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Medical Cannabis: Help and Hype

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Dr. Butowski: Morning. Thank you to the organizers for affording me the opportunity to speak today.

Here are my disclosures and disclaimers. One off topic -- or one-off slide and then back to the slide show. So I don't know exactly why I've been asked to speak and can't be my personal experience of 20 years in the Bay Area with cannabis. I think it has more to do with a lot of empiric experience with patients in clinic that use cannabis for a variety of things.

Probably about 40 to 50% of our patients are using cannabis for some reason and we've actually got some ongoing studies looking at those reasons. We've also had a couple of pharmaceutical preparations in the labs; are so called pre-clinical core animal modeling which I'll touch on. Incredibly difficult to do those studies but perhaps that's why I'm here.

The other disclaimer is this discussion is of a Schedule 1 substance, so it's purely information and you can't take what I say as gospel in any way shape or form. And in case you don't know what Schedule 1 means, it means the federal government thinks it's just as bad so to speak as heroin or LSD or ecstasy or what have you. So that makes research with this -- cannabis -- and I'll talk about what cannabis is in a minute.

It is an unregulated product in all states and honestly, when you go to a dispensary rather than a pharmaceutical preparation, you don't really know what you're buying and I'll touch on why. Again, federal; illegal. State level regulation is different from state to state about how

much you can buy or grow on your own. It's not prescribed, it's given for a certified condition. Oops, too far. One last point about that. If you go to your physician, your oncologist, state by state it's going to be quite different with how you'll be put in touch with a medical dispensary.

In California for instance, you really just show up and say you want X, Y or Z and they have either a physician or someone who's an expert in plant growing take you through your options and/or you find someone like me with a little bit of experience. I also want to make it clear that as far as big organizations at the federal level, like the National Academy of Science, we realize that there's a giant research gap here. So many of your questions I probably can't answer. In fact many of my initial slides are going to be meander and be redundant throughout, in order to hit home some points.

There's a lot more unknown than known about this topic. Groups are just beginning to form, like at UC Davis in California which has a big investigative portion of their university dedicated towards who's growing what, why are they growing it, what's the medical demand, what's the demand recreationally, how is that influencing what kinds of products are available both pharmaceutically and through dispensaries.

Here's an outline. I'm going to touch on these properties; history and properties, use in oncology patients touching on brain tumor patients and again, probably not going to give you as much information as you'd like but I'll give you some. Talking about drug interactions which are important and then real-world considerations of how you make a choice about whether or not and how you incorporate this into your care.

I don't know how many people are familiar with Linus, who was the speediest guy back in the 1750s who was the father of taxonomy. He was the one who named cannabis cannabis if you will. Or at least that's the story. He named cannabis (inaudible 00:51:58) which is the tall, thin weed that will give you an energetic high.

There are other forms of cannabis if you look around the world. There's Indica from India; it's darker, thicker and supposedly cold resistant. It supposedly gives you a lethargic, stoned high.

There's Realis from Russia, which is smaller, shorter and sprouts faster and gives you all sorts of hallucinations supposedly.

In reality these days, you can't tell what kind of high or product you're getting from visual inspection. There's been so much cross breeding that you can't expect to look at a plant and know what it's going to give you. So if you go to a dispensary and somebody looks at the plant and says "Oh, you're going to have this, that and another symptom or benefit." They're probably not in the know so to speak.

There's actually a good program I'd like to plug in, on Netflix by Michael Pollen. I think the title is Explained and then the episode is about this; cannabis in general and why and how dispensaries are going. Check it out, it's only about 30 minutes long.

Linnaeus also noticed that some plants produce only seeds -- those are females -- and some others produce pollen; those are the males. It's the female plants that get you high, not the male plants. Both produce some THC and CBD but the female plants are what are primarily grown in dispensaries for obvious reasons.

There's not just THC and CBD which I'll touch on in cannabis. There's all sorts. There's cannabinoids which affect us and then other chemical compounds like terpenes which give you (inaudible 00:53:31) and flavonoids which give you flare. Again, if you go to some highly sophisticated dispensaries, they'll almost talk to you about cannabis like its wine, right? What variety, what it smells like, what flavor? You name it, you're going to get it.

