Controversy over testosterone therapy lands in Chicago court

By **Robert McCoppin**
Chicago Tribune

SHARE THIS

Fountain of youth generating fountain of lawsuits in Chicago.

SEPTEMBER 21, 2015, 12:42 PM

The ads promise to restore a man's vitality to that of a teenager: one "trick" that makes him strong and energetic, helps him "regain his former glory" and "leaves wives speechless."

The so-called trick is testosterone therapy. Once prescribed mainly for men with "low T" because of sickness or injury, the treatment has turned into a $2 billion annual industry since drugmakers began marketing it for general vigor and to counter the effects of aging.

At the same time, the treatment has caused controversy over possible links to heart attacks and strokes. The FDA has issued a new warning, and thousands of people who took the drug have sued various manufacturers.

Most of those lawsuits have been consolidated into one courtroom in Chicago that could help determine the fate of the novel medical treatment. The cases highlight the potential profitability of anti-aging medications, raise questions about how the treatment is marketed and underscore the difficulties for patients to assess its risks and benefits.

The defendants include pharmaceutical giants like AbbVie Inc., the maker of the most popular testosterone product, AndroGel, and Abbott Laboratories Inc., which owned AndroGel before spinning off AbbVie, both located in North Chicago. They and several other companies are being sued by more than 2,000 men who have suffered heart attacks and strokes that they claim were caused by testosterone therapy.

Among them is Steve Schabel, of Indiana. The married father of three said he started taking testosterone — first in gel form and then through an injection of pellets — in 2013 to treat depression and improve his sex drive.

But about a week after he received the injection, Schabel started to have difficulty breathing, which got progressively worse. At a local hospital, he learned he'd suffered a near-fatal double pulmonary embolism, or blocked veins in the lungs.

"I thought for sure I was dying," said Schabel, now 39. "It was the scariest moment of my life."

Schabel, who said he had no prior history of cardiovascular problems, survived but was told he would need to take blood thinners the rest of his life.

What caused his health crisis is open to fierce debate.

Testosterone is a hormone that produces masculine traits and promotes libido, muscle growth and bone density. Its levels typically decline steadily after age 30, especially in obese men.

Injections of the hormone have been approved for decades, generally only to treat men with hypogonadism, or low testosterone resulting from chemotherapy, genetic conditions or injury.

That changed in 2000, when the FDA approved the hormone treatment in a gel form that men could apply themselves.

The FDA never endorsed testosterone to treat "age-related" hypogonadism and issued warning letters to the original developer of AndroGel, Unimed Pharmaceuticals Inc., then based in Buffalo Grove, stating that it violated regulations by promoting its use for that purpose.

Yet despite limits on how pharmaceutical companies market drugs, doctors are free to use them for unapproved or "off-label" use if they deem it beneficial.

After seeing the huge sales of Viagra, the lawsuits charge, drugmakers seized on testosterone gel as a veritable fountain of youth for middle-age men, marketing it to doctors and patients alike. In 2013, AbbVie and Eli Lilly & Co. spent a combined $120 million on TV ads for testosterone, according to Kantar Media, a market research firm.

The website IsitLowT.com, sponsored by AbbVie, offered a questionnaire asking if men were tired, grumpy or losing athletic ability, conditions that could qualify them as having "low T."

Sales exploded. The FDA reported that in 2013, more than 2 million men, most age 40 to 60, took the treatment, though in a quarter of the cases, there was no evidence that testosterone levels were checked first.

And trouble was brewing. Two studies found that the treatment significantly increased the risk of heart attacks, strokes and death in older men and those with heart disease.

In response, the FDA this year issued a warning of a "possible" increased heart attack and stroke risk, saying the benefits and safety of age-related low-T therapy had not been

proven. The agency ordered drugmakers to put warnings on their labels, alongside previous alerts about other risks, including prostate cancer.

Yet the matter was far from settled. Two other studies reviewed by the FDA suggested just the opposite — a significant reduction in mortality for men taking testosterone — and another study found no change in heart attack risk. This summer, still two more studies found that the risk of cardiovascular problems was actually lower for men taking testosterone.

Critics on both sides have pointed out flaws in the studies. One of the critical studies accidentally included women, while some studies didn't account for risk factors like obesity or appeared to cherry-pick data that supported one side or the other.

