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MEDICO-LEGAL SOCIETY OF NSW INC.

SCIENTIFIC MEETING

WEDNESDAY, 21 SEPTEMBER 2016 AT 6.15 P.M.

THE TOPIC:
THE CASE FOR SHAM SURGERY

SPEAKERS: PROF IAN HARRIS
MICHAEL FORDHAM SC

MS KEELY GRAHAM: Welcome everyone to tonight's scientific meeting on the case for sham surgery. This topic evolved from the Committee's interest in Prof Harris' book, *Surgery, The Ultimate Placebo*. So, we are thrilled to be able to have Prof Harris himself speak tonight. For those who do not know him, Prof Ian Harris is Professor of Orthopaedic Surgery at the University of New South Wales. He is an active clinician and researcher, who directs the Whitlam Orthopaedic Research Centre at the Ingham Institute for Applied Medical Research at Liverpool Hospital.

Providing the legal part of the meeting is senior counsel Michael Fordham, who has always been a big supporter of this Society. Michael was admitted as a solicitor in 1992 and admitted to the NSW Bar in 1996. He was appointed as senior counsel in 2012. His areas of interest are common law, personal injury, inquests, inquiries and alternative dispute resolution.

We will hear from both speakers now, following which there will be the opportunity for questions.

PROF IAN HARRIS: Thank you very much for asking me to talk to you tonight because I like to talk and I particularly like to talk to lawyers. I know there are a lot of doctors in the room and I am used to that, but I like talking to lawyers because I find them quite interesting. I must tell you that interest is not a doctors versus lawyers thing. It is interesting because their perspective is so different to my perspective as a pure scientist. Hence I am very interested to hear Michael's perspectives later. I fully understand that perspective, and find it so interesting because it is very different to the world that I live in.

I am going to talk about sham surgery. I am going to talk mainly about scientific considerations and just touch on a few legal aspects later. Of course, I am going to leave that to Michael to expand on. I am going to talk about the basis for sham surgery, why we need it, the importance of it and some examples of where it has been of practical importance to us and then touch on the legal aspects.

However, first of all, I need to talk about the placebo effect because that is germane to the whole concept. Most of us understand what a placebo is - something that does not work. It is the sugar pill or the saline injection or whatever. We all understand the concept of a placebo. What we do not understand very well is the concept of the placebo effect, because if a placebo by definition has no effect,

how do we get a placebo effect? It is very confusing and also very difficult to explain.

Partly, placebos have an effect because of the way they are given and the environment, or what we call the therapeutic envelope, in which they are given. The actual substance itself may have no effect, but the way it is given can produce an effect. The placebo effect is very over rated. Often when we see people get better after an operation that did not do anything or took a pill that was useless or took antibiotics for the common cold, we tend to say that is the placebo effect. Most of the time it is not and the placebo effect is not very powerful. What normally happens is that the person got better anyway, regardless of any placebo effect. There are other statistical phenomena, like regression to the mean which I would love to discuss but will not, which are examples of how you can take a group of people, do anything to them, measure them again and they will be better. So there are all these tricks.

The way around it is to study it properly. If you looked at things that do have some kind of a placebo effect and you wanted to look at what is the ultimate placebo, it is in the book that I wrote which is the reason why you have asked me here. Surgery is the ultimate placebo because we know from experiments that coloured pills work better than plain pills, bigger pills work better than small pills and in experiments where they have let the patients overhear how much the pills cost, more expensive pills work better than cheaper pills. Again injections work much better than pills. Further the more invasive it is and the more painful it is, the more powerful the placebo effect. It also helps if it has the trappings of science and if it is delivered by somebody who is very authoritative and believes in their own treatment. So the surgeon and the surgical operating room is the perfect envelope for delivering a placebo effect, and yet this is counter intuitive. This is not well understood and this is one of the reasons why I wrote the book.

