Pathologists' puzzle: mystery of the silver-coated heart valve

Dr. Jagdish Butany and the Peter Munk Cardiac Centre's determined team of detectives work to ensure the safety of novel cardiovascular devices

By **David Israelson**

THE MECHANICAL HEART VALVE THAT DR. JAGDISH BUTANY HOLDS IN HIS HAND looks surprisingly unassuming, about the size of a dime. Yet as director of cardiovascular pathology at the Peter Munk Cardiac Centre (PMCC), this particular valve took him on a mission around the world.

The mission was to solve a mystery – what was causing this manufacturer's new model of heart valve to be connected to infections in heart patients, resulting in their bodies rejecting the device and in some cases death.

The mystery started unfolding some 20 years ago, Dr. Butany explains.

"Normally, about 2 per cent of prosthetic heart valves that are implanted do get infected. You make something by hand or with machinery, and somewhere along the line, if the sterilization is not adequate, you can get bugs coming in," he says.

In the late 1990s, one of the manufacturers brought out a new model. It was offered to leading heart institutes at no extra cost because it included only a small improvement – a coating of silver along its edge that was intended to prevent infection.

Trouble is, more patients than usual actually had infections after receiving this device. Instead of the normal percentage of patients whose valves had to be replaced, within months the numbers kept going up.

"When we had eight [infections], I said, 'This is too much.' Unfortunately, prosthetic heart valves behave differently in different people," Dr. Butany says.

While Dr. Butany knew the problem needed attention, he didn't think dealing with this valve would become the cornerstone of his life's work.

There was a great deal at stake, though, not only for some of the over 55,000 people who have heart valves implanted every year, but also for the hospitals that need to make sure the devices work and the companies that invest tens and even hundreds of millions of dollars in developing valves.

Costing at least $4,000 each in Canada, synthetic heart valve looks deceptively simple. It's an outer ring with a disc or a membrane that opens and closes to let in blood and prevent it from flowing back.

As a pathologist, Dr. Butany looks at tissues, biopsies, lab results and even autopsies to determine what went wrong.

He works closely in evaluating and reviewing new devices with cardiovascular surgeons Dr. Tirone David, Melanie Munk Chair in Cardiovascular Surgery, and Dr. Christopher Feindel, Antonio & Helga DeGasperis Chair in Clinical Trials and Outcomes Research at University Health Network (UHN) and across the city.

Many people believe that doctors are highly influenced by drug and health-care companies, but "those days are gone," Dr. Feindel says.

The PMCC is particularly careful about which devices make the grade, Dr. Feindel adds.

"From time to time a new device will come on the market, and we'll start to see one-off or anecdotal situations where it isn't working quite right. Over time we might see a pattern," he says.

Dr. Feindel also sits on a Health Canada committee that reviews heart-related medical devices.

"We meet several times per year, and I sit on the advisory board. We get presentations on various devices that are coming on the market and then we talk about whether we see any pitfalls or have concerns," he says.

"We're not supportive of one company or another. We switch around, and sometimes the companies get upset. We have no problem being critical when it's necessary," he explains.

"On that committee we also have talked about follow-up, where something has already been approved, and we find down the road there are problems. Health Canada has made it very clear that they rely on clinicians [like those at the PMCC] to identify problems."

Pathology is at one end of the testing process that all medical devices must undergo, in many cases following the procedures of the U.S. Food and Drug Administration. (Health Canada tends to adopt the same standards.)

At the other end, before devices even reach the market, they are tested rigorously. Dr. Feindel says he can think of only a handful of situations in 30 years where devices didn't work properly.

But even one that slips through is too many, and problems still can come up, Dr. David says.

"In the worst cases, unfortunately, death is where the problem happens," he says. Even patients who survive a malfunctioning device must undergo removal and replacement heart surgery, and that's when Dr. Butany does his sleuthing.

"This particular valve was a real detective story. I spoke with Dr. Butany and told him something was just not right," Dr. Feindel says.

Dr. Butany took it from there, suspecting that the silver coating was the problem. It had been added by the manufacturer based on the same principle that has doctors apply silver nitrate drops to the eyes of newborn babies – to ward off infection.

His pathology research led him to suspect that rather than protecting against infection, the silver coating on the valves was toxic to cells in the heart muscle.

"I started talking to the manufacturer and continued [investigating]," Dr. Butany says. At one point, he presented them with the unusually high numbers of patients who had to have the silver-coated valve removed.

"They said that I'm biased," Dr. Butany says. The manufacturer had a lot at stake: in addition to the cost of research and development, by 2000 the company had sold 36,000 of these devices worldwide.

Not content to let this accusation sit, Dr. Butany prepared research papers and travelled around the world to deliver them, including a key presentation in Britain, making the case to reconsider the silver-coated valve. The team at the UHN in Toronto stopped using them, but Dr. Butany was determined to trigger a global review.

Late in 1999, the United Kingdom's Medical Device Agency heeded Dr. Butany's findings, issuing a warning against the valve. Australia and New Zealand followed suit.

"One day, about three years after I had my first concerns regarding the valve, I got a call from the manufacturer saying that the device was about to be withdrawn. They made the public announcement half an hour later, that morning," Dr. Butany says.

The process for reviewing devices is always itself being reviewed and fine-tuned, Dr. Feindel says.

"It's a fine line between allowing people to use new devices and being cautious," he explains.

For the future, "I think there are probably ways you could tighten the follow-up. There have been subtle changes in new trans-catheter valves [implanted into aortic valves], for example," Dr. Feindel says.

"We've learned a lot over the last few years, so if there's an issue with one, we need to know if it's a one-off situation, or are there more cases like it?"

01 Discovering the problem with this mechanical heart valve is part of the PMCC's dedication to rigorous testing protocols.

02 From left: Drs. Tirone David, Jagdish Butany and Christopher Feindel strive to fine-tune the process for reviewing new devices.