Some Athletes’ Genes Help Outwit Doping Test

By GINA KOLATA
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The 55 men in a drug doping study in Sweden were normal and healthy. And all agreed, for the sake of science, to be injected with testosterone and then undergo the standard urine test to screen for doping with the hormone.

The results were unambiguous: the test worked for most of the men, showing that they had taken the drug. But 17 of the men tested negative. Their urine seemed fine, with no excess testosterone even though the men clearly had taken the drug.

It was, researchers say, a striking demonstration of a new genetic discovery. Those 17 men can build muscles with testosterone, they respond normally to the hormone, but they are missing both copies of a gene used to convert the testosterone into a form that dissolves in urine. The result is that they may be able to take testosterone with impunity.

The gene deletion is especially common in Asian men, notes Jenny Jakobsson Schulze, a molecular geneticist at the Karolinska University Hospital in Stockholm. Dr. Schulze is the first author of the testosterone study, published recently in The Journal of Clinical Endocrinology and Metabolism.

Dr. Schulze learned from an earlier study that about two-thirds of Asian men are missing both copies of the gene, as are nearly 10 percent of Caucasians. The prevalence in other groups is not known.

Doping researchers said the study raised questions about what to do next.

“It’s disturbing,” said Dr. Don Catlin, the chief executive of Anti-Doping Research, a nonprofit group in Los Angeles. “Basically, you have a license to cheat.”

Should athletes give DNA samples for scientists to analyze as genes like the testosterone-metabolizing one are found to be important? Or would another approach, the so-called athlete’s passport, be sufficient? The passport, favored by the World Anti-Doping Agency, is a record of all of an athlete’s screening tests and would detect results that vary from the athlete’s baseline values — but it would not include gene testing and therefore
may not detect those athletes lacking this gene.

But nothing will happen soon, and certainly not in time for the Beijing Olympics in August.

Testosterone and substances that act like it are the most frequently detected drugs in screening tests of athletes. The antidoping agency reported that these drugs have been implicated in 43 percent of its positive doping tests.

Researchers have long known that some men, Asians in particular, seemed to be able to take the drugs without getting caught, although no one had identified the cause of the phenomenon. Without gene testing, there is no way to know whether any athletes have exploited this doping loophole, but Dr. Catlin says he suspects some athletes discovered their invulnerability by accident and took advantage of it.

Men with the gene deletion still metabolize testosterone, Dr. Schulze says. But, she adds, she does not know where the hormone goes. “We have no idea,” she said. “That’s what we’re trying to find out.”

The gene in question adds a chemical, glucuronide, to testosterone. That converts it from a substance that dissolves in oil into one that dissolves in water and urine.

The testosterone screening test looks for testosterone and another substance, epitestosterone, that is produced in parallel to testosterone but does not have testosterone’s effects. The antidoping agency considers a testosterone to epitestosterone, or T to E, ratio of four or greater a positive test and follows it with a more expensive and definitive test that asks whether the excess testosterone is of human origin or whether it is from plants. The testosterone used in doping usually comes from plants.

When they conceived of their study, Dr. Anders Rhane and Dr. Mats Garle, head of the Doping Control Laboratory at the Karolinska University Hospital, applied for and received a grant from the antidoping agency. Then, to test their hypothesis, the Karolinska scientists injected the men with 500 milligrams of testosterone and looked at T to E ratios over the next 15 days as the testosterone was metabolized.
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