People do not see surgery as a placebo. We all understand that a placebo is out there. Some of us might even be aware of famous cases where drugs were shown to be ineffective, largely antidepressants. These are one of the most common drugs prescribed in the western world but are ineffective or no better than placebo for most of the people they are prescribed for. This is all very well for medications but people do not see that with surgery. Surgery is different. Surgery is literally cut and dried. You take something and you remove it or you add it or you exchange it. How could that not be effective? And yet, that is actually the case.

The reason why we need shams is because science is just a pursuit of the truth. That is all science is. Science does not necessarily tell you the truth, but does give you the least biased, most accurate, most precise and most reliable estimate of the truth. The way to do that is by removing bias with blinding, random allocation, and all of those things that make up scientific experiments. A big part of it is removing any effect that the patient might have from their own expectations. Blinding the patient has been shown in scientific experiments to be the most important thing that influences whether a study is biased or not. If a patient is not blinded and they know they got the real treatment, they are much more likely to get better. That is the most powerful thing. Hence you have to blind the patients if you want to do a proper scientific experiment, that is the least biased experiment. That is the scientific consideration.

I want to dispense with the ethical consideration. It is often thought that sham surgery is unethical. The argument is you cannot do this sham surgery study because it is unethical and the conversation stops there. You think that sounds right, and we cannot do it. When you think about it, it is not really the case. It is not unethical. There is a confusion between the ethics of medical practice and the ethics of science. There is a difference.

The ethics of medical practice says that you should not do something to a patient unless you know that it is going to provide some benefit. Further it says you should not expose patients to any harm at all, even if it is only a needle or a little jab with a knife, unless you know it is going to create a benefit. That is the ethics of clinical practice. But that is neither the ethics of science nor the rigour of science. Science says you must do the best possible experiment to get the closest answer to the truth, and the way to do that is with sham surgery. The ethics of science is that patients sign consents to agree to such experiments. Patients sign up to all sorts of experiments. In psychology, for example people sign up to experiments all the time, where there is a risk of harm with no benefit. That is the reality of science. So when you are doing a sham surgery study, you are doing a scientific study. You are caring for the patient as somebody who has come to you to pay money to get better. You are doing a scientific study.

Here are some examples of the necessity for scientific study. The first one is reasonably famous. In the 1950s it was common to do an operation for angina to improve the blood supply to the heart. The internal mammary artery, which

branches from the same blood vessel that supplies the heart, runs down inside the chest to supply the chest wall but not the heart. It made sense on a superficial level that if you tied off that artery, then the blood would be diverted to the heart improving its blood supply. They did experiments on some dogs and found that tying off the internal mammary artery diverted the blood to the heart increasing its supply and the heart was better. Then they tried it on some people whose angina did get better. As a result of these trials tying the internal mammary artery became a standard intervention for the treatment of angina. Then, after this operation had been practised for some time they did a randomised trial where they opened the patient's chest and in one group tied the artery and in the other one they put the string around the artery but did not tie it off. They found no difference in the two groups. It did not matter whether you tied it off or not. So this operation was completely ineffective as a treatment for angina and yet it had made sense. There were animal studies or lab studies which showed that it probably worked and it seemed to work when it was done it in people.

Therein lies the problem. The above three things are what I call in the book "the wobbly tripod of evidence". Firstly there is biological plausibility, that is, it sounds like it should work. I can explain why it can work. What is wrong with that? I will tell you what is wrong with that. I have a game with medical students where I think up these stupid treatments and ask them to think of a biologically plausible way that that treatment might work for this disease. They can always think up something. Biological plausibility to me just does not cut it. Secondly the same goes for animal experiments. There is almost no connection between animal experiments and human studies.

The third thing is clinical results and this is what drives practice. "I did this tying of the artery on people and I saw them get better. I believe that. I do not believe your study that you did somewhere else." This is what drives practice now. "I did an arthroscopy on someone and I saw them get better afterwards." That is very powerful because we fall for this logical trap of "post hoc ergo propter hoc". This means, as all the lawyers know, "after this, therefore, because of this". Humans are Olympic-grade conclusion jumpers. As soon as they see two things together, they put cause and effect in the middle and it is not normally the case.

