The CCIC Podcast

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This month: Dr. Igor Grant
Interview by Dr. Mark A. Ware

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Introduction

Hello and welcome to the CCIC Podcast. The CCIC Podcast is a series of in depth interviews with leading experts and opinion leaders in the world of medical cannabis and cannabinoids.

The CCIC Podcast is brought to you by CannTrust^{TM}, a Canadian licensed medical cannabis producer.

In this edition of the podcast we are delighted to welcome Prof. Igor Grant from the University of California at San Diego, talking about the problems with medical cannabis access:

"…patients don't necessarily know what they are getting and physicians don't know exactly what they are prescribing"

and medical cannabis policy:

"…the problem I always experience is the relative inability on the part of the public and government to distinguish medical issues from other social, and policy, and criminal justice issues"

Prof Grant is an American psychiatrist who is Professor and Chair of the Department of Psychiatry in the School of Medicine at the University of California, San Diego. He is Director of the HIV Neurobehavioral Research Program, and is Director of the University of California Center for Medicinal Cannabis Research.

We spoke on January 19th, 2015

Ware Welcome Dr. Grant and thank you very much for joining us. I am going to begin with a personal question: **How did you first come in contact with the medical cannabis world?**

Grant Actually my initial work had nothing to do with medical cannabis. When I was a trainee at the University of Pennsylvania in psychiatry I was actually interested in the question of whether cannabis produced brain damage. There had been a number of articles that had come out about amotivational syndrome, basically cognitive deficits and so forth and I was curious whether that was the case. Because certainly when some, many people, including Penn students, seemed to not be suffering those things. So with some colleagues I conducted a study on neurocognitive

functioning in marijuana using and marijuana non-using medical students at the University of Pennsylvania. Based on that study we concluded that, at least in that rarefied population and based on the amount they were using, there was no evidence of cognitive deficit. That was really my first experience with marijuana research. Then a lot of my career has been spent looking at the effects of alcohol and other drugs on the brain and recovery from drug abuse in terms of neurobehavioural functioning.

The actual re-emergence then in medicine - medicinal cannabis - really came about through some inquiries that were made by a lead legislator in the state of California. I can talk about that a bit more if you want to get into the history of it.

Ware Clearly your experience and your background in research and other drug effects led you to become the Director of the Centre for Medical Cannabis Research (Centre), in response to the Proposition 215 in California in 2000. Subsequent to that, you and your organization set up a number of clinical and preclinical studies of cannabinoids and some of those studies have answered some of the questions that people have been approaching. **Looking back on the 15 years since the Centre was first established, how do you think the Centre has responded to some of those questions?**

Grant My own view is that the Centre was enabled to conduct the only really modern clinical trials on smoked and inhaled cannabis in the United States that had been done in many, many, years, using up to date clinical trials methodology. That was made possible, by the way, because the state of California funded the University of California to do this. Without that kind of funding it wouldn't have been possible. Our centre not only did these trials but enabled investigators to go through the many regulatory challenges that are inherent in doing this kind of research. We completed seven clinical trials; most of them concerned neuropathic pain. Each particular study was relatively small in its scope and not long in duration. I think we can safely draw the conclusion that at least in the short term there is good evidence for efficacy in the management in neuropathic pain and similar kinds of pain, from cannabis. We completed another study on multiple sclerosis spasticity that also demonstrated a positive result. I think what I would say the Centre maybe has laid the basis for more mature future clinical trials with medicinal cannabis which I think need to be done but have not been done. I would also add that I am speaking from a strictly Americo-centric experience and I am well aware that in other countries, including Canada, studies have been done, but within the United States I think it is fair to say we are the only ones that have completed these studies in our times.