Most people talk about cannabis in terms of THC and CBD. (inaudible 00:53:52, oil names) The THC is what gets you stoned so to speak or the pshycoeffective component, the CBD is the more healing component if you will. It chills you out a little bit, may not do much beyond that.

The more THC in a plant the less CBD and the reason that's important of course is if you want more THC to get you stoned then that's where you go and if you want to balance that out you go with a higher ratio of CBD. So a lot of patients will get a higher ratio of CBD to THC so it doesn't make them feel too slow.

The systems that these agents work on, or cannabinoid systems are present in every animal on the planet (inaudible). They have an evolutionary role in appetite regulation, helping us to forget in a pleasant way, reducing stress and actually the receptors that are responsible for the euphoria you get after exercise.

These days you can use cannabis, medical cannabis, from a dispensary many number of ways. Smoking, vaping, eating, tincture, cells, you name it. And I'm going to hit home this point several times. The method by which you use is going to affect what symptoms you have, the duration of those symptoms and the intensity of them.

So a deep-rooted history, right? Cannabis goes back to thousands and thousands of years ago. Really first used as grain and fiber, really hemp which is the stems. And then 2-3,000 years ago India and other places used it as medicines to help with anxiety and what have you.

And then in the 1840s actually there was published literature about its use as an anxiety and the like. And then in 1910 it was actually cataloged here in the United States by Eli Billy who probably wishes they never give it up, given the possible benefits of all sorts of things now and the financial repercussions.

However, then it got a bad reputation, right? Because then it got lumped in with the Schedule 1 drugs. In 1937 it was part of the Marijuana Tax Act and thought to be a violence causing drug but interestingly the AMA, American Medical Association, did propose that at the time (inaudible). In 1942 it was removed from the US Book of (Inaudible 00:55:58) and in 1970 was classified as a Schedule 1 drug. And depending on who you believe is part of the War on Drugs and seen as a gateway drug and what have you. Obviously, that has changed to some degree.

And then in 1996, in fact, it became part of the Compassionate Use Act for treating HIV/AIDS, painful diseases and what have you. And there are a couple of pharmaceutical preps that have come out from 1985 onward that are approved first for chemotherapy induced nausea and then AIDS associated pyrexia and then most recently in 2018, there's Canadial approved for seizure control as part of (inaudible 00:56:41).

So a lot of patients use medical cannabis to control seizures or as their preferred seizure medicine. But not necessarily a pharmaceutical prep.

So states -- this is probably an inactive map that needs to be updated I think but, you have both states where cannabis is available medically and states where it's both availably medically and recreationally. The recreational drive if you will, why people are using it recreational is supposedly a far bigger drive financially than the medical needs. So what you're getting on the medical side is often influenced by what people are getting on the recreational side.

Let's talk a little bit about properties. So as I mentioned, you can go to a dispensary today and get all sorts of plant products that are inhaled, that are oral, that are topical, rectal, what have you. Again, the route of administration here is going to affect what symptoms you have and how long they last.

There are four pharmaceutical grade preps. The orange one, the big, small (inaudible 00:57:48) is only available in the U.K and Canada. They use it for spasticities associated with MS and it has a ratio of THC to CBD of one to one. (Inaudible 00:58:00) have been around for a while their THC analogs if you will under Schedule 2 and 3 respectively and are used for nausea primarily, as far as their label goes. And then (inaudible 00:58:11) the medicine is for procedures and (inaudible 00:58:14) Syndrome.

None of these have been routinely tested in tumor models but are available and sometimes patients use them for the things either they're indicated for or either get hold of them for anti-tumor properties, which again, we'll touch on later.

This is a very busy slide but basically, it's just to hit home that there are a number of different places where the (inaudible 00:58:43) system resides both in your brain, your peripheral nervous system and in your immune system as well. Depending on what receptors and the

balance they're going to hit, they're going to have different effects, which I think is better seen in the next slide.

