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MEDICO-LEGAL SOCIETY OF NSW INC.

SCIENTIFIC MEETING

WEDNESDAY, 7 JUNE 2017

AT 6.15 P.M.

THE TOPIC:

MEDICAL CANNABIS - ARE THEY JUST BLOWING SMOKE?

SPEAKERS: DR DAVID GRONOW
MS RUANNE BRELL

MS KEELY GRAHAM: Thank you everyone for coming. Medical cannabis - are they just blowing smoke? We have two fantastic speakers, very well known to this Society for a long time, the first of which is Dr David Gronow, who had a special interest in pain medicine as an anaesthetic registrar in Sydney Hospital back in 1973.

David established a private multi-disciplinary pain clinic in 1981 at the Sydney Pain Management Centre, of which he is still the Medical Director.

David has been a supervisor for advanced training at the Royal Australian College of Physicians, Faculty of Rehabilitation Medicine, and the Director of the Multi-Disciplinary Pain Service at Westmead Hospital from 1999 to May 2017, establishing the training program for the Faculty of Pain Medicine.

He was Secretary/Treasurer, Vice President and President of the Australian Pain Society and has been Treasurer and President of the Australian Pain Relief Society.

He is a past member of the Court of Examiners Faculty of Pain Medicine and is an Accreditation Surveyor for the Faculty. He has been a Surveyor for the Australian Council of Healthcare Standards and is, of course, the Medical Secretary of this Society.

David has undertaken clinical trials in analgesics and written journal articles and has given presentations on various aspects of pain medicine, and consults to many private hospitals and to Sydney Hospital.

It’s interesting conversations with David that led to the concept of this topic. Please welcome David.

DR DAVID GRONOW: Thank you very much. I hope I can keep you interested for the next half hour. Why the topic and why the title - that will be explained by the end of the talk hopefully.

What I want to try and do is give you some sort of background of where this has been, this subject and why there is a difference, if you like, between the popular and the scientific.

Marijuana has been around for 4,000 years. We can see that it’s been used for multiple complaints, some of which are still suggested now. It’s interesting that Emperor Fu Shsi

almost got it right, as we'll see, when he suggested that it could restore homeostasis in the body.

We can see in ancient times it was used for a whole range of other medicinal purposes; some of them a little bit outlandish, but some of them still recommended for today.

In medieval Europe, it was used to treat tumours, coughs and jaundice. In 1854, the US Dispensary listed cannabis to treat the following - interestingly, a hundred years later, now you can't use it for anything - how things change.

Britain in those times recognised it had anti-epileptic benefits and for some of you who are interested, aphrodisiac. India was probably left out a little bit - a panacea for sunstroke and dysentery; but there's not much it wasn't used for.

Things started to change in the 1900s, the Pure Food Act in USA started to require you had to have labelling on the products that were sold over the counter and in the 1900s, 1920s, the Mexicans didn't have a wall, so they managed to introduce cannabis into the American culture.

The Marijuana Tax Act in 1937 really made marijuana illegal and most of the other western countries followed suit following that. Then it became hardly used and not really looked at as a substitute, also because a lot of other things started to be developed that had more specific usages.

What are we talking about? I think this is one of the things that we start to get a little bit confused about in the terminology. It's an ethnobotanical and there are a whole lot of them - these are just a few - which have gone on to produce substances that we use for specific conditions.

Cannabis, interestingly enough, has yet to achieve that. It still hasn't got a single purpose that it's used for, it's still sort of a shotgun type of use and therein lies part of its problem.

When we talk about cannabis, we're talking about the cannabinoids. What we mean by them, there are three different groups of them. There are the endogenous compounds, they're the ones we make within ourselves and they are called the endocannabinoids. Then there are the

phytocannabinoids, which is what comes from the marijuana plant. Then there are the synthetic compounds.

As it happens, these molecules are actually very easy to synthesise and variations of them are very easy to synthesise. You can isolate and vary different compounds. But we're not going to go into that too much.

The marijuana we're talking about comes from the Cannabis sativa most of the time, it's the most common one but also Indica and Ruderalis. There are over 500 compounds in these plants. Over a hundred of them are cannabinoids and the definition of that comes from the fact these compounds are unique to this plant and that's why they're called cannabinoids.

We've got a whole group of them here. As I said, I couldn't put the whole hundred up, but the two top ones are the most commonly identified ones – there's THC, which gives us a cerebral high and there's the cannabinoid CBD, which is said to give a body high. We'll look into those two a bit more.

The interesting thing is if you're going to be using it, particularly using it recreationally, you want to know how much THC there is, because that's the one that gives you the high. We can see the dried flowers give you up to about five per cent of the THC. Hashish gives up to about 20 per cent and hashish oil gives you up to about 50 per cent - so, quite a wide variation.

However, it does depend on the strain of plant that you're taking this from and as of now, there are over 2,000 varieties of genetically modified plants that are available to you. If you want to have a look at those, that's the website that lists them all - leafly.com.

It also depends on the growing conditions. The same strain will develop a different amount of THC depending on where it's grown. Basically, they like to be grown below the 35th latitude, but what's grown in Queensland will be of different content to what's grown in Victoria.

