Quotable Quotes From Prof Barry Marshall:

Genomics: the Now and the Future...

I recently come back from a top genomics conference in the USA and it was so exciting!

The *ultimate* personalised medicine.

It's not going to be long before every Australian will be carrying their genome on a smart card. This is going to be an enormous and unprecedented help to their health. It will give people ownership over their own health.

People need to be responsible for their own health care. Let's take responsibility.

However, Australians currently seem too paranoid to truly embrace genomics. Yet there will soon be 1000s of human genomes publically available.

Currently most human genome sequences in the public domain are de-identified, such as those from the "1000 Genomes" project. (http://www.1000genomes.org/)

The **BIG** announcement – Barry goes Public!!!

I am hoping to be the first person in Australia to make their genome sequence publically available.

My own genome is now being processed at the Lotterywest State Biomedical Facility:Genomics, in Perth.

I already have my genome "SNP" scan report from the company deCODEme (http://www.decodeme.com/) posted on the web.

I'm going to place my ENTIRE genetic code on my homepage and people can investigate it at will.

I have no concerns about everyone seeing my genetic code. I have nothing to hide – it doesn't bother me if people can see that I have the gene for sticky ear-wax, or ADHD, or diabetes for example...

Genetic Information & Health Insurance Companies

There should be no discrimination possible on the basis of mere genetic data.

In the USA it is illegal now to rate a person based on their genetic makeup. That means that health insurance companies cannot charge higher premiums due to the results of a genetic test. As a result, people are freely having their genome tested in various ways.

Australia needs to introduce a similar regulation. We're fortunate in Australia that we have such an excellent health system; so I don't believe that better understanding of genetic make-up can be used to penalise anyone here. However the Australian community is still nervous about public genetic information.

Medical research is so wide open at the moment that I can in the future everybody will be a lot healthier and happier, because of the things that are happening now, in the 21st century, in my lifetime.

Investment in science

Investment into scientific and medical research not only greatly assists health outcomes, but also makes fantastic economic sense.

Take the Human Genome Project as a current and pertinent example. Starting in 1992 it cost \$3.8 billion to sequence the human genome, which is undeniably a huge amount.

However this investment has resulted in a positive economic impact of \$796 billion, and created 310,000 jobs in the USA. <u>In other words, for every \$1 invested into the Human Genome Project it generated \$141 in the economy.</u> So what an important investment this was!

http://www.battelle.org/publications/humangenomeproject.pdf

Science & Ethics

Australian needs to be aware we are not a truly secular country.

We still not have religious people trying to control our science. This battle started 500 years ago with Galileo when he was excommunicated for saying that the earth rotated around the sun, and more recently with Charles Darwin. And it still continues - the GMO debate for example. Natural and alternative medicine might be another pseudo-religious group trying to hold back advances in modern science. Some of this influence filters back into science through Government sponsored and politically loaded ethics committees, whose bible is typically an out-dated NHMRC policy or guideline document. These serve to ensure that Australian medical research lacks spontaneity.

What is ethical or unethical? Your ethics may not be my ethics, or may not be the Pope's ethics...

I believe stem cell research has been stifled in Australia due to religious beliefs. This shouldn't be allowed to happen. Scientific freedom should prevail except in very extreme cases.

Committees

In Australian medical research, we need committees (such as ethics committees), to be run by professionals, not volunteers. These committees play a crucial role and are the first step in clinical research, yet they unnecessarily become a bottleneck, holding up the process.

We need research oversight to be innovative, pro-active, rather than retrospective. Unfortunately guidelines are too complicated and inflexible and they discourage research.

It takes years to change guidelines. We need more of a dynamic process with autonomy for local committees. Too often risk and insurance issues make changes or improvements in research methods virtually impossible.

We don't need gate-keepers for our own genetic information. People should be allowed to know their information if they wish to, and not be "protected" from it.

Self-experiments, like my one with H. pylori, would not be allowed by any present day ethics committee and are impossible to do these days. Perhaps rightly so too!

The immense power of curiosity-driven research

The excitement and power of curiosity-driven scientific research is not knowing where that research will end up. We just don't know where new discoveries will come from. When Robin Warren and I set out to study bacteria in the stomach, we had no idea we were going to end up studying ulcers!

One of the things my wife says is that she actually has five children. She's got the four children and me, and that I never grew up. A lot of doctors seem to be in this category, in that they have always got this childish curiosity...

I suspect I was born with a boundless curiosity and this was encouraged through my childhood.