Ware In many ways California has, in terms of funding and in terms of the number of scientists and clinicians invested in the research, been leading the way for this kind of work for North America. **What do you think gives California the special edge in getting the science done and leading the charge in addressing some of these questions?**

Grant Some people say California is not only a state it's a state of mind; sometimes that's put both positively and negatively. I think that there is a lot of energy in the state; a lot of creative

thinking ranging from our arts and film industry to all of the software development, and so on. I think there is the spirit of inquiry in general in the state. I think obviously many people in California believed back in the 90's that if patients could benefit from cannabis they certainly should have it. That kind of thinking led to the passage of Proposition 215 that you are talking about – which basically says patients should be allowed on doctor recommendation to have access to cannabis for conditions that doctors feel it's appropriate. I think that was one part.

The other part had to do with the legislature itself, which is our state parliament if you will. It had a number of forward looking legislators; including Senator John Vasconcellos - who passed away recently. He was very much at the forefront of trying to see once Proposition 215 passed how could we make this more medically sound, how could we establish that cannabis really worked. I thought that was a rather forward looking way of approaching it from a government standpoint. They really wanted to know the facts so they were willing to put some money into research.

Ware It's clear that they also invested in some policy development and trying to provide a mechanism for access to patients for cannabis. In many ways Proposition 215 led that drive as well. **Again looking backwards at where things have come in California, what do you think went right and do you think there are parts with the Californian experience that things could have been done differently or better?**

Grant California, like many places, has had a split view on this. As a physician, the problem I always experience is the relative inability on the part of the public and government to distinguish medical issues from other social, and policy, and criminal justice issues. So that often we start talking about medicinal applications of cannabis and very quickly it gets into; well should marijuana be legalized, and what about teenagers, and on, and on, and on. I think the legalization of marijuana is a separate question from making it available as a legitimate medicine. In California, coming back to your question, I think there has been some confusion about this to the point that within a couple of years of Proposition 215 – the medical cannabis initiative having been passed – there was an initiative to legalise marijuana which failed. Not by a big margin, but it failed. It shows that within California there was an ability to discriminate between the medical and the recreational use. If I had to predict it further I think that in California there will probably be another proposition to legalize marijuana just as has happened in Colorado and the state of Washington – but we'll wait and see.

What went wrong in general in my view as a physician is not unique to California. Because of this tension between our federal authorities; which have basically taken a position that marijuana is a bad thing it has no medical use and should be what is called Schedule I along with heroin and drugs like that. Because of that tension between the states and the federal government there has been this sort of strange development of marijuana dispensaries and so on and so forth. The problem I have with that is patients don't necessarily know what they are getting and physicians don't know exactly what they are prescribing. That is an unfortunate development. A much better development would have been to make sure marijuana, or

cannabis, can be available from known sources with known potencies through either pharmacies on prescription or some equivalent methodology. Which is what I believe is what is kind of been developed in Canada.

Ware You're right, the Canadian program is almost inverted compared the American one, where we have a federal program which is implemented and the challenge is putting that into play on the ground. It's an interesting experiment going on here; which is to see if we do it that way do we end up a better or different kind of policy and a different response. But clinicians here remain concerned about side effects. Predominantly the ones that seems to keep coming back up are of course the neurocognitive effects of cannabis. Based on the recreational studies that you did with your colleagues, what do you think that the core take away messages that we can draw from your work could be, or could mean, for the medical cannabis community; the users and the care givers that are looking after them? **Is there a takeaway message from your work that you think can be applied to medical cannabis users?**

Grant Yes, and I think here we ought to sharply differentiate between acute effects, or effects that may be measurable when a person has a lot of cannabis on board, as opposed to long term and persisting effects – a permanent injury shall we say. What our work has shown, not just ours but other groups as well using meta-analytic techniques of neurocognitive studies of marijuana users, is that there is very little evidence of long term brain injury or neurocognitive decline among marijuana users if you test them when they are not stoned, or have not recently used - and that makes perfect sense. Nobody questions that cannabis has cognitive effects, and mood effects, and other kinds of effects when people are taking the drug actively. But the evidence for long term harm is virtually nil. I would qualify that in two ways, however. First we really don't know what harm there might be in very young users - that is in adolescents whose brains are continuing rapid development - and what might happen. Here the harm could be not just structural harm, 'oh, their brain looks peculiar after a while', but also the harm in terms of learning and psychosocial development; if you are stoned all the time and not paying attention to class there are be many, many, consequences that are non-neurological but are still very consequential. I think we should look at the adolescents a little bit differently.

