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"Immunisation – The times they are a-changin'"

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PROFESSOR LYTHGO: It is a great pleasure to introduce Professor Ian Gust. He has had a stellar career in medical research, in virology and public health and he is remembered by many generations of medicos as a very inspiring and a loved teacher. He had a 20 year association with the Fairfield Infectious Diseases Hospital. Now, it was the first laboratory to isolate the hepatitis A virus and his work lead on to a vaccine against this virus which was rolled out worldwide. He has also made major contributions to the development of vaccines against hepatitis B and the human papillomavirus.

He was a key advisor in Australia's response to the HIV epidemic and he also introduced and developed early diagnostic essays and established the Australian HIV reference laboratory. He was also a voice of wisdom and humanity in those times of mass hysteria around HIV. I have been told that once, during an interview about the dangers of contracting HIV from kissing or using the same cup, he told the interviewer, with a straight face, that the danger was much the same as being kicked to death by a duck. I have also had reported to me an alleged other more colourful description or illustration of that same risk, but I decided that it was not really appropriate before dinner. We might hear about it later on.

He is the Inaugural Director of the Burnet Institute and Head of Research and Development at CSL and a consultant with the World Health Organisation. It has been an extraordinary contribution to medical research and to public health, but when I spoke to the students and colleagues that he has worked with, it was actually his personal qualities that they remembered him for. He

always taught respect for everyone and they particularly stressed that he was very supportive of the careers of women. Professor Gust will speak to us tonight on "Immunisation, the times they are a-changin'".

PROFESSOR GUST: Thank you very much. Sounded a bit like an obituary. I think most people acknowledge that immunisation has been one of the most important medical advances of the last century but, as I am reminding you here today, as Bob Dylan reminded us, the times they really are a-changin'. And most of those changes have taken place during my working life and through my career, when you think back of the major events, there are many more vaccines and a whole range of combination vaccines that have become available and the quality of the vaccines has just improved out of sight.

A great deal of money has been raised to support immunisation and that has enormously reduced the delay of introducing a new vaccine into the developed world and then flowing on into the developing world and both of those things resulted in enormous benefits in public health. There has been a marked decline in infant morbidity around the world and the saving of about 3 million lives a year, simply through immunisation. But interestingly, over that period of time we have seen a huge increase in the cost and the time that it takes to develop a new vaccine, a transfer of the production of vaccines very largely from the public sector to the private sector and a dramatic decline in the number of research based manufacturers in the world, but that has been counterbalanced a little bit by the rise of a range of generic manufacturers, mainly in the developing world.

We have also seen, recently, a rise in public private partnerships that are designed to try and share the financial and the technical risk in developing vaccines against some of the more complex organisms like malaria, TB and HIV. So this evening, what I would like to do is talk a little bit about the forces that have created those changes and the curious paradox of declining support for immunisation in some developed countries.

Now, by the time that I entered the university as a young seventeen year old, I had been immunised against five infectious diseases. As an infant in the early 1940s, I received, as many of you will have, CSL's triple antigen which was the vaccine that protected us against diphtheria, tetanus and whooping cough, and then also the small pox vaccine. And then later in primary school, I was offered but, because I was skin test positive, did not require CSL's BCG vaccine which was intended to protect me against TB and then, finally, in the second half of the 1950s when I was at secondary school, I recall standing in a long queue at the St Kilda Town Hall with my mother to receive the newly developed Salk vaccine which provided protection against all of the three strains of poliomyelitis.

Now, like most of my generation, infectious diseases were simply part of growing up. I spent several weeks of my childhood isolated at home, sequentially, with measles, mumps, rubella, chicken pox, flu, fortunately without developing any serious complications and then, as a young teenager, developed an unpleasant case of aseptic meningitis right at the time that there was a major polio epidemic in Melbourne that was very, probably due to one

of the strains of polio. Then my next immunisation, like many people of my generation, did not occur until 1967 when I was in my mid twenties and received TAB, not the Totalisator Agency Board but CSL's typhoid, paratyphoid A and B vaccine before sailing off to England as a ship's doctor and that was pretty typical.

