Testosterone Under Attack

Cross your legs, men. A phenomenon called xenobiotic attack is meddling with your manhood, and your family jewels may never hang the same way again

By: Richard Conniff

In 2003 Professional golfer Shaun Micheel took his game to a new level. He won the PGA Championship on the 72nd hole with his 21st birdie of the tournament. Then everything seemed to fall apart.

"I lost my drive. I didn't enjoy practicing anymore. If I made a couple of bogeys, I just wanted to go home," he said at the time. It was more than a slump. He barely even showed up on the professional circuit the following year. At first he thought it was depression. "I seemed to be tired all the time, and irritable. I wasn't myself."

But in April 2005, a blood test showed that, at the age of 36, Micheel had the testosterone level of a 70-year-old. His doctor had him rub a hormone-replacement gel onto his biceps each morning. By September his testosterone level was back to normal.

It wasn't a miracle cure. He still hasn't won another major tournament, though he did manage a second place finish last year. But Micheel is working his way back up the list of money winners. More important, both he and his wife say testosterone has given him back his old, upbeat personality.

Good news for him, but what about the rest of us? Some scientists now wonder if a lot of other "walking, talking, normalish guys," as one urologist put it, are also experiencing a fading of the hormonal basis of masculinity, leaving them feeling less like the men they used to be, less than their fathers were in their time.

Most men can expect their testosterone levels to drop by about 1 percent a year beginning in their 50s. So a man in his 70s might have only half the testosterone he had when he was 25. But researchers behind the Massachusetts Male Aging Study— which has been tracking behavioral and physiological traits for 1,709 men born between 1916 and 1945— noticed something strange. Men born more recently had T levels that were surprisingly low. The 60-year-old in 2003 had about 15 percent less testosterone than the 60-year-old in 1988, according to Thomas G. Travison, Ph.D., lead author of the testosterone study. Sixty was looking like the new 70. Had something happened? Could we be in the middle of some broad biological or environmental change affecting all men simultaneously?

No one was suggesting that men rush out to get their testosterone levels checked (though, okay, I did), much less consider testosterone therapy (and, yes, I am considering it). As one endocrinologist put it, "You need to see more than one study from more than one laboratory before you start waving your arms and shouting alarm."

But the Massachusetts results marked a turning point: Testosterone is no longer just a hot topic for misguided weight lifters or baby boomers with delusions of eternal youth. It's something the average aging male will need to think about, starting with a few testosterone basics.

Testosterone is literally what makes us men. Delivery of the right amount at the critical moment shifts development of a fetus away from the basic human blueprint, which is female, and onto the path to masculinity. A surge in testosterone (from the testes—hence the name) in adolescence boosts us into manhood. And for the rest of our lives, testosterone, or the lack of it, seems to play a key role in muscle strength, lean body
mass, bone density, mental sharpness, and sex drive—the things that often make us feel best about who we are.

Despite testosterone's explosive reputation, there's no solid evidence that it causes aggression or violence. On the contrary, heightened testosterone is often associated with self-confidence and social success. Testosterone levels typically increase to ready us for a challenge, whether it's a football game or a chess match. Testosterone also rises after a victory, causing an increase in confidence that often leads to even more victories, the so-called winner effect. Who would want less of a hormone like that?

And yet the quantity of the stuff, even in healthy young men, is astoundingly small. Most doctors measure total testosterone as the starting point, and for American men under the age of 40, the normal range is 300 to 1,000 nanograms per deciliter of blood. (That's what "ng/dl" means on your medical laboratory report.) A nanogram is a billionth of a gram, and a deciliter is a 10th of a liter. Or, to put it in layman's terms, not bloody much. If you somehow managed to collect all the testosterone from your entire body, it would barely fog the bottom of a shot glass.

But it gets more complicated. Testosterone occurs in the blood in three forms.

About 40 percent of total testosterone is tightly bound to sex hormone–binding globulin, or SHBG, meaning it's not readily available for use by the body. In fact, nobody knows for sure what function SHBG-bound testosterone performs.