There are CD-1 receptors; cannabinoid receptors in your brain and peripheral neurons as CB-1. They're going to modulate neurotransmitters, all kinds of chemicals that effect pain, pleasure, appetite, cognition, perception, movement, what have you.

Then the CB-2 receptors are hit and those can modulate your immune system. Depending on what literature you read actually, often they say it suppresses immune system. Some say that it can augment it, but either way it modulates the immune system in some way that's really not well worked out yet. We think it has an anti-inflammatory role as well and that's the main reason it's used in pain control.

These mechanisms, while some of them need more work too, in just the basic science of them. This is a very busy slide but I wanted to hit home again that CBD is a negative regulator to THC. The more CBD you have the less phsycocomponent of the THC and that's going to balance out your so-called AEs -- your Adverse Events. So when you go into a dispensary you want to know what ratio you're getting.

And then the bottom text is really just to hit home that the reason people are using these are anxiety, depression, pain, anti-inflammatory, sometimes blood pressure regulation and seizure control. So those are the main pathways it hits. I put the busy slides up here so if you want to refer back to them you can understand some about the basic science behind it and then you can refer to.

One question I undoubtably get is what dose do I start at? The answer is; I don't know. This gives you at least a place to start. And again, it comes back to the variety of plant product you're going to use. Obviously if you're going to go with the medical/pharmaceutical preps you're going to likely start with the dosing as they describe. But if you come on with a THC predominant product or mixed ratio or CBD predominant product, this is where most literature suggests one step. Sort of getting into the shallow end of the pool and making your way towards the deep end as you desire. Most patients end up using, if they're going to use for some sort of anti-tumor property, and there is some literature that says it fights tumor growth. I'll touch on that I promise.

Most patients end up using to how it affects their sleep or their mood or their seizure control or what have you and they have to find out the dose that works for them. They end up using and abusing at night. If patients have no experience, they'll end up smoking first, vaping and then they work their way into edible which are a little bit more complicated in that duration and onset -- they lag behind and last longer. This is where I begin but this is based on the literature not based on my personal opinion, so to speak.

So again, this slide just hits home how you use is going to affect what symptoms you feel, how fast you feel them and then how long they're going to last. With those inhaled products coming on very quickly, 15 to 30 minutes, even quicker sometimes and only lasting two or three hours.

If you ingest orally it's going to take longer; it's going to take 90 minutes typically to come on. So if you eat the whole cookie and then wait a minute and think "Oh, I feel fine. Let

me eat another cookie." And then 90 minutes later you're marching in place; right? So you have to work your way up. You'd be surprised how many patients also show up in my clinic with brownies and cookies for the staff and we all have to ask does it have THC in it? It's an important thing in this modern day.

Anyway, you want to be careful with how you use and where you start with that. Especially with some of this -- now you can order it online too. I don't know about Illinoi [sic][1] but in Chicago you can order online and it's delivered to your house. It's easy to use and you use a spray and all the sudden you don't feel anything after two sprays, let me give myself 12. So work your way into it.

And again, just hitting home, there are other ways you can do it. There's these sprays, there's these fancy patches now and even suppositories for some patients.

To hit home the adverse effects; every patient is different. I have a lot of patients that say over time if they ingest the psychoactive component to it, it actually helps with concentration. Everything in the brain has background noise; right? The narrative that we're always telling ourself [sic]; that's what I call background noise anyway. And how we deal with that, especially in modern day era is different, but basically concentration has become a skill in the modern-day society of multi-tasking. Some patients actually say that rather than being neurocognitively slow, that the cannabis they use helps them to focus on one thing at a time. So take it for what

[1] [sic] is used to denote the typed material was transcribed exactly as spoken.

it's worth. But you can wig out on it, so to speak, and that's the yellow box at the bottom. And you can have a bad trip so be careful.

But it can produce other symptoms too, obviously. Red eyes, it can actually speed up your heart rate, it can actually make you nauseated, it can actually make you, if you use too much, feel like you're going to vomit all the time. Some patients say there's withdrawal -- this literature is quite messy. It can make you somewhat irritable, lead to insomnia, heart rate changes and so on.