There are many other examples. Parkinson's disease is caused by lack of the chemical dopamine in the brain. So it makes

sense that if you take some cells that produce dopamine from embryos and you put them in the brain of people with Parkinson's disease, they will probably get better. You then try it on some animals and it works. Finally you try it on some people. Are their symptoms of Parkinson's disease made better? Yes, I think they are. This treatment seems to work. It is the same three things. However when they did the sham surgery study where they drilled the holes in the skull but did not put the cells in, just as many people thought they got better. The treatment did not work at all and yet it had seemed to work.

Knee arthroscopy is the operation that I often write about, because it has been studied so extensively for degenerative conditions. Whether it is osteoarthritis, or a meniscus tear alone you have a meniscus tear. Surely you have to sew the tear together? You cannot walk around with a tear in your shirt. That is a bad thing that has to be fixed Yet the correlation between whether you have a tear in your meniscus and whether you have pain in your knee is almost non-existent.

Most people with a meniscus tear do not have pain in their knee. Many people with pain in their knee do not have a meniscus tear. The two are not correlated. The highest quality studies, the sham controlled studies, have told us that if you have mechanical symptoms, that is a sore knee, you have a degenerative tear in your meniscus and if they pretend to do an arthroscopy on you, all of these studies show no statistically significant difference between pretending to do the arthroscopy and actually doing the arthroscopy and taking out the torn meniscus. The only slight difference is that you do a little better if you have the sham operation. That is the only difference, and yet the operation is still being done. They do one million a year in the USA. We do about 70,000 to 90,000 a year in Australia. I would estimate a high proportion of those are wasteful.

This is the last example but it is a good one because it concerns emphysema. We all know what that is. There is not enough functioning lung tissue making it difficult to get oxygen into your system. Some surgeons thought up a great way of treating it. They took out a bit of the lung and it made the rest of the lung expand. This does not really sound biologically plausible to me but they sold it to themselves. They did it on some dogs and the dogs breathed a bit better and then they did it on some humans, and it was fantastic. They got them to do the oxygen studies, and everything they did was better. Accordingly this operation was widely done. Eventually some doctors wanted to test it. Do not ask me

why, but we are always testing these things after they become common practice. That is just the way it works. They wanted to test it and a famous surgeon in the USA who developed this operation wrote an editorial in a journal and invoked the parachute analogy - which I love. The parachute analogy means that you do not need a randomised trial to show that the parachute works. His analogy was this operation is so clearly beneficial that a randomised trial would be denying treatment to the people that were randomised to medical therapy rather than surgical therapy.

They did the study anyway and in two years they found no difference between whether you had surgery and whether you had medical treatment. The surgery did nothing. The surgeons still couldn't believe it. They looked at the results and they said there was a difference. The people in the surgical group were slightly better at two years or the mortality between one year and two years was a little bit better. However the reason for this was because the only difference between the two groups was that if you died, you died much sooner after surgery. So surgery weeded out the bad ones.

Summaries of the evidence from sham surgery studies show us that most of the time when we do these studies, the surgery is shown to be ineffective. Yet these studies are very rarely done. We did a study looking at the evidence base for surgery and this was very telling. We looked at three large hospitals in South West Sydney. We looked at over 9,000 orthopaedic operations, as I am an orthopaedic surgeon, performed over three years. We asked ourselves what was the evidence for performing these operations? How many of these operations that we were doing every day had been compared to not operating in proper randomised clinical trial studies? We found that only half of the operations that we do day to day as orthopaedic surgeons have been subjected to studies comparing them to non-operative treatment. You might be shocked, thinking how could only half the procedures have been subjected to a study comparing it to non-operative treatment? That number is roughly consistent with other fields of surgery. The punchline in this study though is that of those studies that had been compared to non-operative treatment, in half of those operations the surgery that we are doing day to day was shown to be no better than not doing the surgery.

This highlights two problems. One is an evidence gap. There are operations being performed where we do not know whether or not they are effective because they have not been subjected to a scientific study. The other problem is an evidence practice gap where we have good evidence that this

operation is no more effective than not operating, and yet we are still doing it. So there is an evidence gap and an evidence practice gap.