If you're going to smoke a joint, it basically has a gram of cannabis, containing about 20 to 70 per cent THC. Bioavailability through the lungs is up to about 24 per cent. That means you get about three milligrams of THC, which is enough to give you a high.

If you eat it in a cookie, it takes a little bit longer; it takes two hours to get a peak. It's not quite as well absorbed.

The ratio of THC and CBD, the other common one, is quite important. It's often stated the CBD component, which doesn't give you a high, modifies the THC effect. That's not quite proven yet.

If you're really keen with it, if you do a bit of chemistry at home, you can convert all the other cannabinoids back into THC and get more of it.

One of the things though, is that it is metabolised in the liver by the enzyme group in the liver, and this is important because a lot of other compounds use this to be metabolised, particularly the anti-epileptics, and one of the problems with some of the clinical trials is that if they use this as an add-on, it's been shown that some of the other anti-epileptic serum level goes up. So, how do you differentiate between whether the CBD is giving you the effect or the raised level of the other anti-epileptics?

What are we working on? Why is this having an effect? It's to do with the endocannabinoid system in the body.

This is an interesting and very complex system and it's throughout the whole body, the nervous system. It's involved with how things are expressed and controls the expression of mural and immune transmission.

The system has three broad overlapping functions – it is a stress recovery role, controls energy balance and it is involved in the immune and inflammatory response.

In the nervous system, small amounts are continually being released and then metabolised within milliseconds to help control the excessive synaptic transmission that may occur at any time and that regulates both inhibitory and excitatory neuronal messaging. When we introduce an external cannabinoid; we are saturating the system rather than this fine tuning that's inbuilt.

There are two cannabinoid receptors so far identified and there are two endogenous cannabinoid ligands that work on these, but they're widely expressed throughout the whole nervous system and I'm not going to go through all those. They affect multiple neuro transmitters. They have a wide effect on the whole nervous system all the time.

The CB_2 one mainly is in the immune cells, but is also seen in a much smaller amount in the central nervous system. When you look at THC it's described as a partial agonist on the CB_1 receptor, so it doesn't fully activate it, it partially activates it and CB_2, which is the main one we'll see is used to help control epilepsy, is an antagonist on the CB_1 receptor. It works as an inverse agonist on the CB_2 receptor. People can ask me later about what that means.

What is now available? These are the major ones that are available that are registered or licensed throughout the world. The main places that use this are in Scandinavia, Israel, Canada and there are starting to be some places in the States, as we know.

The main one that's registered in Australia is the one called Sativex, which is a genetically modified plant, ratio of THC and CBD is about 1:1 ratio. We can see there are a whole lot of other ones we'll come to, but the synthetic CBD, as you can see there, is the one being used for resistant epilepsy. We can also see the bottom one caused a major psychosis.

Sativex is manufactured by GW Pharmaceuticals and Otsuka from a GM strain - a genetically modified strain, and it comes as an oromucosal spray. 0.1 ml gives you about 2.7 of THC and 2.5 of CBD, plus some other cannabinoids.

This is the one that's approved in Australia. It's marketed by Novartis. One difficulty is that it has to be kept in the fridge. That's a difficulty because it's an S8 meaning the fridge has to be a safe and there are not many pharmacists that have lockable fridges, nor have a safe for transport, as you would have to do for an S8 drug like an opiate. That's a problem in terms of accessibility.

The current types of medical conditions that can be treated by marijuana are multiple - epilepsy, multiple sclerosis, nausea, vomiting, chemotherapy, neuropathic pain, inflammatory bowel disease, post-traumatic stress disorder, Alzheimers, other dementias, Parkinson's disease, Huntington's disease, feeding disorders, glaucoma, glioblastoma multiforma, Type I diabetes, scleroderma, fibromyalgia. They are all the ones around the world that people are promoting its use for.

But, it hasn't yet established a use and we have to ask why. Why is it that it hasn't managed to find a definitive role as a therapeutic agent? Is it its efficacy, is it

toxicity, is it dependency or just its ability to be delivered to us?

There is a statement that came out by Peter Grimson, he's running a nausea/vomiting study and I think it does give a handle on what the problems are. In a lot of trials, the evidence is unconvincing, involving all the areas that we're going to talk about, but surprisingly the trials have been badly run; they're poorly designed, they fail to account for the placebo effect, there is often inappropriate dosage, small sample sizes, short periods of time and poor documentation of side effects and harms.

Let's have a look at a few of the areas that are promoted, remembering one of the problems of epilepsy is one third of patients are currently pharmacoresistant, that means even with the best mix of anti-epileptics that are available, one third of them aren't totally seizure free, so there is a need for something else.

There is this small group of children who have genetic abnormality, Dravet syndrome or Lennox-Gastaut syndrome that have severe epilepsy, which often leads to premature death, probably about one per cent of the sufferers. It's postulated that in these people they have a defect in this endocannabinoid system and that's why they get their epilepsy.

The CBD group is the most promising. However, interestingly enough, it may not be effective because of its effect on the endocannabinoid system, but on other types of iron channels in the brain, and this is something that's being looked at, at the moment. We may have a total furphy here, this may not be really a cannabinoid effect.

