

Selling That New-Man Feeling

By NATASHA SINGER

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THE LOW-T MOVEMENT

Dr. Harry Fisch, a urologist and fertility specialist, likes to say a man's testosterone level is "the dipstick" of his health. He is the medical expert featured on IsItLowT.com, a site sponsored by the maker of a prescription testosterone gel.

One afternoon a few months ago, a 45-year-old sales representative named Mike called "The Dr. Harry Fisch Show," a weekly men's health program on the Howard Stern channel on Sirius XM Radio, where no male medical or sexual issue goes unexplored.

"I feel like a 70-year-old man in a 45-year-old body," Mike, from Vancouver, British Columbia, told Dr. Fisch on the live broadcast. "I want to feel good. I don't want to feel tired all day."

A regular listener, Mike had heard Dr. Fisch, a Park Avenue urologist and fertility specialist, talk about a phenomenon called "low testosterone" or "low T." Dr. Fisch likes to say that a man's testosterone level is "the dipstick" of his health; he regularly appears on programs like "CBS This Morning" to talk about the malaise that may coincide with low testosterone. He is also the medical expert featured on IsItLowT.com, an informational website sponsored by AbbVie, the drug maker behind AndroGel, the best-selling prescription testosterone gel.

Like many men who have seen that site or commercials or online quizzes about "low T," Mike suspected that diminished testosterone was the cause of his lethargy. And he hoped, as the marketing campaigns seem to suggest, that taking a prescription testosterone drug would make him feel more energetic.

"I took your advice and I went and got my testosterone checked," Mike told Dr. Fisch. Mike's own physician, he related, told him that his testosterone "was a little low" and prescribed a testosterone medication.

Mike also said he had diabetes and high blood pressure and was 40 pounds overweight. Dr. Fisch explained that conditions like obesity might be accompanied by decreased testosterone and energy, and he urged Mike to exercise more and to lose weight. But if Mike had trouble overhauling his diet and exercise habits, Dr. Fisch said, taking testosterone might give him the boost he needed to do so.

"If it gives you more energy to exercise," Dr. Fisch said of the testosterone drug, "I'm all for it."

Recommendations like Dr. Fisch's and the marketing of low T as a common medical condition helped propel sales of testosterone gels, patches, injections and tablets to about \$2 billion in the United States last year, according to IMS Health, a health care information company. In 2002, sales were reported to be a mere \$324 million; around that time, Solvay Pharmaceuticals, which was then marketing AndroGel, began using the term "low T," replacing a previous euphemism for male aging, "andropause." Today the low-T trend is global. From 2000 to 2011, there was "a major and progressive increase" in testosterone use in 37 countries, according to a recent study published in the Medical Journal of Australia.

This marketing juggernaut is running into mounting opposition from some prominent medical researchers and industry experts. They contend that the pharmaceutical industry has vastly expanded the market for testosterone drugs to many men who may not need them and may be exposed to increased health risks by taking them. And drug makers have done so, these critics say, by exploiting loopholes in federal marketing regulations.

Drug makers spent \$107 million last year to advertise the top brand-name testosterone drugs in the United States, according to Kantar Media. That amount doesn't include marketing known as unbranded campaigns, which raise awareness of low T itself. The Food and Drug Administration closely regulates advertisements for brand-name prescription drugs, but does not generally regulate unbranded campaigns. That two-track system, says John Mack, an analyst who runs a blog called Pharma Marketing, has enabled companies to position low T as a malady with such amorphous symptoms — listlessness, increased body fat and moodiness — that it can be seen to afflict nearly all men, at least once in a while. Drug makers also promote low-T screening quizzes directly to consumers, Mr. Mack says, in an effort to prompt men to seek testosterone prescriptions from their doctors.

"You might not have the medical condition as described in the textbook," Mr. Mack explains. "But you may have low T as defined by marketing quizzes, and you go to the doctor and ask for treatment."

David Freundel, a spokesman for AbbVie, declined requests to interview company executives. In a statement, Mr. Freundel wrote: "AndroGel is approved by the F.D.A. to treat adult men with low or no testosterone (hypogonadism) who have been diagnosed by a physician, and has more than 10 years of clinical, safety, published and post-marketing data." He added that the company continues to finance research into the long-term effects of testosterone therapy and that its unbranded informational efforts, like the IsItLowT.com site, "follow F.D.A.'s guidance."

