother to daughter? Or did the high-T mothers treat their daughters differently—pushing them toward more competitive pursuits—than the low-T mothers? And did the extremely challenging jobs bring up the daughter's testosterone levels?

Although his study rated behaviors on a masculine (career-track) and feminine (makeup and cookies) scale, Udry emphasized that what he was looking at is a normal spectrum of female behavior. "By masculine, we're not saying that these women would be mistaken for men," he says. "These are normal women, the kind you and I know. Their behavior is within the normal range for healthy women. Look among your own friends and you'll find a package of behaviors. Some have more feminine habits, others veer in other directions."

I have to admit that when I started reading Udry's study, I fell right into mentally testing myself. Was I high testosterone or low? There are weekends when I love baking cookies and taking the kids to the park. And there are weekends when I can't wait for Monday so that I can escape to the office, talk to grown-ups, even sort my way through a difficult story about the genetics of yeast. Did any of that represent an ebb and flow of testosterone, I wondered. Or, was I getting too weird about this topic? The funny thing was that every female friend I talked to about Udry's study responded by starting to make a similar list: "Well, I wear makeup but I play on the company softball team. . . ." And Udry, while admitting such analyses can be fun, says they are really no more than a game at this point. Although such testosterone-behavior correlations are fascinating, scientists don't know what they mean: "We're working in the dark and we haven't a clue," Udry insists. On the other hand, he says, the findings arc more than pure coincidence.

Alan Booth, of Penn State, has been exploring the connection between hormones and behavior for years. He recently completed a study which highlighted yet another steroid hormone, cortisol, which is made in the adrenal glands. Booth has been concentrating on cortisol recently because of the possibility that, more than testosterone, it drives a flexible response in women.

Cortisol is also acutely attuned to stressful situations. It rises not only in a dangerous situation but in a strange one. Researchers have measured its rise in young children, left for the first time at a child care center. In women or men, a new job, a new city, even going to a party where you don't know anyone can bring up internal cortisol levels.

Again, everyone inherits some baseline quantity of the hormone. The cortisol background may also influence behavior. Jerome Kagan, at Harvard, has found that shy children tend to be generally higher in cortisol than more extroverted youngsters. The high-end concentration creates greater muscle tension, which, Kagan points out, tends to make faces less expressive. An outgoing child tends to have lower cortisol levels, a more exuberant personality, and a face vivid in its reactions to others.

This is a subtle difference. These are all cortisol levels within the bounds of natural variation. We're not talking about children with mask-stiff faces, merely those with slightly less responsive expressions. Still, I could argue that the impact on facial expression could affect a child's life profoundly. We all like someone who openly responds to us, whose affection or humor we can read easily. It's not a surprise that outwardly giving children find it easier to make friends than withdrawn ones. And a sense of rejection may cause a timid child to retreat further. In this sense, cortisol may have an indirect, but surprisingly potent, influence on friendship. But it appears to have other equally strong effects.

In a study of women playing college basketball, Booth tracked both testosterone and cortisol levels in their blood. The women did not spike testosterone; it was cortisol that responded to stress, to the competitive situation. And it went down, especially in the most competitive women. Booth asked women to assess their performance. The more confident a woman felt and the better she judged her skills on the court, the lower the cortisol level.

I've tended to think of competitiveness as being all about intensity and tension. But the cortisol. response suggests a yet another dimension—that good competitors get cool, and relax with the challenge. That's what Booth thinks he sees in women basketball players. The good ones get calm and focused. Competitive male athletes do the same thing; a comparable study of male tennis players found that the better ones had consistently lower cortisol levels and were more relaxed before the game.

Booth believes that for women, the drop in cortisol allows them to approach competitive situations more like a traditional male—focused on the win. "My notion is that for many women, competition sort of runs up against what they'd naturally like to do," Booth says. "It requires some special adaptation to get them into a competitive mode, to put aside a tendency to be nurturing, to look at others as the enemy. I'm persuaded that most of the difference goes back to evolution, to males battling throughout human history. There's just a tremendous gender difference in willingness to get into combative situations. That's not just in a physical sense, but in other confrontations too, say, at the office."

But there are unanswered questions. His study looked at self-assessment and cortisol, rather than linking the hormone to pure performance. There's a possibility that cortisol correlates with op- timism or pessimism about onesself. And there's a real possibility that the underlying confidence or lack of it affects performance. Booth admits that many open questions remain. He plans to look at cortisol and testosterone again. His next study is a long-term one, involving some 400 families. He and his colleagues plan to study both hormones in mothers, fathers, daughters, and sons. One of the pending questions is whether, in a 1990s culture, the girls' hormone levels began to veer toward more masculine levels. If so, would testosterone steadily rise in women over the long term? Would cortisol drop—and would they behave increasingly like men?

"We want to see whether a consistent pattern of parents pushing girls toward traditionally male occupations results in a change," he says. "This is more of an idea than anything else. But in a few years, I hope we'll know more about the reciprocal relationship between hormones and behavior."

In the current study, Booth is particularly interested in whether behavior might influence hormone levels, and whether the resulting hormone levels would influence behavior. And then . . . you can turn the feedback loop forever, it seems. But that variability, that interconnectedness of influence—inner and outer, back and forth—is something we tend to miss when we think of hormones and what they mean. There's a lot of quick political reaction to theories about a cause-and-effect role for testosterone in competition and aggression. Feminists become understandably annoyed by the oversimplified, back-to-the-kitchen notion that women don't have the hormonal underpinnings for competition. And plenty of men—masculinists, if you like—are equally annoyed at being dismissed as a bunch of naturally bad-tempered apes.

Annoyances aside, I think the connections between body chemistry and behavior deserve our attention. Dismissing these theories without giving them fair hearing won't make them go away. I don’t think it's insulting to either sex to suggest that hormones influence our reactions, especially if the suggestion is also that how we behave—even how we choose to behave—can influence the hormones. There may be evolutionary influences on who gets how much testosterone and what it does. Still, we're an evolving species we're not immovably stuck in whatever ancient paths our ancestors trod. Overall, Greg Carey is right: men are more violent than women. If we could explore all the whys—without denying the parts we don't like or agree with—then it might be easier to do something about it. As testosterone's variable nature should remind us, people can change.

From Sex on the Brain, (1997) by Deborah Blum, 158-188