

NOBEL AMBITIONS

Breaking new ground means disturbing some of the old. **Lia Timson** looks at Australia's Nobel laureates, and the struggle for innovation to be recognised.

Things might have improved for scientists since Galileo was put under house arrest for daring to challenge the accepted wisdom of the day. But today's researchers still must contend with the time and effort necessary to prove that the prevalent thinking in their field is wrong before their findings can be accepted.

Professor Barry Marshall and his colleague Robin Warren proved stomach ulcers were caused by bacteria, not stress, 23 years before their experiments were ultimately recognised with the Nobel Prize for Physiology or Medicine, awarded by the Karolinska Institutet of Sweden last October.

The discovery was described as "remarkable and unexpected" and was the catalyst for the cure of the chronic, disabling peptic ulcer disease. It also decreased the incidence of stomach cancers and later made ulcer surgery and years of stress treatment for gastritis redundant (about a third of the population carries the bacteria unknowingly). Patients can now be treated with a short course of antibiotics.

So why did it take so long for *Helicobacter pylori* to gain formal acceptance?

"One of the difficulties when I started was that the standard medical teaching for a century was that the stomach was sterile. Bacteria didn't grow there," says Warren, now retired. "It was just like the Earth being flat. It was a 'fact'. The medical establishment is conservative and doesn't like sudden changes."

While the pair is credited with the discovery in 1982, it was Warren's first observations as a pathologist in Royal Perth Hospital that gave rise to their partnership.

"I found them in one case in 1979, a couple of years before I met Barry. I'm a pathologist. I look at pieces of tissue, trying to work out what's wrong with them for the surgeons who send them down [to the lab]. One of the pieces of tissue was a piece of gastric mucosa from the stomach and I thought I could see a lot of bacteria on the surface, so I stained it with a special stain that shows the bacteria very nicely. I hadn't seen bacteria before in the stomach and no one knew of any reports of them. So I

kept looking and I kept finding more and more and eventually I was finding them in a third of the biopsies."

In 1983, in a letter to *The Lancet* medical journal, Warren summarised his initial findings. In a separate letter Marshall detailed the work they were beginning together. The following year the journal published a co-authored article with detailed proof of their discovery. That's the one Warren believes won them the Nobel Prize.

"Barry first suggested sometime after we published our article [that we may win]. I told him not to be so bloody silly,"

Warren laughs. "When I heard the news last month I got a bit of a shock actually."

Although publication of the articles had taken place – the first step in scientific recognition – the pair experienced great difficulty convincing their peers.

Warren later told a gathering of doctors in Stockholm, Sweden: "I was unable to convince the commissioning [doctors] of the importance of the organisms. While histology suggested the opposite to me, it was hard to prove. I worked in a laboratory without patient contact. I couldn't obtain the biopsies I wanted and the idea of taking biopsies to culture was not considered to be

in the patient's interest."

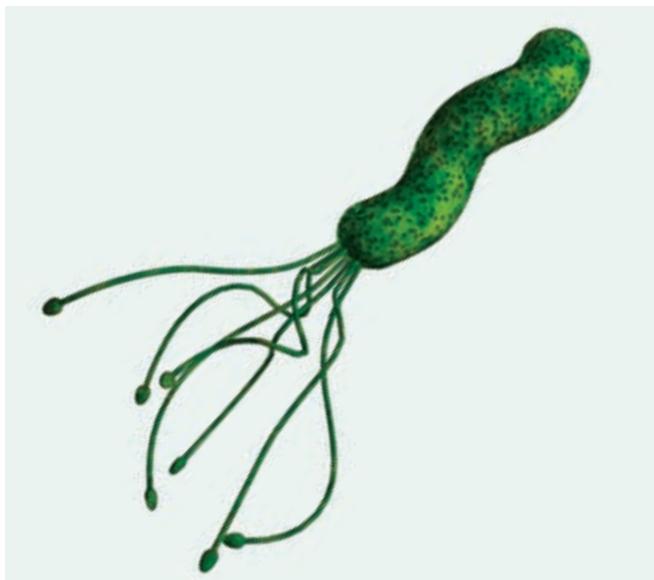
Things changed a little when Marshall, then a young registrar in gastroenterology at the same hospital, took an interest in the research.