Before I conclude I want to raise a couple of legal issues. Firstly there is the ethical paradox in spinal surgery. Spine fusion surgery is a very common operation. There are over a million operations a year in America. There are more spinal fusions done in America than hip replacements. It costs tens of billions of dollars. It is a very high risk operation. It is being done to relieve the back pain of mainly degenerative conditions. It is done for lots of different things, but it is certainly questionable. I do not think that statement is really controversial. I would argue that it probably has very little place and most of the time it is not effective. However people say it is unethical to do the study. Not only is it unethical to do the study, it is difficult to do the study. If I want to fuse somebody's spine and they come and see me with a sore back tomorrow, I would just do it. There is nothing standing in my way other than from their ability to pay the bill.

If I want to do a study on spinal fusions and find out if they work or not, that is its effectiveness, it is very difficult. I cannot do that study without ethical approval, oversight, consent, money etc. All these issues get in the way. I cannot find out if this operation works or not without ethical approval, and yet I can do the operation without ethical approval. What is more unethical: doing an operation on one million people a year at the cost of tens of billions of dollars or doing a study with a hundred people in it to find out whether that operation works or not? The current position is completely back to front. If I want to do a new kind of hip replacement tomorrow, I can just do it. If I want to find out what the results are then I cannot do it without ethical approval. It should be the other way around. We should not be allowed to do any kind of surgery until we have first shown that it is effective.

I think the legal gaze is a bit distracted and these are some things I want to point out with a couple of little examples. Firstly metal on metal hip replacements. In the surgical field these are known as the gift that keeps on giving. I understand it is the same in the legal field. For those of you who do not know, this was a new kind of hip prosthesis that was going to be the solution to all the problems of the old hip prostheses, which in fact did not have any problems. However these new hip prostheses had terrible problems. They all failed and they all had to be removed. The company was sued countless times, including

class actions given the large numbers that were involved. Only the company that sold it was sued. None of the surgeons that used it were sued. Instead the surgeons who used it were paid by the company at very high rates to remove the hip prostheses that they had put in and paid again to put in new prostheses. This was a win/win situation for the surgeons involved. Nobody sued the surgeons who were doing this unproven operation. It was just not on the radar because surgeons cannot be wrong.

Secondly I have a problem with surgery versus non-operative treatment. There is this theory that if we do not operate, it is somehow neglectful or we do not have courage. The reality is often it is the other way around. I have friends who have been sued for not operating. These were operations where there is clear evidence that this operation does not provide any greater benefit than not operating. However the legal mindset is that you just sat there and did not even give them a chance. It is this kind of mentality which is wrong. It is a funny kind of mentality that says that if you do an operation on someone and it goes wrong, well at least he tried.

It is also my view we are just missing the big picture. The big picture is medicine is not necessarily good for you. There is a paper in British Medical Journal this year, which says medical errors are the third leading cause of death in the USA. In Australia there is an old study saying 14,000 people every year suffer a medical error when they go into hospital. Five per cent of them will die as a result of that error. These are huge numbers.

There was a program you can download on Four Corners from about a year ago now, on how much we are wasting on healthcare from over-treatment. I am proud to be part of a study, which commences in January next year, for which there is \$20 million in government funding in two separate \$10 million grants looking specifically at over-treatment and over-diagnosis in medicine.

I will now highlight a few things that have been in the news recently and give you my view on them. Firstly there is the widely publicised matter of the patients with head and neck cancer at St Vincent's Hospital who have allegedly been chemotherapeutically under-dosed. The report on that came out yesterday. Then there is a doctor at St George and Sutherland Hospitals who is likewise in trouble for not giving the full dose as alleged by some other doctors. How much of it is judgment? To put another perspective, a lot of

chemotherapy doctors are seen as used car salesmen trying to sell something that is not very good.