A recent Cochrane review about 18 months ago came out with this conclusion on the effects of CBD on epilepsy, that no reliable conclusions can be drawn of the efficacy of cannabinoid treatments. They could only find four placebo controlled studies for the causes and design with opposing results.

Devinsky, who's written quite a bit on this subject, in a 2015 open label study on this dose of CBD found that there was a 36 per cent overall median reduction of seizures, but 79 per cent had adverse effects, which are listed there and 30 per cent had serious effects. Some of those were in fact worsening of the epilepsy and there were a couple of cases of death, which we are not sure what the cause was.

Interestingly, the author's interpretation of this study was that it might reduce seizures and might have an adequate safety profile, an interesting conclusion. I don't think you could make that conclusion with any other substance, apart from a marijuana one.

This is an interesting one in Colorado, in which of course it's legal to use this substance and of course, what happens, there are a lot of parents that come from different parts of the States to Colorado. 75 per cent in a survey reported that their children had a reduction of seizures by about 30 per cent, but in eight of them they measured their EEG and there was no change.

In 2017 this same author, Devinsky, has done a double-blind trial of CBD, it was an add-on therapy and showed a median of seizure frequency of 39 per cent in Dravet syndrome. However, some had an increase in frequency. The more severe didn't seem to respond but the less severe did.

The side effects were quite frequent and caused a drop out. It was only short term, it was only 12 weeks, so we don't know what happens if you're going to be on these for a lifetime. Do you get tolerant to it? Does the effect wear off and the other difficulty of course, it's a GW Pharmaceutical study, so it is not independent.

Again, John Lawson is running the local study and his overall view is the effects are minor and the majority aren't helped.

Another area is in multiple sclerosis. There have been some studies in this. The cannabis multiple sclerosis study concluded there was no improvement shown in the assessing spasticity on the Ashworth scale. There was an improvement in the subjective perception of spasticity, so, there was a difference between what the patients felt and what could be measured in terms of spasticity.

The MUSEC trial showed an improvement in muscle stiffness, at THC 25 milligrams per day, which is a fairly high dose. An open label study had a high dropout of 36 per cent over a year, but those who did improve seemed to stay improved.

A recent Italian study showed that 70 per cent had a 20 per cent improvement, and only 28 per cent had a 30 per cent improvement of spasm, and again more than a third dropped out because of side effects.

When you do a meta-analysis of 14 studies, only two were of low risk of bias, none met the statistical difference but showed some improvement baseline and none of these were compared to a comparator, so all were compared to a placebo. We can't really tell whether they were any better than what's being used at the present time.

Another study looked at MS sufferers who were using cannabis to those who weren't using cannabis and found that they were worse on information processing, working memory, executive functions and other cognitive functions. These people were having significant central effects.

In pain, it's been postulated again the cannabinoid system is involved in the development of neuropathic pain, that's pain secondary to damage to the nervous system and pre-clinical studies are showing some efficacy, but unfortunately, this has not been able to be translated into clinical practice. THC is the only one that does this and the other cannabinoids don't. Again, we're blighted with the poor quality studies and again, not comparative to what we would use for this condition.

Rheumatoid is another one, because a lot of these are thought to have an inflammatory component to them and we've mentioned earlier this is one of the areas that it is thought it may be helpful. Again, the Cochrane a few years ago found a small significant difference favouring cannabis, but again, those who were receiving cannabis were more likely to suffer an adverse effect. The overall potential harm outweighed the modest benefit; that was their determination.

Canadian survey patients for rheumatic diseases, where again it's freely available, found only just over four per cent used it as a method of controlling their symptoms. Out of those, 46 per cent of them thought they had really severe disease but the physician's assessment was that only 10 per cent had severe disease. So there was a perception problem.

Again, another subsequent Cochrane review found no convincing unbiased, high quality evidence suggesting that Nabilone, which is the synthetic THC, is of value in treating people with fibromyalgia which is one area that it has been promoted.

Other studies looking at pain, Tsang looked again at THC. He looked at eight randomised controlled trials, two perspective trials and one retrospective chart review.

That’s pretty difficult to actually mix those up and assess them.

It was a mixed group of pain. Nabilone is a commonly used adjunct and led to small reductions in pain. All the trials were small, of short duration and bias wasn't controlled.

Pharmacological studies in neuropathic pain, both using non-selective cannabinoid agonist and selective ones, that’s synthetic ones, induced antinociceptive effects in multiple animal models of neuropathic pain. One of the difficulties however was what they actually measured. When you’re looking at neuropathic pain, you’re not only looking at a reduction scoring pain but you’re looking at the other features that neuropathic pain comes with and that’s often spontaneous pain, sleep disturbance, and these haven’t measured whether any of these cannabinoids actually help any of the other manifestations of this pain in patients.

Boychuk’s study looked at what he described as 13 high quality random controlled trials and “these suggested”, he said, “that the cannabinoids provide analgesia in patients with neuropathic pain who are refractory to other treatments”. But a subsequent review again found that he didn’t look at the bias in these patients and didn’t look at the safety and harm.

