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9TH ANNUAL NYS SEXUAL HEALTH CONFERENCE: EMERGING ISSUES AND PRACTICE UPDATES - DAY 3

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[video transcript]

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Dr. Robertson PEP is a practicing neurologist and clinical researcher. She studies chronic pain and judicious opioid prescribing and the neurologic complications of HIV including autonomic neuropathy and HIV associated neurocognitive disorder. She is the director of the Mount Sinai new HIV program, the Parent Project and the autonomic laboratory, a nationally and internationally recognized researcher, Dr. Robertson pap has been funded by multiple grants from the National Institutes of Health, and the Agency for Healthcare Research and Quality. Her expertise has been recognized by her inclusion on numerous committees and advisory groups, including the American Academy of Neurology Science Committee, neurological sciences training review group, global HIV pain Task Force, and Executive Board of the World Federation of neurology, autonomic disorders subspecialty group. Thank you, Dr. Robinson, for joining today. And I'll now turn it over to you.

01:06
Great, thank you so much, Phoebe. This is my financial disclosure, which is a membership on a Scientific Advisory Board of neuropathic x. So here are our learning objectives for today, I'm gonna start by describing the current landscape of medical marijuana focusing on New York state. We're going to talk about the different vailable forms of medical marijuana in the state and how we use them and provide them to our patients. And then we're going to focus a little bit more specifically on people living with HIV. I just like to start out with this orientation slide. So we're sort of all on the same page. Cannabis is one of the oldest cultivated plants. There are two main varieties that you'll hear about when people talk about cannabis, hemp and marijuana. And they're both different forms of the same cannabis plant. Marijuana is the form that's used for both recreational and medicinal purposes usually, and it has two main active components which are both referred to as cannabinoids and cannabinoid just means a certain kind of class of chemicals. One is THC, and that's the psychoactive component and the other is CBD. Hemp on the other hand, by definition is any cannabis plant, which has a very low concentration of THC, 0.3% or less. So this is a somewhat arbitrary definition. So there's nothing really inherently different about versus marijuana. It's just simply that THC concentrations with a legal definition. Any other cannabis that has a higher THC concentration will be marijuana. And hemp is mostly used for industrial purposes. It can be used to make fibers for rope or clothes and certain food items as well. Hemp is also now cultivated a lot for its ability to extract CBD from it but not THC and I'll be talking more about that ladder. There are lots of potentially medicinal cannabis related products and so when people say medical marijuana, they mean a lot of different things. And some of that varies state by state. Sometimes so sometimes marijuana can medical marijuana in a given state could be just the marijuana plant itself, it could be in its most natural form. And other states require that it has sort of more processing so that it comes in more traditionally medicinal forms like tinctures or pills. We also have the CBD products made from hemp, which are sometimes referred to as medical cannabis. And then separate from that are the pharmaceutically manufactured cannabinoids. And so there are synthetic versions of these