The other issue that needs to be tracked is potency. The potency of cannabis, the THC concentration, has been rising according to most surveys. Conclusions that I might have drawn from years of studies going back to the 70's might not apply if we now have instead of 5, 6, 7% THC now its 15-20%. That may be a different story, so we may need to keep an open mind there.

Ware You may have just answered my next question, which is; if you had to pick one study to do next – turning our focus a bit forward looking now – what would you like to see? **What is the most important question in your perspective that could be answered in the near future?**

Grant It's actually hard to answer that in one answer. It seems to me, one thing that would resolve a lot of the immediate issues about should smoked cannabis be permitted or inhaled cannabis or is it just as good to prescribe THC as a pill, like dronabinol – is to actually do a proper study

comparing these modes of administration. Perhaps even having a several armed study that has smoked cannabis, some sort of inhaled cannabis, oral dronabinol, and oral CBD, or something like that. That could answer the question of whether there is any point to using smoked cannabis at all. Is it truly better in the sense that the kinetics are better? Is it better that you get around the inadequate absorption through the gut, or first pass metabolism through the liver? Which have all been raised as issues as to why oral preparations may not work as well as inhaled or sublingual or others. I think that question should be answered in a proper study in a condition where we expect these conditions to work like a painful peripheral neuropathy.

The second question has to do with what are the specific active components of cannabis and can those be developed into forms that can be administered in a way that is more comfortable for providers and patients both; that would be the next phase.

I would like add, of course, our own studies were relatively short term, limited in numbers of cases and the larger trials with a more diverse population, no matter the mode of administration we choose those are necessary. We can't necessarily extrapolate, for example to people who are older with cardiac disease and so on.

Ware Perhaps with existing and changing policies, perhaps with increasing the amounts of money that is being thrown into this space we will see some of these studies emerge and certainly answer some of those important questions. **Looking further down the road, 10 years down the line can you put on your magic hat and look into your crystal ball and see where you see the medical cannabis stage. What do you think it will look like in 10 years' time?**

Grant I would hope that two things would happen. The first, until we figure out what the active ingredients that are therapeutic are or what combination of active ingredients work optimally. I would hope that we would get to a place where patients can be prescribed cannabis, procure it from legitimate sources which are regulated where we know potency, purity. Where there is protection against diversion but not in such a draconian way where no one can really use this medicine. I would like to see this treated as a medicine just like we would for anything else. I would not send somebody to a farmers market to buy penicillin, and neither should we be sending patients with serious illnesses to buy cannabis on the streets someplace.

Point two, in the long-term I think that it will be developed, novel agonists, antagonists, partial agonists, etc. of the cannabinoind system – our internal system – that may become very good medicines in their own right. They may go to the treatment of conditions for which we don't have very good evidence now, but have a few clues including; schizophrenia, autoimmune disorders, epilepsy, and so forth.

Ware Thank you Professor Grant, you have been extremely generous with your time. I appreciate you taking the time to speak with me. **Before I close, is there anything else that you are burning to say to the community that is looking at medical cannabis and cannabinoids, any closing thoughts or wishes that we haven't discussed here today.**

Grant I always like to quip that it would be nice to get beyond the smoke and into the light on this topic and one way we can do this is to have our policy guided by medical evidence, by science, opposed to our preconceptions.

Ware Thank you very much, you have played a great role in helping us find that light and look towards it. Thank you again for your time for this interview and good luck with the rest of your work.

Grant Thank you very much, I appreciate talking to you.

That was Professor Igor Grant, speaking to us via Skype from San Diego. Thank you for joining us, thank you to our webcast sponsors CannTrust, and tune in next month to the CCIC Podcast.

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The approximately 20 minute audio podcast of this interview is available online at www.ccic.net/podcast.

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