Alternative Medicines

- Large amounts of money spent

Americans spent about \$34 billion a year on alternative medicine and procedures, with the out-of-pocket spending on alternative medicine about one third of that spent on prescription drugs. In Australia we spend even more on alternative medicines than on prescription drugs!

- Need for scientific research

We need to have benefits for alternative medicines or treatments that have been proved scientifically to work in double-blind placebo-controlled trials. Alternative medicines currently need no proof of safety or effectiveness before they go on the market. We need rigorous research providing proper evidence to back these products.

- A levy?

I believe that non-validated treatments should incur a levy, which would supplement the medical research funding. This would encourage them to go through proper validation to prove the worth of their products. People spending their money on non-proven medications drains the funds they could be using to look after their own health in proven ways.

Researching "bugs" in stomach

In those days, every single day we would have a new idea.

We were in the right place at the right time.

It was just a wonderful discovery. It was exactly like one of these archaeologists telling us the story of how he discovered this new Egyptian tomb. He was crawling through this little dusky corridor and then, bingo! The door was opened and there was this incredible chamber with all these Egyptian relics in it. It was actually like that with Helicobacter.

There's a lifetime of work in it. There are literally thousands of scientists now study Helicobacter and the stomach. There are a few other interesting issues besides only ulcers.

In England, children with Helicobacter were found to be slightly shorter, about a centimeter shorter than the control group. Helicobacter worsens iron deficiency and is sometimes with low platelets which affects blood clotting. Maybe it sets you up to be more susceptible to other infections that could kill you, such as cholera, and there's some literature on that.

If you ask how bad is Helicobacter, since most people don't even have any symptoms, you could say that in some ways, Helicobacter is kind of like dandruff on the stomach. It's abnormal, it causes an irritation, but many people would fulfill their normal lives and not even know they had it. However, the bug does set you up for an ulcer, or possibly a one percent chance of stomach cancer after age 60. So I'm in favor of treating everybody and wiping the whole thing out.

Medical Research and Collaboration

These days collaboration is so much easier to undertake. The enormous power of the internet enables researchers to talk and interact with colleagues on the other side of the world, to tap into knowledge derived elsewhere.

I've got a lucky combination of a team of scientists working with me on interesting questions that I'm curious about. I also have some connections with industry, so if we have a good idea for a new treatment or a new test, we can quickly make it and try it out on volunteers or patients. Australians are always very, very willing to take part in my research. They say, "Well, he did it on himself, so we can trust him, I suppose."

Novel thinking – going against convention

If your head's just full of that conventional learning (50 percent of which is incorrect), it's very difficult to fit a new concept in. So it's an advantage in some ways if you don't know everything. If the field is not well understood, maybe it's better to find your own path into it and take the leads as they come, rather than saying, "Here's the body of knowledge. I'm going to study this bit, and advance that bit of knowledge." Maybe you just need to be very lateral.

When the H. pylori work was presented, my results were disputed and disbelieved, not on the basis of the science but because they simply could not be true in the context (incorrect) dogma about the stomach. It was often said that no one was able to replicate my results. This was untrue but became part of the folklore of the period. I was told that the bacteria were either contaminants or harmless commensals.

Convincing the skeptics is tough and it does take time, but that is the scientific method. The person who makes the new discovery is a target for everybody else whose duty it is to try to prove him wrong.

So it was initially a campaign, I felt that everyone was against me. But I knew I was right, because I actually had done a couple of year's work at that point with Dr Warren. I had a few backers who could duplicate my results.

And when I was criticised by gastroenterologists, I knew that they were mostly making their living doing endoscopies on ulcer patients. So I'm going to show you guys. A few years from now you'll be saying, "Hey! Where did all those endoscopies go to?" And it will be because I was treating ulcers with antibiotics.

Although less glamorous than high impact papers, reliable cheap and available diagnostics are just as important in medicine as treatments.

THE self-experiment!

We mixed up a complete flourishing growth of bacteria from a petri dish - we calculated out later that it was a thousand million bacteria - and I said,

"Well, here it goes, down the hatch."

My lab technician, who was fairly conventional, was horrified. Maybe he was waiting for me to drop dead, but I said,

"Well, I'm feeling all right. Okay, let's press on." We have ward rounds to do. So, off I went and I kind of forgot about the experiment for a week or so...

I didn't think my experiment was particularly dangerous.

I had to get past this hurdle of fulfilling Koch's Postulates, the rules we have for proving a germ is a pathogen.

I studied the literature, and there were a few subtle hints that people would have no symptoms when they had this infection.