synthetic THC. So these are medications that are either they're very similar to the natural form of THC but are manufactured in a pharmaceutical setting. And then there are other pharmaceuticals that are actually derived from natural cannabis plants. In the US, the only version of this that we have is Epidiolex. And there are other versions that are available outside the US particularly nitpick Smalls. Or Sativex. I also like to point out on this slide that there is terminology that gets used things like synthetic cannabinoids, or synthetic marijuana or fake weed. These terms typically refer to these unregulated manufactured drugs of abuse that are not even necessarily related chemically structurally to cannabinoids, and that they are often highly toxic and don't have any medicinal use. So sometimes these are referred to by street names like spice and Ketu. But they have a lot of different names and there are a lot of different chemical compounds as well, but they really have nothing to do with marijuana other than being a misnomer. So marijuana has been around for a long time. It's used by humans probably originated in ancient Egypt in about 2350 BCE, and it's been present in multiple different cultures and multiple different historic eras and you can See here on the right of the screen different ways in which it's been written in different in different languages. There are different quotations through that have been discovered that refer to the use of marijuana and cannabis for medicinal purposes. So an example here from 1700 BC, shows that it is was used as a treatment for the eyes in conjunction with celery. And in 1640 ad that itch is used for different kinds of pain, which is some of the same uses that we use for today, particularly the pain. I think that this is an interesting quotation to this one from 1640. In particular, that it talks about mixing the juice of the cannabis with oil or butter, which is still done today in the creation of edibles because the the cannabinoids are not water soluble very much, they're much more soluble in lipid. Marijuana also has a really interesting history in the US. In colonial times it was the cultivation of cannabis was encouraged because it was a useful a useful crop, it could be used for making ropes for ships and or clothing. And this sort of continued on until 1906, which was the first time that there was laws regarding marijuana. And this is the Pure Food and Drug Act which require that products that contain marijuana should be labeled as such. And then over the ensuing decades, marijuana sort of became increasingly stigmatized and marginalized in the 1930s there was a real intensification of anti marijuana propaganda. Some of you may have seen this, this classic propaganda film called Reefer Madness, which showed all the bad things that can happen to you if you smoke marijuana. And then this was codified in the 1970s with the controlled substance Act, which still really has implications for us today. Because in this act, marijuana was scheduled was designated as a Schedule One controlled substance, which is a drug that has no currently accepted medical use and a high potential for abuse. So this designation still exists, although there's a lot of talk about whether it's appropriate anymore, but it really impedes it impedes federal laws from changing regarding marijuana and also impedes research. And then the 1980s we saw the war on drugs, there was this three strikes, you're out roll where you could get a life sentence for repeat minor offenses, including drugs such as marijuana. Starting in the 1990s, things started to loosen up. The first legalization of medical use was in 1996. In California, then there was the first legalization of recreational use in 2012. In Washington and Colorado. In 2014, a federal law was passed, which barred the Department of Justice from spending any money to interfere with the implementation of state medical cannabis laws. So while cannabis continued to be illegal on a federal level, and technically the federal government could prosecute the states for their laws, if they weren't allowed to use any money to do it, it essentially tied their hands and so it protected the states from interference. And then

the last big change was in 2018, when there was so there was a budget measure called the farm bill which was passed and it included a provision to make CBD products that were derived from hemp that is a form of cannabis with the lower THC content. It made these products legal. And this resulted in tremendous growth in the CBD industry. And that was sort of the time if IT folks remember where CBD was suddenly everywhere, like, you know, there was CBD water in the CVS, you know, on the corner. And that was because of the Farm Bill. We still have quite a variety of different cannabis laws state by state. And you can see here the dark sort of greenish brown colors. In these most mostly coastal areas, including New York show where both recreation and medical use are illegal. And then the yellowish color is medical use only and then the gray is where there is neither medical nor recreational use. What are the active ingredients in medical marijuana? Well, there are known to be over 400 different chemical entities contained within the natural plant. And about 60 or so of those are designated as cannabinoids which just has to do with the general structure of the molecule. Here's sort of a picture on the right hand side of the screen of what that structure looks like. There are four main cannabinoid compounds and then in particular, there are two of them that tend to get the most attention and that's THC and CBD. THC is the one that has the major psychoactive effects. So it's the part that makes people feel high. And CBD does not have particularly psychoactive effects on its own. There are also other you know, among these other kind of 400 chemical entities. There are many that have been identified, and they're in general referred to as entourage compounds, particularly within the cannabis industry. And these fall into two general chemical classes which are the terpenes and the flavonoids.

10:05

Medical marijuana and cannabinoids in general are able to exert an effect on our bodies because we have endogenous receptors for them. And these cannabinoid receptors were discovered in the late 1980s and early 1990s. And there are two main forms of them that cannabinoid number one and two receptors. And the different effects of CBD and THC and other cannabinoids on the body have to do in part with their affinity for binding to the receptor number one versus the receptor number two. So the receptor number one is extensively expressed in the brain and THC binds the receptor number one particularly well which accounts for its psychoactive activity. And the CB two receptor is more in the periphery. So it has it is largely expressed on immune cells and other cells throughout the body. And this is thought to be the mechanism by which cannabinoids can have an immunomodulatory effect. We have these receptors in our bodies because we do also have endogenous cannabinoids that are made by our own bodies, and those are referred to as endocannabinoids. And there are two examples of them here listed on the bottom of the slide. And then in contrast, the cannabinoids that come from plants are sometimes referred to as phyto cannabinoids. So here are here's that T, a nice table taken from a review article that was published in 2012. That sort of shows some of the different effects of THC and CBD. So, for example, CBD has more of an anticonvulsant effect. THC is more of a muscle relaxant as compared to CBD. In terms of protection against nausea effectiveness is an antiemetic that's present for both appetite stimulation is more of a THC type effect. So what about these entourage compounds that exist in in the cannabis products and in cannabis itself? So this, the idea that these terpenes and flavonoids and other non cannabinoid compounds in the marijuana should have an effect is partially marketing. It's a part of the cannabis industry is sort of idea about what kinds of cannabis will be good for what