Another recent review included six trials with marijuana for neuropathic pain and concluded that it may be useful with some significant side effects such as addiction and worsening psychiatric illness.

Savitex is the one that’s registered here and that’s the combined one with THC and CBD. There have been several clinical trials with placebos and a range of different neuropathic states. The recent meta-analysis of these recommended a weak recommendation against the use in neuropathic pain.

A recent single pilot study compared Savitex with placebos. With chemotherapy induced pain, there are certain groups of chemotherapy that call for neuropathy and showed no global difference in the use.

In the Whiting review studies only found two with low bias and the trend towards improvement but no statistical difference and no change in quality of life and no change in functional performance, which is really quite important when you’re looking at studies on analgesics.

The clinical research of cannabinoids and pain has been hampered by a lot of limitations, a lot of what we've just described, poor sample size, poor methodology, lack of differentiation of the different pain syndromes, not looking at appropriate end points, not properly looking at safety profiles, often poor documentation of adverse events and not looking at long term consequences.

Of course, the problem with blinding these studies is that it is difficult because of the psychotropic effects of cannabinoids.

The Faculty of Pain Medicine has come out with a document in April 2015 - I won't go through all of them, but number 10 states their current belief and this is being reviewed, but it won't change. It does not endorse the use of cannabinoids in chronic non-cancer pains until such time as a clear therapeutic role for them is identified in the scientific literature.

What about the adverse events? They are mainly attributed to THC, but not only and there are no studies looking at the long-term effects of CBD. Short term there is impaired memory, judgement, motor performance, nausea, suicide ideation, dizziness and fatigue, increase in anxiety, depression, social withdrawal and psychosis. We've seen a couple of these this year, the Cairns' murder was a psychotic episode and the Times Square event was a psychotic episode due to marijuana.

Home explosions, there have been 30 of them in five months in Colorado. Why? Because to extract the oil people use butane and that blows the house up.

A meta-analysis of 62 studies showed a much higher serious adverse event rate and dropouts due to adverse events. Long term use is more difficult but the addiction risk is estimated between nine and 17 per cent, with cognitive impairment, behavioural changes, decreased motivation, increased psychotic disorders, immune effects, reduced IQ in children and reduced brain development.

In adults, brain imaging has shown altered function and structure and reduced cortical volume in people who regularly use THC. There's really no good study looking at the long term adverse effects.

So, the three Ps, the promotion of medical marijuana is driven by the populace who believe that sufficient evidence

already exists with the efficacy and safety, and hopefully I've thrown some seeds of doubt of that. There's a created gap between the popular beliefs and the scientific knowledge. The naturalistic fallacy that something that nature produced must be better. However, of course most of the things that they are using are genetically modified. Converting strong beliefs and anecdotes into facts and a desire to control one's own care.

The press promotes the story of the exception, ignoring the overall risk to society and the politicians being persuaded by the vocal passionate pleas against the scientific advice.

I don't think any other therapeutic option would be approved in this fashion.

Where are we up to? There are some trials going on at the moment to try and solve some of these. There's a paediatric epilepsy trial using Epidiolex, which is the CBD one, related to CBD, it's a variation and that's being run by the Sydney Children's Hospital. There's a nausea and vomiting trial being done with a THC and CBD ratio of 1:1 at the Chis O'Brien Lifehouse at Campbelltown and there's an appetite quality of life improvement in palliative care being run at Sacred Heart. That's using this Bedrobinol, which is a spray of 30.5 per cent THC and also at Newcastle.

The future - we do need improved medicines. The cannabinoids do have an effect on many bodily functions but their efficacy and safety must be shown. We still are in the dark of which one, what dose, for which condition and what are the short and long-term safety aspects? We need that debate of the individual development versus society harm.

The synthetic cannabinoids may hold hope in the future, can we develop one that's specific for each of the conditions that may be helpful? That's in the process of being looked at, at the moment. It hasn't advanced all that well, despite that, but still there is hope that there may be an individual synthetic cannabinoid that doesn't have all your negative effects I've talked about in the future. Thank you.

MS KEELY GRAHAM: Thank you David. My understanding now is that there's no significant change to clinical results by use of cannabinoids, but the patient's awareness decreases,

so they often think that there is a change in the results, if they don't blow the house up first.

Our next speaker is Ruanne Brell. Ruanne started her medico-legal career at Blakes, now Ashurst, where she predominantly acted for doctors in complex litigation, particularly obstetrics and catastrophic injury in the Supreme Court, Court of Appeal and High Court.

Then 10 years ago, she moved to Avant as a medico-legal advisor, where she still is, providing telephone and written advice to members on a wide variety of medical and health law issues.

Ruanne is the author of the National Disability Insurance Scheme handbook along with Bill Madden and Janine McIlwraith. She's given a number of presentations on the NDIS and is in the editorial panel of the Australian Health Law Bulletin and has been since 2014, and frequently writes topical medico-legal papers. Please welcome Ruanne.

MS RUANNE BRELL: Thank you. Now that David has told you all about why there's not enough evidence to prescribe it, I'm going to tell you how all our States and Territories have gotten together to try and help doctors be able to prescribe it to patients, but there are some hurdles.