When I spoke to ulcer patients, they couldn't tell me about any illness they had had. They were perfectly fine, and then they developed an ulcer. So I didn't think I would become unwell. I had treated a few patients with antibiotics successfully at that point, so I thought I could probably cure it.

I was a bit overconfident in retrospect. I wanted to make sure that the bacteria did take, because I didn't know whether I'd have the guts to do this every week!

Professor Barry Marshall AC

Current Positions:

- Clinical Professor of Medicine UWA
- Clinical Professor of Microbiology UWA
- Consultant Gastroenterologist (Sir Charles Gairdner Hospital)
- Co-Director of the Marshall Centre for Infectious Diseases Research & Training UWA
- Founder and Director of ONDEK, a biotechnology company
- Founder and Director of TRI-MED a diagnostics company
- Ambassador for Life Sciences for Western Australia
- Western Australian Technology and Industry Advisory Council
- Honorary Patron of Scitech
- Patron of the Monash Centre for Synchrotron Science
- Francis R & Helen M. Pentz Professor of Science at Penn State University, USA
- Visiting Professor, Wake Forest University, North Carolina
- Fellow of the Australian Academy of Science 1999
- Member of the Royal Society, UK 1999
- NHMRC Research Fellow 2009 onwards

Education & Career:

Barry Marshall received a Bachelor of Medicine, Bachelor of Surgery from the University of Western Australia in 1975. Together with J. Robin Warren he proved that *Helicobacter pylori* is the bacterial cause of most stomach ulcers. For decades medical orthodoxy had held that ulcers were caused by stress, spicy foods and too much acid.

Dr Marshall had met Robin Warren, a pathologist interested in gastritis, in 1979 while training at Royal Perth Hospital. Together they studied the relationship of spiral bacteria to gastritis. In 1982 they cultured *H. pylori* and developed the hypothesis that there was a bacterial cause of peptic ulcer and gastric cancer, defying assertions that bacteria could not live in the highly acid environment of the stomach.

After failing to infect piglets with *H. pylori* in 1984, Dr Marshall famously drank a petri dish of the bacteria himself and soon developed stomach discomfort, nausea, vomiting and halitosis.

Dr Marshall went on to do research at Royal Perth Hospital (1985-86) and at the University of Virginia, before returning to Australia. He held a Burnet Fellowship at the University of Western Australia from 1998-2003, continues with research related to *H. pylori* and runs the *H. pylori* Research Laboratory at The University of Western Australia.

Selected Accolades:

(Awarded in conjunction with Dr Robin Warren)

- Nobel Prize for Physiology or Medicine 2005
- Western Australian Citizen of the Year 2006
- Western Australian of the Year 2007
- Companion in the General Division of the Order of Australia (AC) in 2007.
- The Paul Ehrlich Prize 1997
- Warren Alpert Prize 1995

- Honorary Professor at the Third Military Medical University, Chongqing, China
- Honorary Degree of Doctor of Science, honoris causea, University of Oxford, UK
- Honorary Doctorate in Medicine at Örebro University, Sweden
- Galen Medal, The Worshipful Society of Apothecaries, London
- Lennon K. Black Prize for Excellence in Biomedical Research, Jefferson College,

USA

- Elected Foreign Member to the National Academy of Sciences
- Guest Professor of Internal Medicine at Keio University, Japan
- The William Beaumont Prize AGA
- Honorary Degree of Doctor of Science, honoris causea, Polish Academy of Medicine
- The Bulletin Smartest 100 Health & Medicine winner
- Silver Seal, University of Bologna, Italy
- Australian Centenary Medal
- The Keio Medical Science Prize
- Inaugural Premier's Prize for Achievement in Science, WA
- Prince Mahidol Award for Public Health
- Clunies Ross National Science and Technology Award
- Inducted as a Fellow of Australian Academy of Science
- Inducted as a Fellow of the British Royal Society
- Beniamin Franklin Medal for Life Science
- Buchanan Medal, The British Royal Society of Medicine
- The Dr A.H. Heineken Prize for Medicine
- The Florey Medal, Australia
- Kilby Prize, Dallas Texas
- The Gairdner Award, Toronto Canada
- The John Scott Award, City of Philadelphia
- The Albert Lasker Award

Authored books:

Helicobacter pylori (2000)□

Helicobacter pylori in Peptic Ulceration and Gastriti (2001)□

Helicobacter Pioneers: Firsthand Accounts from the Scientists who Discovered Helicobacters (2002)