"Free testosterone" isn't bound to other molecules. But it constitutes just 2 percent of total testosterone.

Fortunately, the balance of total testosterone is bound to albumin and other proteins, and those links are easily broken. So together with free testosterone, this "bioavailable" testosterone is there when the body needs it.

You could look at it this way: Your manhood is based on half of almost nothing. And there's less of it with each passing year.

Measuring testosterone is complicated, because the tests themselves aren't always reliable, and results can differ from one lab to the next. "Normal" levels can also vary dramatically from one man to the next. And they can vary from minute to minute in the same man; testicles seem to do everything in spurts. That's because testosterone levels fluctuate with the little wins and losses of daily life. So if a test suggests that you have a testosterone problem, do not despair: There's a one-in-three chance you'll be back to normal on a follow-up.

But none of this diminishes the mystery: Why would testosterone levels in the United States today be substantially lower than they were 15 years ago? When they saw their results, the Massachusetts researchers thought they'd made a mistake. "We'd used the same lab, the same assay, and the same analyst to gather the data over time," says Travison. "But even so, subtle changes in the way the assay was manufactured could have had some impact."

Then in the summer of 2006, Travison attended an Endocrine Society meeting where another researcher, Antti Perheentupa M.D., Ph.D., from the University of Turku, in Finland, presented evidence of a similar decline. The Finnish results suggested the change was happening among younger men, too. A man born in 1970 had about 20 percent less testosterone at age 35 than a man of his father's generation at the same age. "When I saw another group reproducing our results," says Travison, "that was convincing to me that we were seeing a true biological change over time, as opposed to just some measurement error."

One possible explanation for the decline is obvious: Men are fatter now. In the Massachusetts study, the average 60-year-old man in 1988 was already well past overweight (a body mass index, or BMI, of 25). But his 2003 counterpart was pushing obese (a BMI of 30). And obesity, says Travison, is "a very powerful predictor of low testosterone." Gain 10 percent in your BMI and you can expect your testosterone to drop by about the
same amount. As a result, fat men typically have up to 25 percent less total testosterone than their trim counterparts do. (Fair warning: This doesn't make them girly men. SHBG—the stuff that locks up half your testosterone—also decreases with obesity. That means even a fat man with low total testosterone may have enough of the bioavailable stuff to crush you between his manboobs.)

Taking multiple medicines also tends to decrease testosterone, and a quarter of the Massachusetts test participants were practicing "polypharmacy"—taking six or more medicines at the same time. This was partly because the test group had aged. But in tandem with the obesity epidemic, participants also seemed to be experiencing an Rx epidemic. In 1988, 38 percent of the men were not taking regular medications. By 2003, not one man could make that claim.

Still, obesity and polypharmacy together weren't enough to explain the loss of testosterone. Nor was the dramatic decline in smoking among participants, though quitting can sometimes cause a decrease in testosterone. To filter out these effects, Travison's group looked at a subsample of 500 nonsmokers who were neither obese nor taking a large number of drugs. And even these apparently healthy men displayed the same exaggerated decrease in testosterone.

Scientists have been arguing for years about whether they are seeing a worrisome pattern in male reproductive-health problems around the world—and also about whether environmental factors are to blame. Fertility, which moves in tandem with testosterone, has dropped not only in industrialized nations like Sweden, but also in Sri Lanka, without any apparent change in contraception or abortion rates. Increasing numbers of boys are being born with genital abnormalities, including undescended testicles, and urethras that exit in odd places along the penis. In Denmark, 40 percent of young men have a subnormal sperm count, and the rate of testicular cancer is among the highest in the world. In the United States testicular cancer has recently become the most common malignancy among Caucasian men ages 15 to 35. Some researchers have grouped these developments together as "testicular dysgenesis syndrome," or TDS, with "dysgenesis" meaning abnormal development of the male organ.