Nevertheless, some public health experts warn that the popularization of testosterone drugs is outpacing research into efficacy and possible harms. The drugs' labels warn users about the potential for sleep apnea, congestive heart failure and low sperm counts; the topical gels warn that women and children exposed to the substances could develop male characteristics like chest hair. Others have raised concerns about the potential for prostate cancer and heart attacks.

“The big thing is, we just don’t know the long-term risk of testosterone therapy at this time,” says Jacques G. Baillargeon, an epidemiologist at the University of Texas Medical Branch at Galveston who has studied testosterone-prescribing trends in the United States. “It’s particularly concerning when you see the dramatic increase happening at such a large scale so quickly.”

Seeking a Fountain of Youth

In a TV commercial promoting awareness of “low T,” the shadow of a middle-age man sits on a bench watching his friends play basketball in an indoor gym.

“Feeling like a shadow of your former self? Don’t have the hops for hoops with your buddies?” says the voice-over for the spot, paid for by AbbVie and currently posted on the IsItLowT site. “You might have a treatable condition called low testosterone or low T.”

A few seconds later, presumably after the man is treated with testosterone, the shadow evaporates and a man materializes in the flesh, besuited and smiling. Cue the voice-over: “Step out of the shadows.”

Testosterone, which plays a central role in the development of the male sexual organs, as well as muscle and body hair, has long been a synonym for youthful vigor and virility. And the quest to stave off aging by manipulating the hormone is an old business.

Toward the end of the 19th century, Charles-Édouard Brown-Séquard, a French physiologist, began injecting himself with “juice” extracted from crushed dog or guinea-pig testicles, as reported in *The Lancet* in 1889. Although he contended that the injections were rejuvenating, subsequent researchers came to believe that the placebo effect was at work.

In the 1920s and ’30s, surgeons began transplanting monkey and goat testes into men, says Dr. John E. Morley, the director of endocrinology and geriatrics at the Saint Louis University School of Medicine. But that fad ended quickly after one well-known surgeon implanted goat testicles into his patients, where they apparently emitted a noxious odor.

“This is the hilarious history of testosterone,” recounts Dr. Morley, who in the past received speaking fees or consulting fees from drug makers that marketed testosterone treatments or planned to do so. “It may not have gotten any better. But, gee whiz, it was crazy.”

Researchers were eventually able to synthesize testosterone, and drug makers capitalized on the discovery by using it to develop medical treatments.

The classic endocrine disorder for which testosterone drugs were originally developed and federally approved is called hypogonadism. That condition can be caused by problems like undescended testicles or a tumor in the pituitary gland, typically resulting

in severe testosterone deficiency, along with poor libido, minimal muscles and scant body hair. “That is the real hypogonadal patient,” says Dr. Richard Quinton, an endocrinologist at Newcastle University in Britain, “not the overweight businessman whose erections aren’t as good as they used to be.”

In fact, physicians weren’t precisely quantifying men’s testosterone levels until the 1960s, after the development of sensitive tests to determine the concentration of different hormones in blood samples. These enabled researchers to record men’s testosterone levels over time. Dr. Morley and others have reported that, after age 30, men’s testosterone levels typically decline by 1 percent a year. To the pharmaceutical industry, that decline was ripe for treatment.

But the science here is complicated by the fact that weight gain and illness can be accompanied by decreased testosterone levels. In fact, some researchers argue that declining testosterone may not be attributable to aging in itself, but to the fact that older men tend to gain weight more and develop more diseases. But critics say the pharmaceutical industry has expanded the market for testosterone drugs to men who may not need them and may be exposed to more health risk by taking them.

“Which comes first, the hen or the egg?” says Dr. Farid Saad, the director of global medical affairs for andrology at Bayer HealthCare Pharmaceuticals in Berlin, which markets a testosterone injection called Nebido in 76 countries. “Changes in weight seem to be more important than aging itself.”

Whatever the cause, an age-associated testosterone decline in men was good news for drug makers seeking to expand sales beyond uncommon endocrine disorders. Aging men could be a vast and perpetual audience.