There is a bit of a risk of dependence if you will and habit forming but not in the same way as nicotine or what have you. And again, the literature is very mixed because it's not been followed or studied religiously. And when you go and study a patient population like ours for instance, everybody's using it in a different amount, in a different way and the strain their using is different. So we're recording all that information in the patients that go to our clinic and hopefully we'll be able to provide you with that information in years to come.

And it does cross -- so pregnant patients, it can get to both -- across the placenta and into breast milk. So take that into consideration; that we don't know how it affects fetuses.

A lot of patients ask about evidence of harm -- can cannabis lead to harm? Really the data on almost everything is pretty poor for all the reasons I've mentioned. A lot of it is old and a lot of it is done in patient populations that are using cannabis in very different ways from one patient to the next. The top row, the darker yellow, is perhaps where a better all shift is formed. It can lead to some neuro consequences; reduced memory, potentially pulmonary function, stroke and birth complications. A lot of these aren't well worked out but something to be aware of.

There is an association with heavy use -- and the problem is defining heavy use -- and testicular cancer. And for patients with underlying psychiatric disorders it's thought that it can worsen patients. This is colored by schizophrenia literature and patients that get schizophrenia both often use cannabis to help control their symptoms and then sometimes it worsens. So it's very colored by that and not well worked out.

In terms of other things listed on this slide there's really an inconclusive relationship as to if it causes anything harmful. And again, muddied by the fact that studies -- if we were all using cannabis in the room, we'd all be using it in a different way so you can't draw conclusions very well from that.

Since a lot of our patients are advanced in age, you have to take that into consideration. There's more potential for comorbidity or drug interactions because you have reduced liver and kidney function. Which can mean that the cannabis you're using, whether it's a pharmaceutical or plant product lasts longer. And since you have increased body fat potentially, you have increased distribution. And that can lead to more balance [sic] and falls, potentially more cognitive side effects, potentially more cardiac morbidity in a population already prone to that. It depends; I had an 88-year-old who goes around with a joint in his pocket and basically very anxious man, tried everything that you can think of. That Western medicine would normally think of. Found that when his daughters used cannabis through a joint, he was anxious, he was there, he uses it and changed -- revolutionized his life. He also, somewhat interestingly, out some [sic] five or six years from his GBM? So you never know. Really when assessing for any

patients, including your older patients, you have to do a patient specific assessment and be pragmatic in your approach. I have a slide that will take us through the decision making in a bit.

But you have to decide if you're going to do a plant or a pharmaceutical prepped product and then like I said, start at the shallow end of the pool and make your way into the deeper ends. So low doses, give at night, sleep offside effects, and obviously talk to your treating physicians about what it might interact with.

And basically those are the same counseling points I just mentioned. Are you going to inhale, are you going ingest? Do you want to smoke, do you want to vape, do you want to take some sort of oral product? You want to avoid driving when you first start using it, especially if you have no experience with it. And you want to monitor tolerability in general and there's a theoretical risk of infection in immunocompromised patients. You have to take that into consideration. And as I stated, avoid taking during pregnancy and breast feeding.

So where is medical cannabis or the pharmaceutical preps been used in oncology in general? Well as this study looked at cancer patients in general -- no brain tumor patients lumped in here unfortunately. But more used it for sleep problems, pain, weakness, nausea and lack of appetite. Those are the major reasons. Let's see, in brain tumor patients you have seizure control as well as mood related issues as well into that mix.

I'm going to talk about a couple of different indications along those lines that guidelines exist for, from the NCCN and the Cancer Association and organizations. One is chemotherapy induced nausea and vomiting. Again, these are busy slides with (inaudible 01:08:59) built in for you to refer back to. But in essence cannabis can help or prevent chemotherapy induced nausea

and vomiting. They are associated with approval for that. You can get a hyperemesis syndrome if you use too much cannabis though, so be careful with that.