Further complicating matters, the results appear to vary depending on who does the research. One analysis of various studies suggested that research funded by the pharmaceutical industry was more likely to conclude the treatment is safe.

Because of the contradictory data, the FDA is requiring the drugmakers to conduct randomized, controlled trials, rather than retrospective observational studies, to seek a conclusive answer. Lacking that, doctors wrote in the New England Journal of Medicine that the safety of testosterone products in older men "remains an important public health concern."

Various medical groups have weighed in. The American Urological Association, citing conflicting evidence, deemed the therapy "appropriate" for age-related hypogonadism, with monitoring and discussion of potential risks.

The Endocrine Society endorsed the use of replacement therapy for some men with low-T symptoms but urged caution for men with heart disease.

"What amazes me is the vehemence with which people on both sides of the issue claim benefits or harm in the absence of data," said Dr. Shalender Bhasin, an endocrinologist and lecturer at Harvard Medical School who chaired an Endocrine Society panel on testosterone therapy.

Though he has received grants from testosterone makers, he said, "If there's a hint of a harm and the benefits haven't been demonstrated, it's not appropriate, I think, to use it."

Abbott and AbbVie declined to comment.

Dr. Abraham Morgentaler, a Boston urologist who has been treating patients with testosterone for almost three decades, relies on studies associating low testosterone with higher rates of death and said for some men, the therapy has "changed their life." He said the treatment has become the favorite target of the anti-pharmaceutical movement.

But Ron Johnson, one of the lead attorneys for the men who are suing, charged that drugmakers essentially invented a disease, then got doctors to promote a cure without evidence it was safe or beneficial. He calls the favorable research "biased and false," noting one study excluded patients who died.

A panel of independent doctors almost unanimously recommended the FDA warning, he said, noting testosterone is known to increase red blood cells, which makes blood more prone to clots.

"This is the biggest and most well-orchestrated case of disease-mongering and ... off-label promotion of a drug ever," he said.

In some ways, the controversy echoes the debate over female hormone replacement therapy. Estrogen was commonly prescribed for women as an antidote to the hot flashes and mood swings of menopause, and a protection against heart disease, until a landmark study in 2002 found it increased the risk of heart disease, stroke and breast cancer.

The findings led to a wave of lawsuits that were settled only a few years ago. Now, the National Institutes of Health recommends that each woman discuss the risks and benefits with her doctor, and take the hormone in the lowest does for the shortest time needed.

Dr. Robert Brannigan, a urologist at Northwestern Medicine in Chicago, favors a similar approach for testosterone.

When a man comes in with diminished libido, strength and energy, or depression, Brannigan doesn't dismiss it as a natural part of the aging process but seeks to determine an underlying cause. If the patient has low testosterone, Brannigan will go over the FDA warnings and possible risks and benefits.

If he prescribes the drug, he'll check after a month to see if it is improving the symptoms. If not, he will stop using it and pursue other treatments.

"Most men at Northwestern are not bodybuilders or guys looking to get to super high levels," Brannigan said. "They're guys who genuinely have symptoms and want to see if this is the cause."

He said doctors are eagerly awaiting more definitive research.

"It's murky," he said. "Everybody wants to know what the truth is."

In federal court, the issue will come down to a handful of bellwether cases to be tried starting next year, the outcome of which could be used to settle the rest of the roughly 2,400 suits.

Meanwhile, AbbVie reported that AndroGel generated $320 million in revenues in the first half of this year, but that's down by almost a third from last year.

The controversy also raises broader concerns about medical marketing. In the Journal of the American Medical Association, two Dartmouth College medical school doctors called testosterone therapy for older men "a mass, uncontrolled experiment, which invites men to expose themselves to the harms of a treatment unlikely to fix problems which they may not really have."

In an editorial this year in The Journal of the American Geriatrics Society, two professors call for the FDA and Federal Trade Commission to ban advertising testosterone for "contrived" conditions.

Just as the FDA requires clinical testing to prove the need for a patient to take human growth hormone, the professors suggested, it should require testing and disease diagnosis to justify a prescription for testosterone.

rmccoppin@tribpub.com

Twitter @RobertMcCoppin

This article is related to: Medical Research, Obesity Research, Mental Health Research, Pharmaceutical Industry, Drugs and Medicines, Diseases and Illnesses, Heart Disease