Prior to the 1970s, almost all of the vaccines that were made around the world were used in developed countries and were directed mainly at children, and they were typically produced in government owned facilities and were very inexpensive because the true costs of production were not factored into the price of the vaccine. Now, compare my experience with my grandchildren, of whom there are currently seven but there will soon be nine and assuming no new paediatric vaccines are licensed over the next 15 years and that they do not go overseas with their parents, by the time they finish secondary school will be protected against 16 infectious diseases and two cancers, liver cancer and the cancers associated with the papillomavirus infection.

In addition to that, none of the vaccines that they receive, with the possible exception of flu, will be produced locally and none of them will be inexpensive. The two main factors that have driven those changes, I think, have been for an increasing demand for products of the highest possible quality, but also the rapidly expanding market for vaccines. When you think of it, prior to World War 2, most of the vaccines that existed - and there were not many - diphtheria, pertussis, tetanus, typhoid, cholera - were directed against bacterial diseases and they were made of relatively crude

preparations of killed organisms or inactivated toxins. It was a pretty straight forward process because you could grow bacteria in industrial quantities on solid or liquid media and you could kill them pretty readily with formalin. By contrast, with the exception of small pox in which live vaccinia virus is used to induce immuno vaccines against viruses because viruses only replicate in living cells and cells could not be maintained in culture for long periods of time, so we could not grow the viruses in large quantities, but the thing that changed all that was the discovery of penicillin. It revolutionised the field because it was pretty soon found that if you added penicillin and streptomycin to culture media, you could keep breeding cells in the laboratory for weeks at a time without the danger of bacterial overgrowth so that in the 50s and 60s when I first started to get into the field of virology, the widespread use of cell culture was leading to the isolation of the viruses responsible for a very large number of common communicable diseases, and also the development of a range of new vaccines. And at the same time or at about the same time, the introduction of large scale fermentation and purification technologies enabled us to make vaccines of high quality and at very large scale and then subsequently advances in chemistry, especially conjugation technology have made it possible to improve the immunogenicity of the surface antigens of some bacteria and it is made it possible to develop vaccines against bacterial meningitis and pneumonia and so on, but a second set of factors were also at work.

Whereas vaccines were originally seen as public goods produced by the State, largely for children in the

developed world and sold at cost they have become highly differentiated products produced by the private sector and administered to people throughout their lives used widely in both the developed and the developing world and they are now sold for profit. And several factors have driven those changes. I think the first and the most fundamental one was concerns about vaccine's safety. The second was WHO's role in promoting immunisation and then the final one was resolving the tremendous challenge that was posed by the development and licensing of a vaccine that I was a bit involved with, the hepatitis B vaccine.

Now, in the swinging '60s I was a graduate student at the London School of Hygiene and Tropical Medicine in London. In those times, most vaccines were still being produced by government owned facilities and were lightly regulated, sometimes not even regulated at all and they used methods that had been developed decades earlier. While they were generally fit for purpose, it is not really surprising that the quality and the potency of the vaccines vary greatly from manufacturer to manufacturer and often from batch to batch and that production accidents sometimes occurred. And I remember when I was at the school in 1968, Sir Graham Wilson, who was working there at the time, the former head of the British PHLS, Public Health Laboratory Service, published a book called "The Hazards of Immunisation" and he documented about 600 separate incidents that occurred around the world where people had been damaged by vaccines that had been poorly produced or poorly regulated. By far the most dramatic and important of which was, I think, something called the Cutter incident that some of you may remember. In 1955

when the polio vaccines were just being rolled out around the world, a batch of polio vaccine produced by a small, Californian based family manufacturer, the Cutter Laboratories, was not properly inactivated and that active vaccine was given to about 120,000 children and more than 50 of those kids subsequently developed polio and there were more than a hundred additional cases amongst family members and close contacts and that clearly was something that lead to huge outrage and great public concern that lead to the resignation of some very senior people in health agencies in the United States but also it resulted in the US and other countries giving the national regulatory agencies real teeth and real resources and over the next decade or so, as a result of the tremendously increased cost of compliance for the manufacturers and a rising in litigation claims and the overall low profitability of vaccines, many private manufactures simply closed their plants. The numbers of manufacturers that were servicing the American market fell, in a very short period of time, from 17 to five.