Most of these studies are from the 1970s when I was born and even beyond so, they're kind of old. And now these days, we have a lot better anti-nausea drugs and so it's better to talk to your physician about what you should use based on what type of nausea your having, is it related to a drug or what have you. But certainly cannabinoids can be used and in fact, NCCN does say it is a reasonable option. However this is for pharmaceutical prep grade. There is really insufficient evidence as far as asthma goes for using medical cannabis here. And again, that comes back to the fact that it's muddy. Everybody's using it in a different way, for a different reason. Some people might say its nausea but if one person's vaping and one person's using oral, and so on and so forth, it's hard to draw conclusions.

However, (inaudible 01:10:11) both exist for this and can be used and you should talk to your physician about it. There are standard dosing for chemotherapy induced nausea.

The other is cancer related pain. So pain comes into effect for different number, different mechanisms, inflammation, mechanical invasion, nerve injury, what have you. Like I said, I mentioned earlier in the talk the cannabinoid system is involved in pain transmission, your perception of it as well. Your neurocognitive perception of it and so you can of course use a number of different pain medicines these days. Cannabis has been used successfully in HIV neuropathy and under neuropathic conditions and has potential synergy, beyond that, with opioids. So you can reduce your opioid need as well and you can reduce some of the side effects that opioids cause.

We can skip that actually.

So the guidelines that exist for this -- so the NCNN does advise that Drammanol can be used as an alternate agent to opioid induced nausea. They don't make comment on what you get from a dispensary. And again, ASCO says you might want to talk to your doctor about other pain meds; there's insufficient evidence to suggest medical cannabis as being helpful here. Although lots of empiric and anecdotal evidence exist here, of course.

If you were thinking about using prep -- pharmaceutical preps, I just listed the doses here, I'm not going to go through them and bore you. But again, you can refer back to the slides.

What about cancer associated ataxia, cannabinoids. This is when you're not hungry, not eating and that can be caused from a number of different reasons across different cancer types including brain tumors. From metabolic imbalance, an inflammatory response to treatment, and/or underlying disease and your treatment effects. Especially in brain tumor patients who've been radiated, sometimes your sense of taste and smell is reduced and can affect your appetite. So cannabis can be used here fairly effectively and cause you the munchies [sic] and basically helps with craving or wanting. Or pre-something appetites where I want to eat. But it also enhances your sense of taste and smell and so it can help get you back to where you feel normal with your relationship with food. Where it feels rewards rather than just something, you're engaging in nutrition wise.

It should be noted though that the higher THC that you use, that can actually cause some constipation by reducing gut motility. So again, the ratio of what you're using is to be taken into consideration.

This just shows you that (inaudible 01:13:02) has been used for cancer associated ataxia and give you some background on what other side effects are associated with it and how you can incorporate it, if you want to refer back to this slide and dosing to discuss with your doctor. We can skip that.

So guidelines; cancer associated ataxia, it depends for the NCCN on your life expectancy how you incorporate and use. Again, off medical dispensary you can use as you like but for pharmaceutical preps, they give you some guidance in terms of how bad your appetite is, what your life expectancy is and how to incorporate it. There's very little literature to support this, it's just sort of based on empiric knowledge to consider cannabinoids if you're having a lot of problems. (Inaudible 01:13:55) is sort of a guideline to this process which will hopefully be out in the next year, but in essence it can be used depending on your choice.

So what other roles and symptom management is medical cannabis used for? And as mentioned sleep; insomnia especially. A lot of brain tumor patients have problems falling asleep and staying asleep and choose to incorporate cannabis into their regimen. Mood states, anxieties. CBD is a great anxiolytic frankly with very little side effects. It can also help install euphoria and sort of help give you that exercise euphoria sometimes and lead to better coping mechanisms.

It does help with asbestosity if you do have a neurologic injury that leads to stiff muscle tone -- it can help with that. You just have to be aware that what you're using, if it has THC in it, it can cause gut motility and cause some measure of constipation.

As I mentioned, and this slide hits home, there's really not a great association of cannabis risk. Meaning does it cause other kinds of cancer. Does smoking marijuana lead to lung cancer or other types of cancers? There's really no conclusive evidence at this present, again, that occurs because of the fact that patients are using different products in different ways and as such it's hard to know.