kinds of disorders. So, if you go into certain this is less true in New York State, because of our laws, but in the other states, if you walked into a dispensary, they might tell you, you know, this, this particular strain or form is going to be good for X y&z disorder as opposed to another. There isn't really good scientific evidence to either support or refute that. So we don't know that it's not true, it's just that there isn't really a lot of evidence to support it. So the terpenes are one of the main classes of these entourage compounds. They are a broad broadly occurring Class of, of compounds that occur in lots of different kinds of plants. In general, their job is to protect the plant from predation and attract pollinators. So if you ever, ever used an essential oil, whatever is in that essential oils, probably a terpene. And it comes in different There are eight different classes of them that occur. And they are the parts that is particularly referred to as altering the effect of THC, again, not particularly evidence based, but different forms of cannabis that have different amounts of different kinds of terpenes may be marketed as being, for example, cerebral and euphoric or more of a physical, mellow, sleepy kind of feeling. I mentioned these things because it's it's stuff that comes up with my patients a lot where they'll say like, oh, well, how do I pick one what, which, which one is good for what? And, you know, I like to kind of point out that, although it may be marketed as such, we don't really know that that's true. So let's switch gears a little bit and talk specifically about New York state. So New York State has had recreational cannabis legalized in the past couple of years and has ever had medical marijuana for several longer years. The legislation that was passed in 2021 was called the New York State cannabis marijuana regulation and taxation act. It the Act established the Office of cannabis management. It also expanded the list of medical indications for which medical marijuana could be recommended and permitted home cultivation for medical purposes. And I'll go over that in a little more detail. It also provided for the oversight and of the production and quality control of the products and for the taxation structure. And it had a very sort of social justice bent to it in that it specifically indicated that 40% of the proceeds should go to education 40% to community reinvestment, particularly toward communities that had been disproportionately impacted by drugs themselves and then also the war We're on drugs, and that 20% should go to drug treatment and public education. Um, it also provided for people who had been convicted of something that would now be illegal to be able to have their cases re examined. So as most things involving the government, this took a long time to actually kind of get up and running. So the law was passed in 2021. And then the first legal recreational marijuana dispensary opened in December of 2022. So just a couple months ago now, and this was in New York City, and it was actually opened by Housing Works, which folks from the New York City area who take care of people living with HIV you might be aware of is a sort of an institution that's been around for a long time as a social service agency serving people living with HIV. So there are also other, since since this is open, there have been there have been others as well. And I'm sure that the recreational marijuana dispensaries will continue to grow quickly now that they have their infrastructure in place. So as for the medical marijuana program, this has been around for much longer, it was legalized in 2014 by the Compassionate Care Act. And the ACT stipulated that medical marijuana could be recommended to patients who had certain medical conditions. This is in contrast, still to the federal law, which is still that marijuana should be illegal federally. And so the state law in New York as it is, in many states conflicts with the federal law. So to issue a certification for patients, any kind of a diversity of healthcare providers can do this. So it doesn't have to be an MD It can be do pa nurse practitioner, I think midwives and dentists are now allowed as well. But you have to be licensed, you have to be a licensed provider and then