Now, as a manufacture of modern vaccines requires access to highly skilled staff, large long-term investments and a tolerance for risk, most governments in the developed world decided to exit the field and their facilities were either closed or sold which also simultaneously solved the problem of governments being both the producer, the regulator and the major purchaser of the products. Finally, to avoid totally destroying an industry which fulfilled an important public health function, many governments introduced no-fault schemes which compensated individuals who were inadvertently

damaged by immunisation providing the damage was not caused by negligence on behalf of the manufacturer.

Vaccine production moved into the private sector and the industry began investing in innovative products that would command a price premium and then give them a return on their investment and the first of these to be licensed was the hepatitis B vaccine, which was developed in the 1970s and was first licensed in the United States in 1981. Now, Hep B as some of you probably know is a blood born infection. It is rightly feared because some individuals are infected fail to clear the virus and those people become chronic carriers not only posing a risk of transmitting the disease to others but there are significant risk of developing chronic liver disease or liver cancer later in life. As the hepatitis B virus could not be grown in cell cultures and still can't be grown in cell cultures, the only way to produce a vaccine then was to harvest the plasma from chronic carriers and then purify and inactivate the excess viral coke material. It was a very complicated process. It required huge quantities of plasma from healthy, paid donors, dedicated production facilities, a complicated purification process, a three stage inactivation process, lengthy testing in colony raised chimpanzees and then eventually clinical trials in many tens of thousands of people who were at risk. The vaccine cost the original manufacturer, Merck Sharp & Dohme, about a billion dollars - 1970 dollars - a billion dollars to develop and they anticipated that it would have a relatively small market in the developed world so in order to recoup their investments, they initially priced it at $40 a dosage, it was a three dose

regimen, so it was $120 for the vaccine alone without the cost of administration of the vaccine. So the vaccine, initially, was really only used by people who could afford to pay, very largely, people in the healthcare professions or people who had the industrial clout to get their employers to pay for them - you know, like police and emergency service workers and so forth. But two guys, two actually quite good friends, Jean Stephenne and Francis Andre, were at that stage working with a small French pharmaceutical company that produced vaccines. It was called RIT in Rixensart in Belgium. It is now part of GSK. They recognised that hepatitis B was a global problem, it had a potential global market and that it might be possible to produce the vaccine much more economically and with greater scale if they were able to harness modern recombinant DNA technology, which they did. They introduced the gene coding for the surface antigen of the virus into the common baker's yeast, they were able to grow those modified organisms and scale in industrial sale. Fermenters used the purified antigen as the basis of the vaccine which licensed as Engerix B. Engerix B was a real trailblazer in the vaccine industry. It was the first vaccine to - first of all to be produced by recombinant DNA technology. It was very widely promoted and it was widely used and it became the first human vaccine to generate global sales of a hundred million dollars a year which, in those days we thought, was an enormous amount of money. And that gave GSK and other research based companies the confidence to invest in a whole range of new products and later because of the economies of scale, GSK was able to introduce a tiered

pricing system so that sales in the developed world effectively subsidised sales to poorer countries.

Now, from that very modest beginning in the mid 1980s when the total global market for vaccines was about three or four billion dollars the vaccine market has grown exponentially. Last year it was 32 billion dollars, reckoned to reach a hundred billion by 2025. And interestingly, since all of the research based vaccine companies are all part of larger pharmaceutical companies, the sales of vaccines are actually only a very small part of the market for all biological products which is dominated by monoclonal antibodies. There is an even tinier proportion of the market for prescription pharmaceuticals.