You may be wondering after hearing David talk why we're actually even having this process evolve and that's mainly because the media have been calling for it, and anecdotally we know that patients are walking into consulting rooms and asking doctors for it.

From an MDO point of view obviously we need to provide some advice about what can I do, how can I do it and is it advisable to do?

These are just a very small snapshot out of hundreds of headlines that you've probably seen over the last three to six months and beforehand, saying increasingly, as you can see, that there is at last some evidence to back anecdotes about medicinal cannabis in seizures. There are patients calling for it, the media's covering it, but what actually is it and what can you do?

David has talked about the clinical aspects of it and what it actually is as a substance. I'm just going to talk about what the law says it is and then go through very briefly, mainly focusing on New South Wales, how patients can actually get access to it in New South Wales and what

you need to be aware of. I'll just cover a little bit about the other States and Territories, because some of what they've done is relevant.

Basically, David left off at the US taxing marijuana and it becoming illegal. The illegal status of cannabis was entrenched into the single convention on drugs and that was reflected in the Commonwealth legislation as well.

What they did through an amendment brought in last year, was actually to create a category of cannabis, being medicinal cannabis, which is basically something derived from cannabis that actually has properties to cure or alleviate the symptoms of a disease.

It is still very clear that all other forms of cannabis are illegal. What some of the States and Territories have done is provide for people to be able to carry what they see as cannabis for medicinal purposes, but this is actually about how doctors can go about prescribing it.

Unfortunately, there are different schemes in all the different States and Territories. Some have no scheme or no additional legislation, some have their own State-based legislation and in addition to that, the Commonwealth through its Federal legislation and also the Therapeutic Goods Administration and the Office of Drug Control have provided for how people can apply for licences to cultivate marijuana and then manufacture it into medicinal cannabis and supply it under prescription.

There are very strict, obviously, licensing arrangements for being able to manufacture and cultivate marijuana and the difficulty is that it ultimately will fall to the doctors on being able to source these, if they do indeed decide to provide a prescription for a particular patient.

Once you have your Federal supply scheme, what the Therapeutic Goods Administration have also done as of November last year, is changed medicinal cannabis from being a schedule 9 prohibited substance to an S8, a controlled drug.

David talked about one of the forms of an S8, which is actually registered, but otherwise, all other forms of medicinal cannabis do remain unregistered. For a doctor, that means one has to fulfil the normal requirements of an advice to a patient about how to provide medicinal cannabis and how to advise patients about the risks of doing so.

The supply and production, as you can see, is complex, there are lots of steps to go through, but once you've gone through the Commonwealth process, where do we end up?

Basically, concentrating on New South Wales, there was an amendment to the Poisons and Therapeutic Goods Regulation last year and essentially in New South Wales general practitioners or other specialists can apply to the TGA and to the State system for an authority to prescribe medicinal cannabis as an S8. They have to get a State authority and then get a Commonwealth authority through the TGA Special Access Scheme. Now, as a result of a TGA decision, that's only through Special Access Scheme category B, medicinal cannabis is specifically exempted from any category A prescriptions.

Some of you may have seen some of the press talking about that as a step backwards because previously it could be accessed for terminally ill patients through a category A potentially.

New South Wales and Tasmania have come to an understanding about the supply of the cannabis products for the New South Wales' trials and they're actually being cultivated and provided through Tasmania. The ultimate aim for some of the Tasmanians is that they may (a) get the benefit of the findings of those clinical trials and (b) exchange information and develop a relationship with New South Wales.

But in the meantime, Tasmania has their own scheme, as do the ACT, the Northern Territory and South Australia, all currently don't have any specific legislation. South Australia has followed an interesting step of actually introducing what's called a Patient Access Pathway where there is some cannabis product available as an S4 and that was only announced about six weeks ago, but otherwise a State authority is still needed as an S8.

Interestingly, in WA, again while there's no legislation, the Health Minister in WA has recently called an emergency meeting to understand why doctors in Western Australia are not prescribing medicinal cannabis and not seeking to prescribe medicinal cannabis more, which is quite interesting when we've all just heard from David about why there doesn't really seem to be sufficient clinical reason for doing so.

Beyond that, in Victoria and in Queensland, are the two other States where legislation has been brought in and

Queensland have taken the extra step of actually bringing in, quite usefully, some clinical guidelines about the things you need to be aware of when considering whether or not to prescribed medicinal cannabis and how to go about doing it.

These are obviously guidelines only and they're State-based, but at the moment there are no Commonwealth guidelines, although these are in draft form and being considered, but it means that for doctors in other States and Territories, they are a good reference document for trying to understand the sorts of things that may be needed to be considered and reviewed and covered in any application for an authority prescription.

We are basically left with no consistent legislation. We're left with one set of clinical guidelines in Queensland. We've got the TGA having down-scheduled medicinal cannabis to an S8 and therefore it being accessible through either the Special Access Scheme or the authorised prescriber system through the TGA.