registered with the state in order to prescribe these these products. So and you also have to do a special training, which is a two hour course, that can be accessed online. And so these are the courses that that satisfy the the requirements. They're all available on the Office of cannabis website, which is actually very comprehensive and well organized. So they tell you if you want it to be a provider of medical marijuana, how you go about doing that. And then once you have your training, you can go to the New York State House commerce website, which is most which is probably familiar to most of us, it's the same place that you go to check, I stop, and then you can register yourself there. And then that's also how you ultimately register patients for medical marijuana. It's a very, it's a fairly straightforward process once if you are a registered provider, then when you go into the into the health commerce system, you have this app here, which is the medical cannabis, DMS. And if you click on it, it just walks you through the process of certifying a patient, you issue the new certification, you put the patient's information and last name, date of birth, and then you just enter some simple kinds of demographics and such. And it takes maybe five to 10 minutes, it's pretty, it's pretty straightforward and simple to do. And I mentioned before that the law has written stipulated certain conditions that you have to have in order to be qualified to receive medical marijuana. And this is the list that we have currently at is kind of expanded over the years. At first it was just a few items. And then they've been kind of progressively adding more conditions. And now this is almost moot because they have this other this other category which you can check. So you don't even have to specifically have one of these diagnoses, which seems to make sense since that since recreational use is legal now and you don't have to have any diagnosis for that. But they've made this more liberal as well. In addition to indicating what the diagnosis is, by the way, if you do happen to indicate HIV AIDS as the diagnosis, then there is an extra step usually, to make sure that the patient is consenting to having that information shared with the state, you can use that diagnosis. It doesn't show up on the patient's card or anything. But some patients just prefer not to have it there for the sake of privacy. In addition to those those conditions, you can overhear in the bottom give some recommendation as to what kind of formulation you are recommending that the patient has. You can also free text in here. any limitations on what you would like the patient to be able to receive. This is a little bit of a moot point again now that we have recreational marijuana because it's not like you're giving them access to something that they couldn't get otherwise. And I think most providers don't spend a lot of time making specific recommendations since they're for the most part not binding. And you can just for simplicity check off per pharmacist consultation, and most dispensaries will have someone available to help the patient decide what they want to purchase.

19:56

So the patient then so you will then print out a form and such as this, and then it gets signed and sent to the patient. And then at the moment, the patient has to go in and log in to a computer system and put in some more additional information. This is about to be discontinued. And I haven't done this, you know, in the last month or so. So I don't know if it has been discontinued yet. But soon, they won't have to do any of that. And they'll just get this card in the mail, the card itself doesn't expire. So once they have the card, they can keep it forever, but the registration does expire. So you just as the provider have to go in and renew the registration once a year. And, you know, it's my practice that this should be part of a regular prescribing type of relationship. And so I have my patients, most of my patients who are prescribed for I see

for something else anyway. And so I'm seeing them more frequently. But I have a few that I just see for for this. And so those just come in once a year to sort of check in and see how they're doing and renew the prescription, or the registration. I try to avoid saying the word prescription because it's not really like prescribing because you can't be specific about it. But sometimes I forget. Okay. So if we do want to recommend something to our patients, and I usually do have a pretty thorough conversation with them, relations that are available, and what they might choose, I find this graphic to be kind of helpful in in consulting patients about the uses of THC versus CBD. So I think the simplest way to think about it is that CBD is like is a good place to start. If patients want to, it's really important to them that they not have any psychoactive side effects. So people who are working and have in require a lot of concentration, you can take CBD and and most people will not feel anything from it, they'll be able to go about their day and not feel sedated at all. CBD is also CBD and isolation is also indicated for the treatment of seizures, it's usually not a first line seizure treatment. But if that's if for some reason, that's what you were using it for, then you would definitely want CBD. And probably some of this the anxiolytic kind of effects may be CBD more may be better off with CBD. The flip side of that. And what's related to it is that THC consumption has made people feel paranoid. So if that's a concern, then CBD alone may be better. In the case of my patient population, almost always people who I'm registering have experience with with marijuana in the past, so they know how it affects them. So a lot of this is sort of moot. But those are some of the things that I do counsel people about. THC, on the other hand, is probably more helpful if they are looking for something that's an appetite stimulant or for GI symptoms. Or if they want the sedating effect, like if it's something in terms of like want needing to go to sleep or insomnia. So there are different routes of administration available within the MediCal program. And I'll show you some of the specific products just as examples on the next slide. But there's three main routes. One is a vaporized or inhaled route. This has the shortest onset of action and the shortest duration of action. And, and typically requires some kind of vaporization device. As medical providers, we kind of tend not to like to recommend that people smoke things. But smoking would also count as as the inhaled route. The transmucosal route is typically what I recommend most to people, it's kind of a nice middle ground, it has an a relatively rapid onset, a longer duration. And it kind of comes in it can come in like a little dropper or a spray where they can put it sublingually or in the side of the cheek and it can be absorbed through the mucosa. Patients just need to be counseled not to swallow the liquid. And nothing bad happens if they do but it's just much less effective. Because instead of transmucosal route, then you're basically getting an oral route, that the oral route has the longest onset time and then also the longest duration of action. One main downside to the oral route is that any cannabinoids that are taken that way undergo first pass hepatic metabolism, so you lose a lot of the product out of that. And the other thing that people need to be a little bit aware of is that because the onset of action can be pretty slow. Some folks may feel like they haven't taken enough and then may take more and then all of a sudden feel a little bit overdosed because they've they've not anticipated how long it takes to work. So that's something that I like to counsel patients about. I think the oral route tends to be less popular, just because people are kind of over having too many pills already and don't really want to go that way. So within New York State the the medical dispensaries are very distinct from the recreational dispensaries and they are really tightly controlled. So they usually heard used to medical marijuana, they do sort of a soup to nuts like they do they produce it, they package it and they sell it in the dispensaries, they are produced the the medical marijuana is typically