The other factor that influenced the vaccine industry has been the huge increase in funds available to procure and deliver vaccines to the developing world. In 1974 just after the eradication of small pox, WHO became very excited about the possibilities of immunisation and they embarked on a new program to expand the use of six widely used and then very inexpensive vaccines, TB, tetanus, diphtheria, whooping cough, polio and measles into the developing world and the program was known as EPI, the expanded program on immunisation. They obtained funds from donors. They used UNICEF to procure and distribute the vaccine and the EPI has been one of WHO's great successes. The global immunisation rates rising from just a couple of per cent in 1974 to about 75 per cent by 1986 but by 1986 it became apparent to a lot of us who were involved in the program that the system was really, tremendously fragile. UNICEF was never sure how

much its donors was going to provide or even if their pledges would be honoured. It was unable to enter into contracts in advance. It was forced to buy a vaccine every year on the spot market and as a result manufacturers were sometimes unable to meet UNICEF's needs and there were frequent interruptions in supply in the developing world. But more importantly than all of that was that there was no mechanism to introduce a new vaccine like the hepatitis B vaccine into the program and when we went to WHO and UNICEF advocating that they did, they vigorously fought tooth and nail for two or three years against the other because they thought it would be the straw that would break the camel's back.

So in 1986 after a rather boozy dinner at a little cafe in First Avenue in New York, a group of people that you see here, who were all involved in public health and the development of vaccines and so forth, decided to form a little ginger group. It was a catalytic group which we called the International Task Force for hepatitis B Immunisation to try and draw attention to the problem and try and find a way forward, something that WHO was not able to do. And our strategy as a group was to force WHO to confront the issue by demonstrating the public health importance of the disease in a number of major developing countries and then create pressure from its constituency, demonstrate that it was possible to add hepatitis B vaccine to the EPI without it overburdening the local immunisation program. More importantly, I think, we sought to encourage new manufacturers to enter the field and to create some competition between suppliers, hoping to bring down the price to a level that poorer countries

could afford which we guessed would probably be about a dollar a dose. Now, we got a generous grant from the MacDonald Foundation and conducted some pilot programs in Indonesia, in Thailand, China and the Cameroons and then we were lucky enough to identify a Korean supplier who was prepared to provide the vaccine at a low price as a kind of lost leader, they were trying to get into the field, and then over the next five or six years produced such compelling data and persuasive arguments that, in 1992, the World Health Assembly recommended addition of hepatitis B to the EPI, a decision WHO finally endorsed about a year later. So the hepatitis B vaccine was introduced into EPI. It is now being provided to more than 85 per cent of children who are born around the world at a price - and UNICEF can currently buy it in admittedly, in multi-dose vials for about 25 or 30 cents a dose.

Most of the vaccine is for manufacturers located in the developing world. The task force also recognised that expanded immunisation programs would not occur without political commitment and better coordination and greater resources, so through its advocacy, it managed to get immunisation on the agenda of the 1990 Children's Summit of New York and to have ambitious targets for coverage included in the millennium developing goals. In 1999, a new organisation GAVI, the Global Alliance of Vaccines and Immunisation, was established to bring industry public health officials and donors together to improve coordination of activities and while all those were steps in the right direction, it was impossible to provide more vaccines to more children by simply slicing the pie into

smaller and smaller pieces; what we needed was a bigger pie. And then we had a bit of luck. As you are well aware, in 1997, Bill and Melinda Gates decided to establish a foundation and they turned to a friend Gordon Perkin, who ran a small Seattle based NGO PATH, for advice on investments that might enhance global health and Gordon told them that immunisation was an area in which huge advances in global health could be made using existing technology provided additional funds were provided and the programs were managed properly. Those were things that really took Bill Gates' attention. So they took his advice and shortly after made an initial investment of a hundred million dollars into, what was then known as, the Children's Vaccine Program and subsequently a global frame has been established for purchase of vaccines for the poorest countries and to strengthen their immunisation programs and Bill Gates and Warren Buffett have been major contributors, as have the governments of many countries, including Australia. And they have recently pledged to donate a further 10 billion US dollars during the current decade.

