Will a Nobel ever be awarded to someone in sports medicine or science?

By Dr J

It is a time for great celebration that we have just had two Australian medical doctors awarded the Nobel Prize for medicine and physiology (Robin Warren and Barry Marshall). Their discovery was that the bacterium *Helicobacter pylori* is in fact the major cause of stomach ulcers which can now be successfully treated with antibiotics. Those of us in sports medicine should greet this award with a similar level of elation that we felt, for example, when Cathy Freeman won the 400 m at the Sydney Olympics. Admittedly the Freeman gold might have warranted more instantaneous joy in that the 'event' lasted less than a minute but there are more than one hundred Australian Olympic gold medallists yet only a dozen Australian Nobel Prize winners.

The only Australian Nobel Prize winners in medicine and physiology are:

- Warren and Marshall in 2005 for their discovery of *Helicobacter pylori*,
- Peter Doherty (along with Rolf Zinkernagel, a Swiss working in Australia) in 1996 for their discoveries in immunology,
- John Eccles (along with Hodgkin and Huxley of the UK) in 1963 for his discoveries regarding nerve cells,
- Frank Macfarlane Burnett (along with Peter Medawar) in 1960 for his discoveries in immunology, and
- Howard Florey (along with Fleming and Chain of the UK) in 1945 for the discovery of penicillin.

In terms of the impact on improving the human condition, the discovery of penicillin (which was the biggest ever breakthrough in the field of antibiotics) would rank as highly as any of the Nobel prizes awarded for medicine. Alexander Fleming is credited with discovering that the mould penicillium could inhibit the growth of bacteria, but the Australian Sir Howard Florey (who has an institute named after him in Melbourne) is considered to have been most responsible for introducing the antibiotic penicillin to clinical practice.

Warren and Marshall deserve the highest of our praises for making a discovery which vastly improves a common disease in clinical medicine, for being prepared to challenge existing dogma about the causation of peptic ulcer and, locally, for conducting all of their work within Australia (in the city of Perth). You should take any chance you get to read about the story of Warren and Marshall, including the free text in the Christmas edition of the *Med J Aust* at

http://www.mja.com.au/public/issues/183_11_051205/van11000_fm.html

With respect to the field of sports medicine, a recent Nobel award has major relevance (Paul Lauterbur and Peter Mansfield in 2003 for the discovery of magnetic resonance imaging). In 1998 three Americans (Furchgott, Ignaro and Murad) shared the Nobel Prize for medicine for their discoveries with respect to the role of nitric oxide in the cardiovascular system. Their work has probably inspired that of George Murrell and Justin Paoloni who have discovered that nitrates can improve the clinical outcome of tendinopathy, which may one day be worthy of a major international award in the field sports medicine. George Murrell has just won the FE Johnson Memorial Fellowship of the NSW Sporting Injuries Committee for 2005, whereas Justin Paoloni has already won the David Garlick Memorial Scholarship for this work.

There was an IOC Olympic Prize in sports science and medicine which was awarded every two years between 1996 and 2002, but not awarded in 2004 because of the withdrawal of sponsorship from the Pfizer company. This award, if it is resurrected, may possibly be seen as the "Nobel" equivalent in sports science and medicine. Yet it would only be an equivalent for as long as it was considered impossible for a sports medicine researcher actually to win a real Nobel Prize.

Those small-minded folk who think that I have tenuous grip on reality would probably suggest to me that sports medicine experts should stick to the task of proving to the Australian Government that we actually exist as a distinct area of medicine before anyone starts worrying about winning the Nobel prize for a sports medicine study. Even though we tend to equate sports medicine with sports injuries, if we start to think along the sports and *exercise* medicine paradigm, perhaps it won't be long before we see an exercise medicine Nobel laureate. Researchers such as Jeremy Morris, Ralph Paffenbarger and Stephen Blair must surely be close to that elusive Nobel for their work proving that exercise can prevent heart disease and cancer.

If we switch back to Marshall and Warren, there are lessons for us to learn. Firstly, that you can be an Australian and living and working in Australia and still beat the rest of the world to making a unique discovery. Secondly, even if your abstract is rejected from your society's annual conference (as it was – see the MJA article for evidence), it doesn't mean you won't end up winning a Nobel Prize for the research. Thirdly, you can be a touch on the eccentric (mad) side, as Robin Marshall obviously was when he drank a helicobacter solution to give himself gastritis, and it may actually help you be a great scientist. Fourthly, you might do well to think that infection could have an undiscovered role in a common condition where the ruling view is that is has no role.