A FDA study in 50,000 men did show that heavy cannabis was associated with a higher incidence of testicular cancer. This is very biased though, as most of those patients were very sedentary and had other risk factors so it's hard to know.

I'm sure you're all dying to know what about its role in brain tumors. There's a wealth of pre-clinic literature that's out there, that's in its initial stages or infancy. I really just have this slide and the next to talk about what role it might have in brain tumors. There's a lot out there; again, it depends on the product you're using. And to get a pharmaceutical prep to use in an animal model or the dish model takes three or four years of effort to get approval for both by the federal government, the state government and even at a liberal place of work like mine -- UCSF -- they won't help you store it.

The FDA has to come and inspect my lab and my office to see that I can take this much cannabis. Which, of course, you can buy on the corner of the street a hundred times, and then I have to lock it behind three doors in a cabinet that's attached to the wall that's also locked. To do any kind of research you need that set up. The FDA comes to inspect you with literally a book, a paper book, that they then check off with you in terms of all the security that you need. It's

extremely interesting; this very antiquated way of regulating this and needs to obviously needs to change.

So it's very difficult to do. You're not allowed to use dispensaries in research on any academic campus that I know of, because of the legal ramifications. That being said, what literature is out there that supports that cannabis -- both THC and CBD or any combination -- may have a role in fighting brain tumors. But the role has been unclear. There's five potential mechanisms that have been supported that it's cytotoxic. That it kills tumor cells. That it's cytostatic; that it stones them and gets them really tired and they don't grow. That it can fight blood vessels associating with the tumor, prevent invasion of mobility, it may even have an anti-stem cell like quality to it.

But again, what's been used has been different. Different studies; a lot from Spain. Not reproduced yet anyway and need to be studied. Unfortunately, one of the companies that was in the U.S. that was supportive of this ran into problems with the federal government about their other drugs in the opioid world and therefore at present doesn't have the resources to support cannabinoid research. But maybe we'll get there with some of our European partners.

As I mentioned, relative to brain tumors and brain [sic] in general, there is epidyalects that is approved for seizure control. A lot of patients use medical cannabis that they get from dispensaries for this purpose. I mentioned that there might be a role in fighting glioma in general. We know that glioma has those receptors; CB-1, CB-2 sometimes presenting on the tumor itself. We know that the drug gets into the brain from the psychoeffective component of

course. There's also actually animal modelling that supports, although it's very small, that cannabinoids can be neuroprotectors of the normal brain during radiation.

This is a very hot topic where I live. How much cannabis should I go on during radiation? I don't know. I know that the literatures are quite small, I know that we're working on it. Again, we're in process of having an application in to use cannabinoids to study this in a radiation model but it's probably going to take another year or two to get federal permission and then probably a year on top of that to get state permission. So talk to me in about three or four years.

GW did have a clinical trial, I put the link up here, that was in the U.K. They gave Cativax which is that pharmaceutical prep approved for MS patients for (inaudible 01:19:13) and they give it to brain tumor patients -- glioblastoma patients. It wasn't randomized but very small study that the patients who got Cativax plus radiation and Temodar did better than the patients who didn't get Cativax. What their next step is, I'm not sure. The U.K. and Europe have regulation also that needs to be thought of. We're hoping that they proceed.

You can also get product, cannabis product, from NIDA which is a federal agency and then put that in clinical trials. Columbia does have a trial with that. I don't know how or who that got that from but great for them. We've been trying for years and just can't do it and can't get permission. UC Davis is about to be able to grow its own product. We're hopeful that in four or five years from now that we'll actually have clinical trials for glioma patients as well.

So drug interactions; I'm not going to take you through these slides in great detail, but you do need to know that whatever cannabis product you're on can interfere with your other

medications. It doesn't interfere with Temodar, it doesn't interfere with CCQ, but it can interfere with some of the other medications you might be taking. Lots of slides, but these are just a list of some medications that other cancer patients or some brain tumor patients use and you should discuss with your physician whether the cannabis you're using is either speeding up your metabolism or potentially slowing it down.