The existence of GAVI and the global fund has resulted in improved immunisation rates in many poor countries, the introduction of vaccines against, not only hepatitis B, but Haemophilus influenza b, rotavirus, papillomavirus and a huge reduction in mortality in children less than five years. While the importance of immunisation is clear, in many countries, the absence of epidemic disease has lead to a level of complacency. Now, my parents needed little encouragement to have their kids immunised. They were born in Europe at the turn of the

last century and like this family, commemorated at a graveyard in St Andrews that I tend to visit for other reasons, had both lost siblings from infectious diseases. Later, they nursed my older sister through a severe attack of diphtheria and both of us through the big 4, measles, German measles, mumps and chicken pox. My father's good friend, Alan Marshall, who wrote the book that many of you will have read, I Can Jump Puddles, was a constant reminder of the threat posed by paralytic polio.

But our children's generation has had none of those experiences. Widespread use of vaccines has reduced the incidence of many previously common childhood diseases to such an extent that modern parents are largely unaware of the threat. We now have the curious paradox that, while we have never had a better opportunity to protect our children or grandchildren against a wide range of diseases with products of remarkable quality, many of the public regard the benefits of immunisation as a matter of debate and much of the information provided by those opposed to immunisation is based on misconceptions, anecdotal data and misrepresentation. It strikes a chord amongst people who have neither the time nor the expertise to review the data because it plays on fears and prejudices. There is an inbuilt tendency to ascribe a causative relationship to events that are temporally related and to seek an answer to serious illnesses whose aetiology remains unknown, especially if the antecedent event was sponsored by government. So little surprise that the recent vaccine scares sought to implicate immunisation as the case of unexpected deaths and of SIDS, autism and of multiple sclerosis. When you add to that the distrust of the

medical profession and of the motives of the pharmaceutical industry, you have got a dangerous mix which is easily inflamed by media with a voracious appetite for controversy.

This next image, which is a pretty shocking image, I think - accompanied a story in India's leading weekly news magazine, the equivalent of Time Magazine, a year or so ago, following the deaths of several children shortly after they had received a new four component vaccine recommended by WHO. Many children in India die early in life at the time when vaccines are given, it is not surprising that sometimes deaths occur following immunisation. A very speedy and independent review found that the deaths were unrelated to immunisation but the damage had been done and public confidence in the program was so great that the Indian government replaced the vaccine, which was intended to simplify administration, with two others containing the same four components but at a significant programmatic and economic cost. The medical profession is not without its share of blame either. In the 1970s when I was working in Glasgow, Professor Gordon Stewart, a very personable and articulate Scottish epidemiologist persuaded a generation of British mothers that whooping cough vaccine was associated with brain damage and caused a dramatic fall in immunisation rates from over 80 per cent to down to about 30 per cent, which was then followed almost immediately after by two major epidemics and a large number of deaths and it took several public enquiries and more than a decade to elapse for the immunisation rates to recover.

In the United States, with its focus on celebrities

and glamour, the leading anti-immunisation advocate is Jenny McCarthy, a former Playboy bunny, who is the mother of an autistic child which she attributes to immunisation. She is attractive, articulate and her bizarre conspiracy theories have the support of the one of the most influential people in the United States, Oprah Winfrey. While both Stewart and McCarthy clearly enjoy public attention, I have no doubt that their views are genuine but by contrast, Andrew Wakefield who first drew attention to a possible link between the measles vaccine and autism has been found, not only to have falsified the data, but to have benefited financially from a relationship with lawyers representing damaged children and have potentially benefited from his interest in an alternative vaccine. Although he is now debarred in the United Kingdom, he still has a large number of supporters in the United States who simply refuse to acknowledge the evidence and believe that he is the victim of a giant conspiracy, so what can we do? Well, I think the first thing we need to reassure ourselves is that immunisation rates still remain higher in our community, they are still over 90 per cent, and remember that concerns about immunisation are not new. In 1802, when vaccination was first becoming popular in Britain, this cartoon appeared in the Watchtower suggesting that people who are immunised are probably going to turn into cows.