One of my all-time favourite articles I have ever read was called "A New Germ Theory" written by Judith Hooper and published in The Atlantic Monthly in February 1999. This article focused on the theories of Greg Cochran and Paul Ewald, who believe (via Darwinian theory) that any common medical condition which has been around for generations but which substantially reduces human fitness should be considered an infectious disease until proven otherwise. For example, not only do they believe that peptic ulcer is caused by an infectious agent, they assert that cardiovascular disease must be too, along with diabetes, rheumatoid arthritis, Alzheimer's disease and many cancers, etc.

If you consider this concept to be preposterous, remember that mainstream gastroenterologists have only accepted in the last decade that *Helicobacter pylori* causes peptic ulcers. There is some evidence that various chlamydia organisms are associated with cardiovascular disease, although this has not yet been proven to nearly the same degree as the helicobacter/peptic ulcer connection. For a summary of of the Atlantic article, please refer to: http://www.injuryupdate.com.au/forum/showthread.php?p=1066#post1066. And for a more formal reference, try Cochran GM, Ewald P and Cochran K ("Infectious Causation of Disease: An Evolutionary Perspective) in Perspectives in Biology and Medicine 43(3), Spring 2000, pp. 406-448.

It is worth noting that the "New Germ Theory" does not pose a threat to the importance of public health, because of the ability for microorganisms to evolve rapidly. For example, the HIV virus is an infection which is known to mutate according to its environment. In Africa, where unfortunately sexual practices are not generally very safe, HIV is far more virulent, as it is usually given ample opportunity to spread from victim to victim, even if the victims die relatively quickly of the disease. The strains of HIV which are seen in Western countries have, by contrast, become far milder, presumably due to the widespread institution of safe sex practices. Because there is less opportunity for the virus to spread from patient to patient, it 'evolves' to become more benign, as it would be disadvantageous to kill its hosts before there was a chance to spread.

If, for example, the proponents of the "New Germ Theory" are right about Type-II diabetes, that it might involve an infectious agent, then it would still be important to push the public health message about exercise and good nutrition. In a society where there is a high population of overweight and obese people, if an infectious agent can cause diabetes in these people, from an evolutionary perspective it can afford to be a far nastier agent, as the potential pool of victims is huge (and from the agent's viewpoint it will not affect its spread if a few victims die of the disease). In a society (which unfortunately is now a hypothetical one) where everyone exercised regularly and ate moderate amounts of food, if you were a diabetes-causing virus you would quickly mutate to a more benign form. It would be very costly to kill your victims due to the difficulty in finding replacement victims (given that the virus might need a high-fat host environment in which to live). Therefore, even if there are infectious agents that cause diabetes that we are yet to discover, we can limit their spread by increasing rates of exercise and improving nutrition.

Which diseases in sports medicine might be caused by infection? The number one candidate, in my view, would have to be "chondral degeneration" in the knee joint, in particular. How many times do you see a patient go in for a knee arthroscope for a meniscal tear, and in which the surgeon also finds grade 1-2 chondral degeneration in the joint, followed by a rapid deterioration after the arthroscopy? A year later another arthroscopy is performed and this time the patient has grade 4 chondral damage (that is, frank osteoarthritis) and a disability that will last a lifetime. Of course, the ruling dogma is that the "early" chondral damage seen in the first arthroscopy constituted a joint "weakness" that after further "mechanical loading" deteriorated to frank arthritis. Yes, I believe that early wear of the knee joint can later become advanced wear, but in the average patient this normally takes 20-30 years. How come it can happen to some poor victims in under 12 months when they don't run a single step due to the fact that they have a knee effusion for the entire year? In my mind, the likely culprit is an infectious agent and, sadly, the likely source of entry to the joint is the initial knee arthroscopy itself.

OK, some of you sceptics out there who may actually be medicos who have treated patients with chronic effusion post-arthroscopy may be able to tell me that:

1. Whenever you have sent a knee effusion in this scenario off for a culture it has always come back negative AND
2. If you have ever happened to treat a patient in this scenario with a standard antibiotic (eg, Amoxil) it hasn't helped with the knee effusion.