There are plenty of experts who question the evidence of such a syndrome. But Mitch Harman M.D., Ph.D., an endocrinologist at the University of Arizona college of medicine and the director of the Kronos Longevity Research Institute, sees the shadow of Silent Spring. Back in 1962, when Rachel Carson published her environmental classic, estrogen-like substances in the insecticide DDT were making eggshells so thin that they were crushed by nesting parents; populations of eagles and other large birds plummeted. And today? Dr. Harman says, "I'm concerned that we're just pouring chemicals out into our environment that are endocrine-suppressing, estrogen-like compounds," possibly causing similar disruptions in human reproduction. The authors of a recent article in the Medical Journal of Australia likewise suggest that from early fetal life onward, male hormonal and reproductive functions are under "xenobiotic attack," meaning chemicals not naturally found in the body appear to be disrupting normal biological development.

For instance, 90 percent of American men have evidence of chlorpyrifos in their urine. This shouldn't be surprising, since up to 19 million pounds of the stuff was distributed across the United States in 1999 alone, much of it in household products like tick-and-flea powder for pets, lawn treatments, and common insecticides. Though residential use is now restricted, chlorpyrifos is still common in agriculture, as well as in some professional applications; for most people, diet is now the main source of exposure. In a recent Harvard study, men with the highest chlorpyrifos exposure typically had 20 percent less testosterone than those with the lowest exposure.

Carbaryl is another possible culprit. Detectable levels turn up in 75 percent of American men, and having it in your urine appears to be associated with reduced sperm count and liveliness, or motility, as well as increased DNA damage. And yet we still apply carbaryl to lawns and gardens at a rate of up to 4 million pounds a year, mostly by way of an insecticide known as Sevin. There should be a bumper sticker: Honey, the lawn shrunk my testicles.
Phthalates are also everywhere, almost certainly including your own body. Manufacturers use them in colognes and cosmetics and as softeners in plastics. Baby bottles now come "phthalate-free," but hospital intravenous bags generally don't. And yet some phthalates seem to have all of carbaryl's unpleasant associations with reproductive health. And not just in men: Last year Greenpeace issued a warning against the danger of phthalates in your girlfriend's sex toys. Then the Danish Environmental Protection Agency came riding to the rescue, declaring such toys safe--as long as she keeps it to an hour or less a day.

Scientists can't say that any of the suspect chemicals actually cause the reproductive effects that are occurring. They can only point out troubling associations. But these associations seem to be proliferating. About 50 new chemicals come onto the market weekly, says Dr. Harman, and while testing for carcinogenicity is required, "there's no systematized testing for subtle endocrine effects."

We're not likely to have good answers anytime soon. The reproductive problems of human males will remain understudied, says Dr. Harman, in part because federal research dollars are being diverted to issues like biological warfare and terrorism. "We might just wind up disappearing from the planet quietly," he says, "because we were too busy fighting wars to figure out that our reproductive systems were going south."

All this could Make testosterone therapy a more likely part of your life as you age. Demand is already booming. Last year, according to IMS, a pharmaceutical information company, U.S. doctors wrote more than 2.5 million testosterone prescriptions, and the market was worth more than $500 million to pharmaceutical companies. That's double what it was 5 years ago. If the decline in testosterone levels turns out to be real, the market could easily double again, with 6 to 12 percent of men in some age groups likely to qualify as "hypogonadal," to use the medical profession's distinctly depressing term. (Loosely translated, it means "tiny testicles.")

Misuse of testosterone-based steroids to build muscle is booming. It's already twice as common as heroin abuse among U.S. 12th graders. Baby boomers have also latched onto testosterone therapy as an anti-aging remedy, despite a dearth of supporting evidence.

At the same time, Australian andrologist David Handelsman, Ph.D., worries that doctors are failing to diagnose cases of genuine testosterone deficiency, resulting in "lifelong consequences" for younger men. As a result, testosterone therapy "suffers simultaneously from both overuse and underuse." And yet evidence about whether such therapy is safe or effective is "shockingly weak," says the Mayo Clinic's Victor M. Montori, M.D. "There is no way for physicians to be certain when prescribing testosterone that, on average, it's doing more good than harm."