But before you go to a Commonwealth authority, depending on the State or Territory, you need to get State approval and that certainly applies in New South Wales. Then once you've got the State approval, to be able to apply for the TGA approval you need to identify your supplier and you need to name them. You need to work out that they can supply it and then you also need to provide all the scientific and clinical evidence to justify why you should be able to get the authority to prescribe medicinal cannabis for that patient.

In most States and Territories where that system exists, it's a 12 month authority. In Queensland, it's for three months.

So, assuming that you've considered that; we're in New South Wales and we've got two different examples. We've got a patient in front of us who is a 24 year old with chronic non-cancer pain and he's heard some friends talk about how medicinal cannabis has really helped them. He goes to his doctor and he says, can I get medicinal cannabis?

On the other hand, we've got the 40 year old patient, they've got MS, so we know that there is some evidence to suggest that it may be beneficial for MS, but you're the neurologist and you're wondering can you prescribe medicinal cannabis for that patient.

Much like any other situation, you've still got your overriding duty of care to your patient; so that's still relevant and if there is some sort of adverse outcome, you're going to need to justify that it was standard practice at the time, according to the peer test that's set out there.

You need to talk to your patient about what it might be able to do for them, the risks and benefits. You need to be able to provide them with sufficient information about what those risks and benefits are and as the TGA has specifically set out, the patient has to be informed that it's not approved in Australia, of any known side effects and possible benefits, and of course, that has to include that there is limited clinical evidence that there are side effects that we don't know about, particularly long term.

For a terminally ill cancer patient, the lack of long term side effects may not be relevant but for a number of other patients, that may be very real and very relevant. Say, for example, the parents of a child with epilepsy, even though their symptoms might be horrendous and quite debilitating, the long-term effects may still be relevant for them.

You also need to consider whether or not there are any alternative treatments, what's been tried, why it hasn't worked or why it may not have worked and whether there are any other alternatives still available.

This is a step where those Queensland guidelines might become useful, because even though they are State-based, they do still talk about some of the things that you need to consider and it makes it very clear that medicinal cannabis is not meant to be and will never be a first line treatment.

You might be talking about some of those clinical indications but the long-term issues are going to be particularly important.

In addition to the Queensland guidelines, the Commonwealth is in the process of trying to finalise some draft guidelines on a Federal level. At this point in time they are directed to epilepsy and to palliative care patients and the use of medicinal cannabis in treatment for those two sets of patients.

Those are being considered by the Australian Advisory Council, of which they've had two meetings as yet and they're still considering those guidelines before they get finalised and released and are available generally, and should be considered when considering any prescription for medicinal cannabis.

At the first meeting the members of that Council did say that they were encouraged by some of the evidence available, but they believed that further research was required, further clinical trials were required, and generally speaking there was a consensus that there was very limited understanding and limited evidence available to the medical profession in Australia when considering whether or not they could prescribe medicinal cannabis.

As you can see there, the clinical guidelines talk about some of the contra-indications. One of the relative contra-indications is that it's not recommended for people under 25; so, the 24 year old patient is not looking very good, because you're going to have to get over that hurdle if you're trying to prove to the TGA and your State authority that a prescription is indicated.

They talk about paediatric and elderly patients being relative contra-indications too. So paediatric patients, when a lot of the trials have focused on paediatric epilepsy, again are looking interesting.

There it just says as you can see in the clinical guidelines, nicely in bold down the bottom, that they really need to be aware that doctors prescribing medicinal cannabis have to take full responsibility for the use of the product over any other unauthorised product and that's where the discussion with the patient, the warnings, and of course, the documentation of that discussion and the warnings, becomes very important.

Interestingly also, one of the main sticking points when looking at medicinal cannabis is obviously that under the Crimes Act it is an offence to drive under the influence of a drug. The THC component of cannabis particularly has an effect on driving and the clinical guidelines make it very clear that cannabis generally will influence driving.

As a doctor prescribing medicinal cannabis, it is important that they warn their patients that they cannot drive if taking it. Again, for a terminally ill cancer patient, they may have already ceased driving. Inability to drive may not be that important. Regardless of the patient's

circumstances, it must still be covered with them, addressed with them and documented, but that is often a hurdle that many patients are not able to accept and at this stage there's no level or acceptable concentration that would enable a patient to drive and still take medicinal cannabis.

Once you've gone through that process, you've explained it all to the patient, you've warned them that they can't drive, you've got their written consent that they understand all those warnings and that they're willing to take on that risk and go through the process with you, you then go and apply for your State approval process.

You've explained to the patient all of the clinical indications. You've talked to them about why it's being used, how it's being used. You need to have a plan in place of monitoring to ensure that you can be aware of whether or not it's having any effect, but also whether or not there are any adverse effects of it, whether or not it's causing any harm to the patient and judging from what David said, the chances of it doing more harm than good may be quite high.

If you manage to get over those hurdles, then you go to the TGA Special Access Scheme. Again, as an unapproved drug, this is your course of action, either through the Special Access Scheme or as an authorised prescriber, and as I mentioned at the beginning, you also need to identify where you are getting the supply from.