This is where a read of the story of Marshall and Warren is extremely valuable. They only managed to culture *Helicobacter pylori* when one of their plates was accidentally left in a laboratory over the Easter break. Normally in pathology if a culture is not positive after 48 hours,

the plates will be discarded and a negative result recorded. *Helicobacter pylori* managed to evade detection for many years because it takes longer than 48 hours to multiple on an agar plate. When you think about it, based on Darwinian theory, if you are an infectious agent in modern times (such as a bacterium, virus or fungus) what would be the most important characteristic you could evolve to ensure your survival? The mainstream thinking is that "antibiotic resistance" (or anti-viral resistance) is the major evolutionary defence mechanism that microorganisms have. What about inability to grow on an agar plate in a pathology lab? Wouldn't that be a far more valuable characteristic to develop compared to antibiotic resistance? If you are resistant to an antibiotic, the humans will just hit you with a different antibiotic until they nail you. However, if you refuse to conform to their belief that they must be able to see you grow within 48 hours on an agar plate in a pathology laboratory, they probably won't even know that you exist and therefore won't be throwing any antibiotics in your direction in the first place.

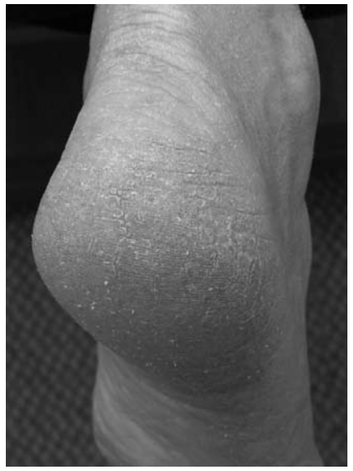
If the bacteria (or other non-bacterial microorganisms) which are most likely to infect a knee after an arthroscopy happen to be resistant to amoxicillin and don't grow on agar plates, then they can continue on their merry way eating through the layers of articular hyaline cartilage whilst the doctors who are supposed to be treating the patient nod their heads about the inevitability of cartilage breakdown. I can remember a case from my intern year of a woman who had a persistent effusion after a knee arthroscopy and was stuck on my orthopaedic ward for weeks due to severe knee pain. Eventually the pathologists isolated *Kingella kingii* bacterium from her knee, but it was thought to be possibly a benign pathogen.

There is a case report which suggests this may be a cause of septic arthritis in *J Rheumatol* (1981 May-Jun;8(3):501-3): "Septic arthritis due to Kingella (Moraxella) kingii: case report and review of the literature", by Vincent J, Podewell C, Franklin GW and Korn JH. This short PubMed abstract states that Kingella (Moraxella) kingii, a gram-negative bacillus, was isolated as the cause of septic knee arthritis in an adult. Three previous cases (one adult and two children) of septic arthritis due to Moraxella species have been reported. All cases have been characterised by difficulty in identifying the organism, indolent clinical course and slow response to antibiotic treatment.

Does this (underlined section) sound to you like the standard progress of a post-arthroscopy patient with a chronic effusion? What if there are actually dozens of organisms out there like *Kingella kingii*, which can chew through knee articular cartilage but are difficult to identify and don't respond to standard antibiotic treatment? Apparently *Kingella kingii* does not grow well in the laboratory within 48 hours and if not transported in blood culture bottles so, from a routine tap of the knee joint, a *Kingella kingii* infection will generally return a negative result (just like *Helicobacter pylori* used to do with peptic biopsies). For more info, read http://www.medterms.com/script/main/art.asp?articlekey=33658.

One of my personal areas of clinical expertise is the treatment of Achilles tendinopathy, and I occasionally think about whether an infectious agent might be responsible for the failure of Achilles tendinopathy patients to repair their degenerative lesions. We know that tendon degeneration is very common (eg, the Jill Cook studies on patella tendons) yet we know that many people with tendon degeneration don't get pain and many cure their own radiological tendinopathy spontaneously. Could it be that those who don't spontaneously cure possibly have an infectious agent responsible for the ongoing degeneration? I'm not saying that this is necessarily the case, but I can hypothesise that it wouldn't be an in-your-face bacterium like *Staphylococcus aureus*, or someone would have already cultured it.