So is it safe to use testosterone therapy, even under a doctor's care? Does it cause prostate cancer, as some suggest? Here's where the debate stands now: First, the fear isn't that testosterone will cause prostate cancer. It's a natural product of the human body, and no evidence anywhere has ever shown it to be a carcinogen. Scientists worry instead that adding testosterone may fuel the growth of small cancers that already exist, undetected and harmless, in the prostates of many older men.

The only reliable way to gather scientific evidence on the prostate-cancer question would be the sort of large-scale, long-term study endocrinologists have tried and failed to get the government to undertake since 1999. That's roughly the same period in which testosterone use doubled in this country. So men are, in effect, undertaking the same experiment themselves, on their own bodies--haphazardly, and with no way to track the results.

The debate over testosterone levels was kind of a parlor game for me when I started researching this article. I'm married, a father of three, and neither overweight nor a smoker. I lift weights, and I row crew 6 miles a day in season. My appetites and my outlook on life have always seemed healthy. It never occurred to me that my testosterone levels might be low. Using testosterone therapy to prolong the illusion of youth made about as much sense to me as hair plugs.
Then I had a blood test, and my total-testosterone level came back way low. It looked like the batting average of an okay hitter in a bad month near the end of his career. Suddenly, I listened a little more sympathetically when Abraham Morgentaler, M.D., an associate clinical professor of urology at Harvard, started making the case for testosterone replacement therapy. "What's amazing to me is the passion this testosterone issue generates in people," he was saying. "There are a couple of issues that come up. 'Why can't we just age normally? Why do we have to have 70-year-old men chasing their wives like they did when they were 25? Why can't they just be 70?' And I think it's the most ridiculous argument. Bad vision is age related, as are bad hearing, bad joints, bad hearts, bad blood vessels. Even cancer is age related. We treat all these things so we can live longer or happier. And the change in hormonal levels? If it's treatable and the therapy is safe, reasonably speaking, why would we want to withhold treatment from somebody?"

The case for considering testosterone therapy became even more compelling this past summer, when researchers at the University of California at San Diego released results from their long-term study of men over 50. Participants whose testosterone levels tested low in the early 1980s but who were otherwise healthy had a 33 percent higher risk of death over the following 2 decades. Another study, from the University of Washington, looked at men over 40 who already had health problems, and found that low testosterone dramatically increased their risk of death.

But I didn't immediately try to alter my T levels. (See "Become Mr. T" for natural ways to do it.) The standard medical guidelines for treatment are strict. I qualified on the first count: "unequivocally low serum testosterone levels." But I didn't have "consistent symptoms and signs" of low testosterone.

For doctors who take the conservative approach, the symptoms that matter most are physical changes, such as shrinking of the testicles, development of breasts, a decrease in spontaneous erections, or a loss of muscle bulk and strength. Doctors who take a looser approach often recommend therapy to men with the sort of complaints almost everyone experiences at some point: "Do you tire more easily? Is it more difficult to get and stay in shape? Is there less desire to exercise? Have you lost some of the zest for life?" I didn't fit either set of symptoms.

Given the nuances involved, anybody thinking about testosterone therapy needs to consult a specialist. My doctor, an endocrinologist, pointed out that, despite the low total testosterone, my free testosterone was normal. He also discovered a slight thyroid hormone deficiency, a potential cause of low testosterone. So while he wasn't ruling anything out, it didn't look like T-time just yet.

Those are the kind of judgments a lot more men will be making over the coming years, as the population ages and further evidence comes in on health and reproductive issues. For some men, both young and old, testosterone therapy will seem like a miracle, a second chance at life as a man. But the effects can also vary dramatically from one person to the next. So for other men, it won't make much difference at all. "I'll be 64 in April," says one endocrinologist, whose total testosterone is "sky high" at 640, "and I don't feel the same as I did when I was 44. There's more to aging than hormones."

So which are you? And what should you do? A good doctor is the place to start, but even doctors have no certain answers, and your government has guaranteed doctors won't get answers for decades to come. So when it comes to doing the right thing about testosterone, the truth is that you're pretty much on your own.

The question remains: Are you man enough right now? Will you be, 10 years from now?