In combating the views of the anti-immunisation groups, both education and attitudes and beliefs of the health care workers are really critical. Probably the country that does it best is Cuba, which has one of the highest immunisation rates in the world. They begin

education on the value of vaccines in primary school and they repeat the message frequently to students and parents throughout life. In every country the attitudes and the enthusiasm of doctors and nurses to immunisation is critically important. Although this can be achieved by the education alone, incentives to achieve certain targets have proved helpful. And finally, public health authorities learnt that they need to market the benefits of immunisation in the same way that a company might market a new labour saving device using super clear messages and the strategic marketing skills of the modern advertising agencies.

There are no easy solutions and while technology may eventually enable us to administer a variety of vaccines in a single encounter, retaining public confidence in the benefits of immunisation and maintaining high coverage rates remains a continuing challenge. Thank you.

PROFESSOR LYTHGO: Professor Gust will take some questions. Michael Gronow will be walking around with his microphone there, if you would like to stand and introduce yourself before a question.

SPEAKER: (Indistinct) Melbourne University. How do you combat someone like Oprah Winfrey who – it is shocking that she uses her publicity to promote an anti-vaccine campaign. How - I mean, so many people feel that she really knows everything. How do you combat something like that?

PROFESSOR GUST: With great difficulty. For a very long time, the medical profession and the public health establishment has kind of tiptoed around the area, not wanting to take people like her on head on but recently a wonderful advocate of immunisation called Paul Offit, who is an

American paediatrician, has decided to take up the cudgels and he is tackling those people head on. He has written a series of wonderful books about it. He is a very passionate advocate and he is able to just take apart the arguments in a very convincing way and I think you probably have to do that.

SPEAKER: Thank you for a lovely presentation. Can I ask you to try and project ahead in thinking about the hepatitis C and HIV, what sort of things are going to need to occur or what directions do you think we need to head in order to try and develop appropriate vaccines for these significant illnesses.

PROFESSOR GUST: Thanks Greg. The two diseases that you have mentioned pose peculiar problems for the development of vaccines because when you think about all of the vaccines that we currently have, they are based on imitating a natural experiment that in nature somebody gets infected and if they recover they develop immunity and so what we are trying to do is to replicate that. And in the case of HIV, natural immunity does not occur and in the case of hepatitis C natural immunity does not often occur, it occurs but often. So we are trying to do something that nature has not yet been able to do and currently with the technologies that we have available, I think it is pushing the technologies beyond where they are capable of going. I have been, as you know, very much involved with attempts to develop HIV vaccines for the last 20 years of more and we have made fledgling steps in that direction and it is reasonable to think that with the technology that currently exists, that we may be able to develop a partially effective vaccine in the next 20 years, but that

is not good enough. I think that the things that are going to enable to us to crack those barriers are technologies that we probably do not yet have access to and I hope that they will be developed soon.

PROFESSOR LYTHGO: Could I just ask, is it less important with HIV now with the drugs that are you used to antiviral agents agent Hep C?

PROFESSOR GUST: Well, no. The short answer to that is no because first of all, if you are infected with HIV and you require treatment, you require treatment for the rest of your life. The treatment is rather onerous. It is not without certain complications and it is very expensive and having every infected person in the world on HIV medication forever is probably unsustainable for the moment. So then in terms of controlling the epidemic and preventing the accretion of more cases, a vaccine would be tremendously important.

PROFESSOR LYTHGO: Yes, I was thinking more of Hep C.

PROFESSOR GUST: Well, again, the Hep C is a tremendously important global disease. The drugs that are available now are superb, but they are not available widely around the world. There has been no program equivalent to the PEPFAR program that President Bush funded to roll out HIV medication around the world. There is no equivalent for HCV.

PROFESSOR LYTHGO: No.