I regularly notice that many of my Achilles tendinopathy patients have cracked heels, presumably due to low-grade skin fungal infection (see figure). A lot of the general population also has low-grade fungal infection of the heel, but is it more common in Achilles tendinopathy patients? I don't know, but perhaps one day in the future I will do a case-control study to test this hypothesis, and on another occasion I might treat some of my non-response Achilles tendinopathy patients with Lamisil to see how they go.



The great thing about being involved in science is the thrill of watching our knowledge base evolve. Fifteen years ago the internet didn't exist and, 25 years ago, no one suspected that *Helicobacter pylori* was a common cause of peptic ulcer. If you are working in sports and exercise medicine, you are working in an area which, despite its snubbing by the mainstream medical profession, is one which is critical to the advancement of human health. Maybe we won't see a Nobel Prize-winning discovery in sports medicine in our lifetime, but maybe we will. What is assured is that there will be new and successful ways to prevent and manage major sports injuries that are discovered in our lifetime, and that some of them will be discovered in this wonderful country of ours.

The new Australian Sports Anti-Doping Authority

Adam Firth

The year 2004-05 has been a landmark in Australia's anti-doping effort, Chairperson Brian Sando says in the latest -- and probably the last -- annual report of ASDA before the Government turns it into ASADA, the Australian Sports Anti-Doping Authority.

Acting Chief Executive Kim Terrell points out in the report that the establishment of ASADA, implementing one of the biggest testing programs ever undertaken in Australia and the work on the 2006 Commonwealth Games will be high priorities for 2005-06. For example, the Agency will conduct more than 7,000 drug tests in 2005-06 -- on average, that's at least 19 athletes tested every day of the year.

Sport Health here publishes extracts from the report on issues of special interest to its readers, such as no advance notice testing, trends in notifiable events and the prospects for an online athlete whereabouts system.

On 23 June 2005 the Australian Government announced its intention to establish the Australian Sports Anti-Doping Authority (ASADA), which from early this year will take over from the Australian Sports Drug Agency (ASDA) as Australia's NADO under the World Anti-Doping Code (WADC), but with significant additional functions to ASDA in the fight against doping in Australian sport.

No doubt ASADA is motivated at least in part by the Australian cycling controversies of the past two years and the experiences in the United States with the BALCO scandals. Its enabling rules and regulations are not yet finalised and accordingly this article can only make comment on some features that have been announced and in relation to such a body generally.

ASADA's powers

It has been confirmed that ASADA will replace ASDA in handling the responsibilities of sample collection and testing, and education and advocacy. It will also play a role in policy development relevant to sports doping, and most significantly will act as the investigator and prosector of all allegations of anti-doping rule violations relating to sports whose governing bodies in Australia sign on to use ASADA for such purposes.

It will be a condition of government funding and other support that sports submit all their anti-doping operations to ASADA, and ensure that their members and staff cooperate fully with ASADA in the performance of its functions. It will also be a requirement that the sport accepts any adverse finding of ASADA against any of its athletes (or other persons within the sport's jurisdiction), ensures that infraction notices are served on such persons and enforces penalties imposed in accordance with the sport's anti-doping rules. The Government has used purse string control to good effect in forcing all Australian sports to sign on to the WADC and it can be expected that it will pursue use of ASADA with the same intent.

More specifically, in addition to ASDA's existing powers, ASADA will have:

- power to conduct investigations on the basis of information acquired from its drug testing and other activities, or where it has received information from any other person, or on its own initiative;
- power to receive, use and disclose (where appropriate) information from Australian Customs Service or other law enforcement agencies where relevant to a possible anti-doping policy breach;
- power to present the prosecution case before a tribunal (whether or not ASADA investigated the case). This may include prosecuting adverse analytical findings in respect of a sample tested by ASADA; and
- the ability to publish results of any hearing where it is in the public interest.

The effect will be to have a common procedure and consistent practices throughout Australian sport in pursuing anti-doping rule violations and enforcing anti-doping policies. Consistency between and within sports can only be a positive thing in reducing uncertainties that have in the past been seen in anti-doping matters in Australia and around the world.

The most significant new features of ASADA are its investigative and prosecutorial functions. An independent, government-funded body fulfilling such a role has been sought by many sports organisations in this country for some time as the burden of anti-doping policy enforcement distracts time and resources from developing their sport, their competitions and their athletes. This is particularly the case