You literally have to name the contact details and the supplier needs to be involved in the process prior to seeking the authority from the TGA. As of about four weeks ago the TGA now actually have a list of the authorised suppliers on the Office of Drug Control website, which actually lists the name, company, contact details and the actual specific drugs or concentrations that are available through them.

You have to be able to confirm that the company is able to provide that supply as part of the process of seeking authority.

The other interesting thing that's happened in Queensland is that there is an exception from a protection from liability included in that Act. Whether or not it protected a medical practitioner from any action from a professional conduct point of view, from the wording it

would suggest that it doesn't, but obviously it's untested and it hasn't gone through the process yet.

If you didn't get the impression from that that the process was overwhelming, this flow chart should confirm that it is. I think, really it's going to be that middle step in terms of actually being able to provide, document and supply to the State authority, as well as to the TGA in the process of seeking that authority, that you've got the requisite clinical evidence and support that is really going to be the stumbling block.

But in the meantime, the press keep talking about it, patients keep asking for it and so it's really a matter of taking each patient as you find them and applying the guidelines and the law to each individual situation and seeing whether ultimately you want to go through the journey with them and make the application. Thank you.

QUESTIONS

MS KEELY GRAHAM: Thank you. We have a short while for some questions, if people have questions.

QUESTION: People who smoke pot, are they all smoking the same stuff?

DR DAVID GRONOW: No. It's going to depend what strain of marijuana plant they're using. Hydroponic growth has higher concentration of THC. There's the amount of THC, which is variable in concentration and over the years the concentration of THC has increased enormously.

If you go back 50 years ago, you'd probably be battling to get 0.1 per cent, now we're talking about five to - if you're talking just about marijuana, not hashish, we're getting up to 20 per cent easily and hydroponic probably gets up to 25 to 30 per cent, but then there's the ratio of the THC to CBD, which is different in every strain of those 2,000 plants that are available.

If you go to Colorado, you can order one of those strains and decide which one you'd like. It's a bit like going to T2.

QUESTION: Who pays for the cost of the drug if you do get it through the approval process and how much does it cost?

DR DAVID GRONOW: The current stuff is extraordinarily expensive. I think it's in the order of - the registered

stuff is about, depending on how much you take a day, $100 to $200 a day. Yes, it's very expensive at the current time.

MS KEELY GRAHAM: And who pays for it?

DR DAVID GRONOW: We're not talking about marijuana, we're talking about that list I put up of those ones from - now you've got to remember that if any of you had been wise enough to invest in a marijuana company in the United States, whether it be supply or even giving the farm machinery, they have gone up in 18 months by 5,000 per cent on the Stock Exchange; it's big business. The other P is proprietary.

MS KEELY GRAHAM: David, who pays - the patient, the private health fund, the government?

DR DAVID GRONOW: The S8s, yes, you have to pay the company. Say it's under the Special Access Scheme; I don't think the government has brought in any financial support that I'm aware of at this stage, unless you're in a clinical trial.

DR GREG STEWART: Greg Stewart, South Eastern Sydney Local Health District. We're responsible for a drug and alcohol service, and I was told by my director of drug and alcohol the other day that half the marijuana that's being prescribed under the scheme, and I think because they'd be under trials, Sativex trials, that they probably are provided free of charge.

DR DAVID GRONOW: Yes, if you're under trial, yes, that's being supplied. The one thing, you can become a registered supplier. To date, only 25 are in Australia and 23 of them are in New South Wales.

DR GREG STEWART: Just another comment, you'd be unlucky wouldn't you, as a prescribing doctor if a 24 year old came along and said I've got terrible chronic pain and you were convinced and went through the process and he got his dope, and then he sued you. Wouldn't you be unlucky?

The more serious comment is this, I come to these lectures all the time, there's not a lot to see here, is there? We've got a drug that maybe or maybe doesn't work. We've got a regulatory framework that allows it to be prescribed. The only contentious thing in all of this for me was why in heaven's name are we saying that a person who smoked

marijuana five days ago is incapable of driving? Why does the law say that? It's just silly.

If you've drunk six glasses of wine, then clearly, you're much less capable of driving a car.

MS KEELY GRAHAM: Not if I drank it five days ago though.

DR GREG STEWART: No, immediately. But a law that says if there's any THC in your system, you are therefore in breach of a law that's about not being able to look after motorists--

DR DAVID GRONOW: The problem is that, first of all, there is evidence, significant evidence, that THC increases motor vehicle accidents and motor vehicle deaths.

DR GREG STEWART: Not five days later though.

DR DAVID GRONOW: No, that's the next point. There are no studies on how much you are affected in terms of your motor skills and there's no study on that; and therein lies the difficulty.

Unfortunately for those who smoke it, the sensitivity of these tests is getting more sensitive than they used to be, but the difficulty is, we don't know if you've got a half-life or if you're safe or do you have to get down to a quarter, and it does hang around in the body for a long time.

If you're a chronic smoker or a chronic user of THC, so if you're using it - and for most of these conditions the clinical effect only lasts for about four to six hours, so you're going to have to be using it four times a day. If it's Savitex, you're going to be using THC four times a day, so you're going to have a build-up in your body for quite a long time.