produced from genetic clones. So like all the plants are exactly physically the same. And that way they're like they can kind of control their product better they are producing an indoor facilities that are also under tight security. So again, a very controlled product. The state keeps an up to date list of all of the dispensaries that are licensed to practice and that you can see here, the link for that most most of these dispensaries now also sell online that sort of started picking up during COVID. So you can see. And that's sort of a nice place to start for some patients because they can go online and look at all the different products that are available. These have also become much more diverse over the years. When we first started out in the medical marijuana program, they were really just the the sort of vape pens, the tinctures and the pills, and now particularly with and this was sort of liberalized slowly, slowly without changing of the law over time. And then when we went to having recreational available then this sort of opened up the door to have lots of different products. So now this is just like a smattering of different products that are available. From some of our medical dispensaries, you can still see sort of these ones that are more traditionally medical looking like little white pills or you know things that you might dispense in a dropper as a as a sublingual tincture. And then we have things that really don't look very medical at all over here that just looks sort of more like traditional marijuana. These are just some other examples. There have been all kinds of different things. Some patients have used these these devices. These are called these volcano devices that take these little pods and look like you want to get coffee out of them or something and they vaporize the product so that it's below the level of burning so you don't get a lot of the the purportedly anyway you wouldn't get the ill health effects of smoking but you'd still get those vaporized products. They're also lozenges, sprays, and things you can dissolve into water to make tea. So those are sort of a summary of the products that are available under the New York state medical marijuana program. We also have a lot a lot of CBD products out there in this country. And that, as I mentioned, is because of the 2018 farm bill which legalized all CBD products that are hemp derived. So you may remember that hemp and marijuana are the two forms of cannabis. And they are arbitrarily distinguished by their level of THC. So if your plant has a fair strain of plant has a low THC content, then it is a hemp plant, and you can grow it in a much less controlled environment. So you can see you know, it's grown out in the field like a regular kind of agricultural product, as opposed to under these very tight indoor facilities.

28:04
So it's legal to make it anywhere, you know, in the US. But there are certain caveats that that plagued the industry a little bit. So it requires an awful lot of hemp because it has this this form of cannabis has low cannabinoid levels, it requires a lot of hemp to make enough cannabidiol or CBD to sell. And so because of that, and because it's a traditional agricultural product, there's potential for contamination with pesticides, microbial contaminants like mold and bacteria, heavy metal from the soil. It's a bio accumulator. So it can suck up heavy metals if the soil has them in them. And then you have to use solvents to get the CBD out of the hemp. And so there can be residual solvents in it as well. The industry has also been pretty inconsistently regulated at the federal level. So there's been a lot of variability in the quality of products that are available. So this was these are just a smattering over here on the right of like the many, many, many different things that are available online, including CBD water and creams and gummy bears, and really pretty much anything you can think of. And there was a little bit of a bit of an expo ze done by the Associated Press A couple years back now showing that a lot of these products are