THE CRAZY PATHOLOGIST

"Someone suggested he come down and see that crazy pathologist who was trying to suggest bacteria cause gastroenteritis. He burst into my office one day without knocking and demanded to see my work. He was quite a wild young man," remembers Warren, who is 14 years Marshall's senior.

"He was the first person to actually show an interest, so I was quite happy to show it to him."

Marshall agreed to send Warren a number of biopsies to see if the findings could be replicated. "They were. So he became



Left: Helicobacter pylori - Marshall drank a glass of it and consequently suffered from a two-week bout of gastritis.
Right: Nobel laureates, Robin Warren and Barry Marshall



more enthusiastic and we became collaborators. Barry was the only person who believed me at all for about five years.”

Together, they studied a further 100 patients as well as Marshall himself, who drank a glass of the Helicobacter pylori and consequently suffered from a two-week bout of gastritis.

While being a volunteer guinea-pig would be frowned upon today, at the time there were compelling reasons for the experiment. Not the least, the need for proof.

“In retrospect, my experiment could’ve gone wrong,” says Marshall, now senior principal research fellow, microbiology and immunology, at the University of Western Australia.

But the excitement of the discovery and the possibility – however remote – of a Nobel Prize were good incentives.

“The Nobel Prize helps innovation because it helps create a parallel scenario. Someone young on a low salary, slaving away on weekends trying something new, everyone says he’s a fool, but he says ‘just wait till I get the Nobel Prize’.

“I can’t say I was really like that. But it helps. It’s like the Olympics for science,” says Marshall.

The pair received a number of other prestigious prizes on the way to the Nobel, each with its own benefits and small monetary reward. But it is the latest that has finally given them licence to spend a little. They each received a slice of this year’s total prize pool of 10 million Swedish kroner (about one million euros) on December 10.

“It’s good I can share with the family, take them to Sweden. It’s much better value to know that I can temporarily afford to board the dog for \$30 a day while we’re away,” Marshall laughs.

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Seriously speaking, Marshall is pleased the prize didn’t come earlier in his career as now he feels better prepared for the notoriety that follows such honours.

He is also thankful for the doors it opens – “we now go straight to the top of government or academia” – particularly as he’s spent the past year trying to attract seed funding for his current Helicobacter project. His company, Ondek, is working on development and possibly commercialisation of an ulcer

vaccine for developing countries.

According to the Australian Bureau of Statistics only 11% of all Australian venture capital invested in the year to June 2005 was devoted to young biotechnology, pharmaceutical and health projects. That’s \$116 million out of a total of \$1 billion.

The manufacturing and transport-related group attracted the largest share of venture capital, with 38% of total investment, followed by retail, services and real estate with 26%. Marshall says the health funding is clearly not enough.

FRUSTRATION SURFACING

“The mining industry seems to be able to test [the ground] anywhere and immediately attract funding. It’s not like that in biomedical research,” he says, revealing two decades of frustration.

“Innovation means you try to do something no one has done before. There’s a risk in it. But the Australian community is risk averse. They want to know what the answer is before they give you any money.”

Marshall says businesses and governments need to reward risk-takers to truly support innovation. He hopes Australian private investors will eventually join their American counterparts in viewing biomedical research as a high-risk, high-return investment.

“We need investors in their 50s or younger, with millions of dollars who can get a few of their friends to share [in a fund]. We can’t have mums and dads [as shareholders].”

While the federal and state governments have established a number of grants for research over the years, Marshall says

the bureaucracy demanded by such schemes defeats their original purpose.

“To get \$50,000 from the [WA] government to pay one salary for a year, I reckon we’ve put in \$25,000 worth of effort into the application. We’re grateful for that, but if you spread \$10 million a year on Western Australia, [the result] is pretty thin on the ground. But if we had the [funding] done by private investors, we’d be multiplying it by 30,” he adds.

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