There's more information available about this topic from each of the pharmaceutical preps to the link that you can refer to.

So real world considerations. What do I use is going to be the question. Go and use your pharmaceutical prep, do I go to my dispensary? Technically in California I'm not allowed to tell patients, "Hey go to this or that dispensary." It's against the law, their supposed to find it for themselves. But I can tell you that the answer depends on you. Where do you want to start, what's your previous experience with it? Do you want to know that what you're getting product wise is consistent and standardized? If so, you have to go with a pharmaceutical prep. If you're willing to take more of a risk, you go to a dispensary or grow it on your own. Got [sic] a lot of patients that grow it on their own, especially in Santa Cruse. If you've ever been to Santa Cruse, you'd get the joke. It's actually not a joke, it's openly used by everybody. You don't have to have a tumor.

It depends on if you want quick onset, do you want it to last longer, do you want it to help you sleep? All those things have to be taken into consideration. I gave you the dose of guidelines earlier, that's my best guess at rough starting. You then have to find for yourself. I

will tell you; most patients end up using in a manner that benefits their symptom relief. Whatever's the most important to them.

Be it mood, be it seizure control, be it what have you. And often it becomes a very social thing with the remainder of the family members sometimes as well. This is my step wise approach. Again, I'm not going to take you through each box, but it does depend on those things I mentioned plus what other drugs you might be on and what other symptoms you might have neurologically from your brain tumor or from treatment. And then, I think, it should be openly discussed with your treating physician.

I get patients who call me all the time and say "Oh, my physician's not very open to it. They tell me to stop. They're uncomfortable, they don't know what it does." And I say "Well, you know, here's some resources that you can refer to" and I'll show you in a bit. But in essence, sometimes you have to educate your treating physician that this is here and present and this is something you're interested in. And then to ask them to engage in a conversation about it.

I find that most treating physicians are open but most don't know a great deal about it, because frankly, there's not a great deal to be known about it yet.

One other thing to take into consideration. If you're going to a dispensary and/or buying online, you have to make your mind up about how do you value that source? Is it someplace or some person that can tell you about what pesticides they're using, what heavy metal might be in the ground, what other kinds of side effects of toxins are you exposing yourself to? And the testing is different per state. So we have testing in California that contacts dispensaries and puts out information about them, but I'm not familiar with each state's reporting guidelines for those

types of things. But it is something that's generally available online and you can generally ask the dispensary. And/or online source that you're getting it from.

So UCSF is not allowed to store marijuana as I mentioned. Most academic centers fall into the same issue so in fact, visitors and patients are not allowed to bring it. There's national news five or six years ago where an MS patient lit up in the lobby. Not smart to light up a joint and she got kicked out and made the news and so on and so forth. Because it's illegal, right? From a federal level and we might use funding, especially some people in office right now.

But we want to be kind and you have to understand your own academic facility or hospital's facilities policies on use. Especially if you get admitted, you probably have to supply it yourself and medical staff won't be able to help you with it.

The perfect challenge for research is all the things I mentioned. Again, there's more unknown than known. The legal barriers are really what prevent me from making any further headway at present, either preclinically or clinically. Hopefully those things come to the forefront of consciousness in the nation. Both from a medical point of view but also from a legal point of view and that we can make some inroads as to whether this has a true role in just either symptom relief or tumor treatment within the fairly near future.

Here are some resources that I've relied on over the past few years. And websites that can give you some information. Obviously, this is a moving target itself and I'm happy if anyone in the audience thinks I should add to this. Frankly, most of this has been supplied from patients to me, rather than relying, again, on my own personal experience.

So I thank you for going on this trip with me and I'm happy to take questions.

[Applause.}

Q: I'm Trevor from Indiana. So is it help or hype?

A: My own personal opinion is that there's definitely symptomatic help for all the things I mentioned. Sleep and what have you. Mood regulation, it's a great seizure medicine in my opinion. You do have to find how and what you're going to use for your own personal liking. In terms of symptoms or side effects it produces.

