

Testicular cancer rates baffle

Researchers are trying to find out what is causing an increase in testicular cancer cases.

From The Australian
By Dr Christine White
23 Sept 2006

SEVEN years ago, Gerard Butera went to the doctor expecting a prescription for antibiotics or bed rest. "I just had a bad cold. But because I was a new patient, the doctor decided to give me a thorough going-over. And he found a lump in my testicle."

Butera was immediately sent for an ultrasound. At 9pm that night, the doctor turned up at his door, wanting to deliver the results in person. "He told me that the lump might be cancer." One week later, Butera was in hospital having his testicle removed. "That week was surreal," he says. "I had always considered myself fairly healthy – I ate well, played basketball. I had a healthy lifestyle."

Testicular cancer is the most common cancer in men aged 20 to 34. It's a condition in which the cells within the testis grow and divide abnormally, causing a tumour that may spread to other parts of the body. While it's relatively rare, affecting about 550 Australian men a year, the disease is on the rise in developed countries.

At the Monash Institute of Medical Research in Melbourne, doctor Kate Loveland and PhD student Vinali Dias are trying to discover how and why testicular cancer develops. Dias presented her most recent findings at the recent annual meeting of the Society for Reproductive Biology on the Gold Coast.

Worldwide, the incidence of testicular cancer has more than doubled in the past 40 years, and there has been a 34 per cent increase in the number of Australian men diagnosed over the last 10 years. But we still don't know what causes it, or why it's becoming more common.

By comparing healthy testis tissue with pre-cancerous or cancerous tissue, Dias has found that a hormone called activin might play a role in the development of the disease. Activin is important for the normal development of the testes and sperm production, but its action is not always beneficial. "Testis cells are only able to respond to activin if they have activin receptors," says Dias. "We've found that one of the activin receptors is not there in healthy testes, but it appears in cancerous testes. It may be that the cells respond to activin in a different way when they become malignant." Unfortunately, a blood test would not pick up changing levels of the activin receptor in the testicle. But if cancer was suspected and a testicle removed, the tissue could be examined under a microscope to see if the activin receptor was there or not. If it was, it could mean that the cancer was ready to spread.

Associate professor Mark Frydenberg, chairman of the Department of Urology at Monash Medical Centre, hopes that this research may one day help to diagnose and manage patients more effectively. "Once cancer is identified, it would be really helpful to know whether or not it is likely to spread, or metastasise," says

Frydenberg, who has been treating testicular cancer patients for more than 15 years. "Sometimes the disease stays quiet. But 30 per cent of men with testis cancer will relapse in the first 12 months and have to move on to chemotherapy. At the moment, identifying these men is a bit hit or miss."

Speed of diagnosis is important. The five-year survival rate for patients with "stage one" testicular cancer – the stage at which Butera's cancer was originally detected – is around 99 per cent. But once the cancer spreads, the chance of surviving past five years drops to between 80 and 90 per cent.

After his surgery Butera was desperate to know if his cancer was going to spread. He had blood tests, a chest X-ray and a computed tomography (CT) scan of his abdomen, and there was no sign of metastasis. "I was offered radiation and chemotherapy," he says. "In an ideal world, that would get rid of any other cancer cells in my body. But it was a huge dilemma – did I want to put my body through all that, when it might not be necessary?"

Based on all his test results, Butera's doctors said there was an 80 per cent chance that the surgery had completely removed his cancer. "So there was a lot of deliberation and stress. I spoke to all the specialists. In the end, I decided not to have the post-operative treatment. That was in 1999." Six years later, in November last year, doctors discovered that the cancer had spread to the lymph nodes in Butera's abdomen. "They found it during general surveillance – I was having checks every few months. They put me straight onto chemo."

Men in Butera's position, with early-stage disease that has relapsed, are usually given four cycles of chemotherapy. Each cycle lasts 28 days, during which time the drugs are injected directly into a vein, and circulate throughout the body to kill the cancer cells. But healthy cells are also affected. "I had all the usual side effects of chemotherapy – nausea, hair loss, weight loss, nerve damage in my toes and fingers, tinnitus (ringing in the ears) and lethargy," says Butera. "And of course, infertility will probably be an issue."

Testicular cancer strikes men in the prime of their life, often while they are in the process of having a family. While the removal of one testis does not affect the sperm production of the other testis, both radiotherapy and chemotherapy can lower sperm counts temporarily – or permanently. Doctors recommended that Butera freeze away a sample of sperm before starting chemotherapy, just in case the treatment caused him to become infertile. "When the time comes to start a family, I'll have the option of seeing a fertility specialist," he says.

When his chemotherapy was finally over in March this year, Butera was given the all-clear. But he finds it hard to celebrate. "I thought I was over it six years ago, but that wasn't the case." Throughout his ordeal, Butera's partner Lisa has stood by him. While they may still face further challenges, he says that their relationship has become stronger and deeper as a result of his illness. "I've learnt to appreciate life more," Butera says. "Making myself happy is now much more of a priority."

Frydenberg says that predicting relapse is one of the top priorities for testicular cancer research. But there are many other areas where research is desperately needed. "There are a few issues with the diagnosis of testicular cancer," he says. "We have a number of good cancer markers that we can test for in blood, but 30 to

50 per cent of men with testis cancer don't have high levels of these in their blood. If we had another marker that we could screen for in a blood test, that would be extraordinarily helpful."

Loveland hopes that her team's research will one day help to develop a new blood test for testicular cancer. Dias has found that if a man has low levels of the hormone testosterone, his testicles have more of the activin receptor. So testing for hormones in the blood could give another clue as to whether a cancer is there and ready to spread.

After dealing with testicular cancer for years, Butera is well aware of the need for more research. With no history of testicular cancer in the family, Butera is still baffled by why he has been struck by this disease. "Not much is known about what causes testicular cancer," he says. "There's talk of bike riding, even tight underwear. But there's a lot of uncertainty and contradiction."

In fact, scientists believe that a man's likelihood of developing testicular cancer is largely determined before birth – a combination of his genes and the maternal environment he encounters in the womb. There are many factors that could affect the developing testicles at this time, including the mother's estrogen levels, and environmental pollutants such as plastics and pesticides.

Research published this year in the *Journal of Urology* (2006;176:734-737) suggests that maternal smoking during pregnancy can also affect the baby's testicles, leading to a condition called cryptorchidism, where the testicles don't descend properly into the scrotum. This condition is one of the risk factors for testicular cancer.

"The most important thing to remember is that this is a disease of young men," says Frydenberg. "They should be doing regular self-examination and not be shy about reporting anything unusual to their doctor. Don't put it off for months – the sooner it's caught the better."