A review done in Sydney in 2004 looked at all the randomised trials of chemotherapy for adult malignancies, comparing them to no therapy. They found that the contribution to the mortality or survival in cancer for all adult malignancies, which is the five-year survival rate, was around 60 per cent on average - some cancers being worse and some better. However the contribution from chemotherapy was around two per cent. You can see that for some cancers you are looking at having some six months of awful chemotherapy to gain an extra three months of life. That is what chemotherapy offers and yet it is being argued that the lower dose and the higher dose made the difference between life and death. I doubt it, but that is the way we see it. We see things as so clear cut. Lawyers see things as clear cut. However I cannot do that.

Why is more treatment better? We always think that more chemotherapy is better. There is a famous example from the 1990s which I touch on in the book where it was thought chemotherapy works for breast cancer. Well perhaps it works a little bit. As chemotherapy works for breast cancer, then if we give people a lot of chemotherapy it will be even better for them. The problem with high dose chemotherapy is it knocks out your bone marrow and you die.

The answer to this problem was a technique called bone marrow rescue. They take some of your bone marrow, before giving you massive doses of chemotherapy (enough to kill you) and then give you your bone marrow back and it grows again. In essence you have an auto-bone marrow transplant.

Bone marrow rescue sounded like a good idea. Hence it was tried it on some people to see if it worked. And work it did! Lives were saved left, right and centre and so it was demanded. However it is obviously a high cost procedure. By the end of the 1990s insurance companies in America were being sued for about \$100 million for not covering people for bone marrow rescue for breast cancer. That is how effective a procedure it was, and this was the legal side of it. In 1999 there were about three or four randomised trials published which showed bone marrow rescue was not effective. It offered no survival advantage whatsoever and exposed patients to risk. This again demonstrates how a procedure becomes common practice, people sue to gain access to it, because they have to have it. However it just did not work. It never did work, and yet we thought it did.

Another example I just love is the little study from Sydney where they looked at older patients on multi-medications. This is very difficult for them. They are on seven or nine different medications which they are taking at different times of the day. The patients were divided into two groups. One half had all their medications stopped. These patients did not take any medications at all. The other half of the patients were kept on all their medications. There was no difference in outcome between the two groups. There was no difference in mortality. Their blood pressure stayed the same. The only difference was the people who had their medications stopped were less likely to fall over and hurt themselves. More medicine is better? I do not think so.

My last example is the very serious one of the wrong gasses that has been in the news. I do wonder if the legal gaze is distracted when we hear and when we read in the papers that a baby died after being given nitrous oxide instead of oxygen in an operating theatre. This is obviously a disaster in anyone's terms but what did we think of? We thought of how the pipes were connected. We thought about how the pipes were labelled and who labelled them and who joined them up. These cases occurred after caesarean sections. Australia has one of the highest caesarean section rates in the world. Elective caesarean sections are commonly done in Sydney but there are risks involved. However we do not ask ourselves why was the baby being born in theatre? Or why were they not being born in the labour ward where they do not have the pipes and the tubes? The other thing is that when you are resuscitating a newborn baby, you want to give them oxygen. That is what they tried to do, but there was nitrous oxide in the pipe labelled oxygen.

There have been large scale randomised studies done on oxygen versus air in resuscitating newborn babies. Typical of these studies is one in the Lancet in 2004. This found no advantage to using oxygen over using room air in resuscitating newborn babies. In fact the summary was the pooled analysis showed a significant benefit in infants resuscitated with air. Oxygen was harmful and yet it sounds good. Surely as oxygen is good then more oxygen is better; just as more medicine is better. No, it is not. It is just the opposite. You have to study things scientifically to know that. Sounding good is not enough.

In summary, a high proportion of surgery is either not effective or we just do not know whether it is effective or not. True effectiveness is determined by scientific enquiry and there is not enough of that. In order to do that properly you need sham surgery. Our default position is to operate.

If somebody comes to see a doctor, their default position is to do something. I get this criticism from my colleagues all the time. "We cannot just send them away" or "We cannot just do nothing". Yes we can and often it is safer to do nothing.

My question to the next speaker, and to the audience, is how can the legal profession help steer surgery away from over-treatment? Thank you.