There was just one problem. The F.D.A. approved testosterone treatments like Androderm, a skin patch, in 1995, and the original AndroGel, in 2000, for men with classic testosterone deficiency, and the agency prohibits pharmaceutical companies from marketing branded drugs for uses that have not been federally approved as safe and effective.

In 1997, for instance, the F.D.A. admonished Unimed Pharmaceuticals, the developer of AndroGel, saying that the company had violated federal regulations.

Even before the gel went on sale, Unimed was preparing to market it for “andropause” — in other words, for symptoms of male aging, according to a continuing whistle-blower lawsuit asserting that Solvay, which acquired Unimed, promoted AndroGel for unapproved uses. (AbbVie, a spinoff of Abbott Laboratories — which acquired Solvay in 2010 — is not accused of any wrongdoing.) The F.D.A. cited Unimed for a news release promoting AndroGel for potential uses “such as the treatment of geriatric hypogonadism in elderly men.”

Three years later, the agency issued another letter to Unimed, emphasizing that AndroGel was approved for “primary” testicular problems and secondary problems like pituitary or hypothalamus disorders.

“Claims and representation that suggest that AndroGel is indicated for men with ‘age-associated’ hypogonadism or ‘andropause’ are misleading,” the F.D.A. letter said, according to the complaint.

Tests That Anyone Can Fail

Do you have a decrease in libido? Do you have a lack of energy? Are you sad and/or grumpy? Are you falling asleep after dinner? Have you noticed a recent deterioration in your ability to play sports?

More than a decade ago, a Dutch pharmaceutical company, Organon BioSciences, asked Dr. Morley to devise a screening questionnaire covering symptoms common to older men with low testosterone. The way Dr. Morley recalls the drugmaker’s instructions, “they said, ‘Don’t make it too long and make it somewhat sexy.’ ”

In return, he says, Organon gave \$40,000 to his university for research into the effects of testosterone on muscle. Along the way, Dr. Morley’s quiz acquired an official name that emphasized its intended audience was older men: the Androgen Deficiency in Aging Males, or ADAM, test.

That test has become standard fare on brand-name drug sites like androgel.com and on informational sites like AbbVie’s IsItLowT.com — where the ADAM test has been re-branded as the “ ‘Is It Low T?’ Quiz.” If the questions drive many men to identify themselves as low-T sufferers and visit their doctors seeking remedies, well, that is their purpose.

The test has also become controversial. Most of the questions invoke symptoms that are so general that they could apply to many men who are clinically depressed or simply having a bad day — or even to women, says Dr. Adriane J. Fugh-Berman, an associate professor at Georgetown University Medical Center in Washington.

“There are tests that everyone will fail — that is the idea,” says Dr. Fugh-Berman, who directs PharmedOut, a Georgetown project that educates doctors about drug marketing claims. “ ‘Do you feel tired after dinner?’ Depends how long after dinner. We all do eventually. It’s called sleep.”

In 2010, the Endocrine Society, a professional medical association, issued guidelines on testosterone therapy advising doctors that there was little evidence to recommend self-reported quizzes.

Dr. Morley recalls that he drafted the questionnaire in 20 minutes in the bathroom, scribbling the questions on toilet paper and giving them to his secretary the next day to type up. He agrees that it is hardly a perfect screening tool.

“I have no trouble calling it a crappy questionnaire,” he says. “It is not ideal.”

He says he believes that the test does catch a subset of the aging population, like older men with low bone-mineral density and decreasing strength, who might benefit from treatment; he prescribes testosterone injections for some of them.

In his email, Mr. Freundel, the AbbVie spokesman, wrote that the ADAM test “is designed to help men assess their risk for low testosterone and determine whether they should speak to their doctor about low testosterone testing.”

He added, “For men concerned about low testosterone, we encourage discussion between physicians and patients that leads to proper diagnosis based on symptoms, lab tests and a patient’s other health needs and underlying conditions.”

But researchers like Dr. Lisa M. Schwartz and Dr. Steven Woloshin, professors at the Dartmouth Institute for Health Policy, say disease promotions and quizzes do more than just worry men into visiting their doctors. The implicit message is that taking testosterone will improve men’s energy and mood, the pair wrote in a recent article in JAMA Internal Medicine.