If you stop it, then you're going to be affected by THC for several days and your motor skills will be affected for several days.

If you just have a joint on Saturday night, then you're probably right, by Tuesday probably your motor skills are normal, but it still will be picked up.

So, it really is how much cumulatively you've been using it and that is a significant component to it.

QUESTION: On the adverse effects, compared to tobacco smoking, what are the adverse effects of marijuana? Is it in the same category?

DR DAVID GRONOW: There's no real science on that, but if you smoke it, there are carcinogens in the other components of the marijuana flower; whether it's as bad as nicotine is not known but it has been shown that regular smoking does cause chronic bronchitis and it can go to producing bronchiectasis.

But whether that goes on to producing cancer, in itself, is not known, because a lot of people smoke nicotine as well as smoke marijuana, but the evidence is available to suggest that it could be as bad, but it's not proven it is as bad, yet.

The problem is that we don't know what the long-term effects of this are going to be on people. We do know that people who are chronic smokers become totally withdrawn from society and do have quite significant cognitive and memory effects and basically become disabled.

We then go back to individual cannabinoids, are they going to have the same effect as THC? We don't know that yet.

MS KEELY GRAHAM: To both of you, have you found many applications to go through all these hoops to seek to supply it? If so, has it been supplied with this requirement for locked fridge trucks and if so, or if not, has there been much notification about a failure to supply it or you supplied it when you shouldn't have? Have there been claims related to it in your experience?

MS RUANNE BRELL: From the point of view of the newer concept of medicinal cannabis, other than, I suppose those products that have been used like the Sativex, it's just not been nearly as widely taken up as perhaps the media coverage would suggest and at this point in time the main concern is really trying to understand - it was literally as of four weeks ago, so, it was down-scheduled in November last year, but it was almost impossible to actually find out how to get it in New South Wales or across the country until three or four weeks ago.

The other thing in New South Wales is that there is a scheme where you can actually become registered as a terminally ill person using medicinal cannabis and that was probably more common where patients may get given leniency if pulled over by the police holding cannabis, but the main

problem is actually just access and understanding where to be able to obtain it, if indeed you find a patient where you can justify prescribing it for them.

DR DAVID GRONOW: So far in our practice, once you start explaining the risks involved of taking it, none of the patients have persisted with the request.

One of the first things, of course, you can't drive and that loss of independence is significant for a person who's in their 30s, 40s, 50s, or even I had one patient's daughter came in and said can't you prescribe some medicinal marijuana for my mother? When you told the mother, she actually had tried it and said it was the most horrible thing she'd ever had, but despite that, the daughter still thought it might have been a good thing.

But once you explained all the things that could happen and you can't drive, it often just ends the discussion.

One of the things I have in terms of that though, if you're prescribing THC in any of its forms, do you actually have to notify the RMS as a prescriber?

MS RUANNE BRELL: That's a whole other fitness to drive discussion, but generally speaking the obligation would be on the patient having been warned that they can't drive, not to drive and to disclose any condition that affected their driving, depending on how serious you thought the risk might be if they continued to drive.

QUESTION: Given the vagaries around the indications for the use of cannabis and the different clinical scenarios, if a practitioner took a position that cannabis was sort of a cure-all, they've had efficacy and all of these things, epilepsy, MS, pain relief, etcetera, when would you consider a practitioner was actually reckless in the prescribing?

MS RUANNE BRELL: I think based on given that we've just gone over all the lack of clinical support for doing so, if a particular practitioner decided that it was some cure-all and started prescribing it, presumably they would be doing so outside the State and Commonwealth authority scheme because they wouldn't have sufficient evidence to support it.

If they were doing so without appropriate authorities, then they would obviously be at risk of sanctions much like prescribing any S8 without an authority and presumably also

they could potentially be at risk of a finding of negligence and potentially at mandatory reporting risk because arguably, they might be acting so far outside standard practice if they were prescribing medicinal cannabis as their first line treatment for every and any condition in patients that presented to them.

I think that practitioner would be at real risk if it was their go-to medication for all presentations.

DR DAVID GRONOW: In New South Wales it will only ever be allowable for epilepsy, nausea and vomiting and palliative care. All the other things that I mentioned, you will have no chance of getting approval for.

That's provided what happens with these clinical trials and no one's really said from the government point of view what standard of proof these clinical trials have to show for them to continue to approve it through their system. This is still an unknown.

The clinical trials, all of them are doing a pilot study, of about 30 patients, which is very small. If they show a positive outcome, they're planning to do a second trial of about 200 to 300 patients, but even that is actually quite a small sample size to get any power in the study.

We don't know what the end point is going to be of these, what's going to be acceptable. We're going to have to wait and see. That hasn't been pre-determined. We don't know what's going to happen with the results of these clinical trials.

I suspect they'll show some degree of positivity, but how much? With the nausea and vomiting ones there's a total lack of other trials comparing these substances with the current antiemetics. All the studies that were done 15 to 20 years ago against the older ones, and they were about the same in those studies.

This is what we don't know, so it's still a bit of a melting pot.

MS KEELY GRAHAM: Thank you very much.

MEETING CONCLUDED