As far as anti-tumor; I don't know. In the lab we found some interesting results that we weren't able to publish because of the legal problems that the company had with their other drug pipeline and we've not been able to build on that because GW won't supply it to us. It's another company that has problems.

We're doing a study with all our patients now. All patients that come to UCSF get interviewed about their cannabis use and we're looking for whether or not there is a common thread. It is interesting when we look at our long-term survivors that almost 80% of them are some type of cannabis users but that doesn't mean anything, right? It's still a gray area and most patients use. So draw conclusions from that as you will.

Q: What are your thoughts on pediatric use? You touched on the elderly but I'd like to go on the other spectrum.

A: Sure. Well, I don't treat kids so it's hard for me to know. The peds are UCSF anyway are very cautious about it because of obvious potential issues of abuse so to speak, but also the stigma of it, right? And it's funny how that differs even in the Bay Area. That being said that at

least one of our Peds Neurooncologist, especially for older patients, will use -- for symptom relief if applicable. For nausea, for some of the neuropathy associated with chemotherapy. Because frankly for some patients it's less sedating than opioids or what have you.

So again, I think a pragmatic approach is reasonable. Whether it has an anti-tumor effect in the pedes population, again, I can't answer. And I think that (inaudible 01:27:41) even smaller than for adults.

Q: Because of our Draconian laws, where -- outside of the country -- is the best research being done?

A: Probably Spain and the U.K. The Spanish have more lenient laws, so to speak and most of the literature comes from there. To some degree from the U.K. and a healthy amount from Israel as well. But there almost always very small studies.

Q: Hi, thank you so much for your presentation. My name is (inaudible 01:28:18), Senior Health and (Inaudible 01:28:19) Specialist with Brain Tumor Foundation of Canada. My first time at this conference, it's amazing. Well done.

Just a comment really. Interesting to hear what's happening here in the States versus Canada. Cannabis is now officially legalized in Canada as of this year. So all the dispensaries are done, they're illegally. What we have are cannabis stores where you can go in across the country at any time to purchase cannabis but then there's clinics as well, with physicians and nurses as well who are educated on medical cannabis. They are educating people on cannabis as well. Just kind of an FYI, just wanted to mention that to the audience that we're seeing some big researches as well.

I'm not sure if you know, Dr. Butowski, but there's an association called the Canadian Consortium for the Investigation of Cannabinoids and I've had the opportunity to attend one of their conferences. And it was just amazing to see the number of physicians that attend this conference every year. Just to learn from each other on cannabis and medical cannabis. So if anyone is interested in more about that the short form CCIC. They're a federally registered Canadian nonprofit organization focused on basic and clinical researchers, healthcare professionals and educators are promoting research and evidence-based education concerning medical cannabis. So just FYI.

A: Great, thank you. I appreciate it. Any others?

Q: I have a question.

A: Yes.

Q: The 80% of patients you observed with long time survival, as you mentioned, they used cannabis. Do they use topical, ingestion, inhalation?

A: Sure.

Q: That's one question. The other thing; is there other (inaudible 01:30:11) such as young age? I tried to eliminate other possible factors for him.

A: Yeah, of course. So again, I think the population we've studied that led to my interest in determining whether cannabis is playing a role here, is oftly [sic] biased by the fact that in the Bay Area it's been acceptable to use for 20 years. So all patients are; what else can I do, what else can I do? And cannabis is a very easy answer where I live.

I would say if we went back and studied our population and did really poorly and also find the same answer that 80% of them use, I just don't know. So most people, I think, end up using some kind of very sophisticated use like vaping or some type of edible because it's thought of as more healthy than smoking. But again, they use it in different forms, different strengths and what have you.

I can't comment on whether or not it's affected or has led to other behaviors that have increased survival or frankly -- there doesn't seem to be any common thread beyond the known molecular features for long term survivors that are present. Except I hasten that maybe Jeff one day will be able to testify personality profile in those patients who have a somewhat more optimistic determination towards their disease also do better than patients who do not. Which is a bit of an unfair statement but how you meet with psychology behind it is as important as anything, right? The mind set I think is extremely important.

Thank you.

[Applause.]