The F.D.A. doesn’t regulate how doctors practice medicine, and physicians are free to prescribe drugs as they deem appropriate. Some doctors believe that testosterone can be a good treatment to increase energy. Nevertheless, the F.D.A. has not approved testosterone for such uses.

“None of the testosterone products have indications for weight loss, increasing energy or improving mood,” said Andrea Fischer, a spokeswoman for the F.D.A.

The agency prohibits drug makers from marketing unapproved uses for brand-name drugs — because these “off label” uses have not been federally vetted for safety and efficacy. But Ms. Fischer declined to discuss testosterone ads, saying the agency doesn’t comment on brand-name ad campaigns that had not been subject to regulatory action.

Drug makers’ unbranded promotions talking up a disease or a condition are typically not subject to the same scrutiny. Ms. Fischer said that if the F.D.A. determined an unbranded “disease awareness” campaign to be false or misleading, the agency could refer the matter to the Federal Trade Commission for investigation. She declined to comment on whether the agency had done so regarding low T.

‘Enhancing Awareness’

Earlier this year, Medical Marketing & Media, a trade magazine, named two AbbVie executives as “the all-star large pharma marketing team of the year” for promotions of AndroGel and unbranded efforts to advance low T.

“It didn’t hurt that baby boomers have proven less than shy about availing themselves of any product that they believe will increase their quality of life,” an article in the magazine said. The article lauded AbbVie’s DriveForFive.com, an unbranded site that encourages men to have regular checkups and to ask their doctors about five tests, among them tests for cholesterol and blood pressure — and testosterone.

Mr. Freundel of AbbVie described the effort as “a national disease-awareness initiative aimed at encouraging men to take a more proactive approach to their health.” The F.D.A., he added, encourages companies to develop such initiatives “because they serve an important role by enhancing awareness of health conditions.”

Critics, however, see the site as another tactic to create testosterone takers out of generally healthy men, using the kind of unbranded campaign that federal regulators don’t typically police. Dr. Fugh-Berman of Georgetown refers to this kind of marketing as “disease mongering.”

In contrast to the promotion of testosterone tests on DriveForFive.com, for instance, the Endocrine Society recommends against screening the general population. For one thing, men’s testosterone levels fluctuate so wildly — depending on time of day, sleep quality, whether they just ate, whether they are taking care of a newborn and even how their favorite sports team is faring — that a single low testosterone reading may not indicate a problem. For another thing, the society says that there is a lack of medical consensus on the extent to which testosterone deficiency “is an important health problem.”

For men with serious symptoms, testosterone deficiency can be debilitating. A decade ago, Dr. Fisch, the talk-radio urologist, diagnosed testicular failure in a small-business owner from New Jersey. Now 52, the patient, who has been taking testosterone shots for eight years, said he felt that the medication had significantly increased his strength, energy and libido.

“I’ve run half-marathons, which I could never run before,” said the business owner, who asked that his name be withheld. “I wonder what I could do if my hormone levels weren’t balanced, if they were what they were before the shots.”

Yet some researchers warn that men whose problems are not caused by low testosterone are also taking the drugs, potentially putting them at unneeded risks for side effects.

A recent study published in JAMA Internal Medicine reported that about a quarter of men had received testosterone prescriptions without having had blood tests to check their levels.

“A lot of these men don’t have clear, unequivocal indications for this drug,” says Dr. Baillargeon of the University of Texas, the lead author of the study, “and yet you see the aggressive advertising on ESPN, on radio, on the Internet.”

Dr. Saad of Bayer acknowledged that occasionally men who are not truly deficient may be treated with testosterone therapy. “This is something that worries us and we would not encourage,” he said.

For his part, Dr. Fisch says many medicines follow a parabolic pattern of prescriptions — first used for limited purposes, then overprescribed, followed by a pullback to a more targeted group of patients. Testosterone drugs, he says, may go the same route.

Still, Dr. Fisch, an occasional paid speaker on men’s health for AbbVie, says he remains bullish on low T. But he prefers his own euphemism for aging: “the male biological clock.”

“This is a huge industry,” Dr. Fisch says, “and I expect it to grow even bigger.”