MR RADFORD: My name is Nicholas Radford. My paediatric colleagues tell me that studies in the developing world comparing the outcomes with live vaccines versus killed vaccines seem to show that the use of live vaccines is associated with an improvement in morbidity and mortality

from all causes, whereas the use of killed vaccines not only seems to not confer any added benefit but also actually is associated with an increased morbidity and mortality from all causes in children. Is there anything in this and if so what?

PROFESSOR GUST: I do not think so and it is also counterbalanced by the fact that many of the enterically transmitted live vaccines do much more poorly in the developing world because of the interference from other intercurrent infections. Rotavirus vaccine, for example, is much less effective in the developing world as it is in the developed world but oral polio vaccines have often had difficulty and required multiple doses to have the same effect as three doses would have in the developed world because of the other intercurrent infections that kids are suffering at the time.

SPEAKER: You have talked about some of the modern diseases immunisation against Hep C and HIV, but the two classic infectious diseases of humankind for like yonks, tuberculosis and malaria. Is there any progress of either of those fronts and where might that come from?

PROFESSOR GUST: There is progress but it is slow and there are major initiatives, both of them largely funded by the Gates Foundation, to develop malaria vaccines and TB vaccines of which the malaria vaccine is the further advanced. That vaccine has gone into man and is partially effective and has been developed in conjunction with industry at the moment, but I do not see a highly effective vaccine against either of those on the horizon at the moment.

SPEAKER: Professor Gust, Peter Wearne paediatrician from

Bendigo. If I could just return, for a moment, to anti-immunisations - I can talk a bit about around my town where the anti-immunisation practices are, but I won't. But could you just comment upon the tension between the governments and public health experts and how much parental autonomy you may allow and how much you can legislate for, for public good. Do any countries have this right? Are any countries doing this properly?

PROFESSOR GUST: Well, yes. They are basically countries with totalitarian governments or one party states and they are able to do it very effectively. Where we have to do it by persuasion, it is very much more difficult. There are pockets of - as you are referring to, there is a famous pocket outside Albany in Western Australia, there is another one in Queensland, where people who have alternative philosophies and alternative lifestyles reinforce each other in fears about immunisation. I have had a personal – I am running out of time, but I have had a personal experience of that some people in the audience will be familiar with and might be worth recounting. We have several - four boys and a girl. Seven or eight years ago, our daughter had a child and about six months later my wife inadvertently opened an envelope on the table from the local council which was sending her a reminder of notice that her son had not been immunised and I thought it was an oversight, so she mentioned it to Anna and Anna had said, quite unbeknownst to us, that she and her partner who was a naturopath had decided not to have the child immunised and not only that but he had persuaded all of her girlfriends who had children at about the same time not to have their children immunised either. My wife who

is also a physician found this too much to handle and said, "You have got to do something about this." So I tried appealing to reason. I asked to meet with them and to have a discussion about it and I started talking to them in a reasonable, calm, scientific kind of way and to every argument that I had, they had something that they got off the internet that they could just bounce straight back at you. It was like playing squash; the ball just kept zipping back over your head. And I thought, I am losing this argument. I am done. What am I going to do? So the only thing I could think of was to get down in the gutter and get nasty. So I told them about my experiences at Fairfield Infectious Diseases Hospital with the kids who came in with complications from these diseases and what happened to them and how, in the middle of the night, you would have to get up and cut their throats and stick a tube in so that they could breathe and how they ended up in iron lungs and really laid it on. At the end of it they were all in tears and they all went off and got their kids immunised.

PROFESSOR LYTHGO: I think that is a good point to finish and start eating. I will ask Will Edwards to come and thank Professor for us.

MR EDWARDS: Professor Gust, what a wonderful talk. Thank you very much. It took nearly 200 years for us to exploit vaccination for small pox. It seems you have pushed the margin so that we, perhaps, use vaccination better now. You have certainly pushed the science. We should thank you for this and thank you for a wonderful talk tonight. Professor Gust, many thanks.

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