either not what they say they are and that they don't really have very much CBD in them. Or even worse, I guess is that some of them are contaminated with other things. This particular study, they were looking at CES, they had 350 different products. And this is a little bit of a biased sample because they were products that were particularly identified by consumers as being suspicious in some way. So probably worse than a more general sample. But anyway, 128 of them tested positive for some extraneous, chemical and then including gummy bear products, which I think are particularly worrisome because they're attractive to children. And then they noted that three of these samples even contained illicit fentanyl, which is obviously very concerning. So, for my patients, I just, I think it's nicer to just use the New York state registered products because that program I know is very tightly controlled. But if they do want to order something online that's CBD based, there are ways of knowing whether it's a high quality or not. So there is something called the US hemp authority. This is not a governmental body at all, it's an industry self regulation group. So you have to take it with a little bit of a grain of salt. But they do at least have on their website, a list of their standards, and it's a pretty detailed and transparent list. And then they evaluate companies, and see if they meet their standards or not. So they do have a certification list on their website of, of companies that they approve of. And then I think what's also more more objective, and often easy to find on the websites of the CBD companies are these certificate of analyses. And in particular, there's a lab program called ISO 170 25. That is like a is a highly regulated form of lab testing. So you can know that it's a standardized form. And so these tests, this is an example here in the yellow Have a good one. So what you want to see, for example, is that it does not have any THC in it. So here, D nine THC was not detected. But CBD was detected, and it was 99.4% of the weight. So that's good. They tested it for heavy metals, and there were no heavy metals present. And then they tested it for bacteria and yeast and mold. And that was not not present. And it should be dated as well. And kept up to date. So you want to see that one of those is a pretty recent testing. So one thing that patients will will sometimes ask is, well, what dose should I take? And that is a really tricky thing to answer, because it's not really very well studied. So for CBD alone, that answer is maybe a little bit easier. No, notably, the efficacy of CBD alone without THC is not proven for most disorders. So with the exception of epilepsy, so it's really hard to say what a dose someone should take when we don't really have evidence that it's that it's, you know, efficacious at all. But you know, I tried to be helpful with this with this question. And so what we can say is that well, with Epidiolex, at least, which is an FDA approved, plant derived CBD, we know what the dosing is because it's gone through the regular FDA regulatory process, and that initial dosing is 2.5 Mix per kick B ID. So if you're in 150 pound person, say would start with 175 B ID, and that's an oral dosing. So you know, for for an adult, then you can say maybe something like 100 to 800 milligrams would be a reasonable oral administration of CBD. We know that transmucosal and inhaled versions are much more bioavailable and much more gets into the body. And so you know, you want a much lower dose there and so something like maybe five to 30 is reasonable. For THC, this is like really even less well established, because a lot of the studies done, were done on like smoked and smoked marijuana cigarettes. So knowing exactly what the dosage there is, I think is tricky. But we do know at least what the dosage is on the synthetic pharmaceutically manufactured forms of THC. So the comp the one that we're probably all most familiar with is Dronabinol or Marinol, which is synthetic THC that's FDA approved for the treatment of appetite. So as appetite stimulant and then also as an anti emetic. And Marinol comes in capsule form the dosages of 2.5, and five and 10 milligrams, so at least

we know sort of what that dosage is. The other pharmaceutical cannabinoids NAB alone is very similar. nitpick smalls is the version of the natural plant derived THC CBD in a one to one ratio, but we do not have that in the US. It's approved in Canada and Europe. And Epidiolex is the version that we do have in the US. I was pretty excited about that when it first came out because I was thought that it would be a potentially nice thing to be able to provide to my patients. It is very difficult to get covered by insurance because it's only FDA approved for the treatment of Lennox gusto and Dr. AIDS syndromes which are these rare childhood epilepsies. So sometimes you can get it approved for someone with a different kind of epilepsy, but it's pretty hard to get entirely off label. Oh, and I think I failed to mention before with the the medical marijuana with the New York State products, none of that is covered by insurance so it's all out of pocket and it can be quite pricey. I'll just pop back up to that other slide. So you can see some of the prices over here. Not really non trivial, you know some of the ones that are the whole flower so like the least processed versions can be can be cheaper because they don't go through the kind of processing. But still it can be the expense can be an issue for patients. Okay, so a little bit about cannabinoid research. This has been researching cannabinoids in the US has been notoriously difficult and most of that stems from the fact that it is a is a controlled substance and a schedule one controlled substance like I spoke about before. And actually up until 21, all cannabis research in the US that actually used the plant version of cannabis, had to use cannabis coming from one single source, which was via the federal government, the National Institute on Drug Abuse, or NIDA, that has loosened up a bit, there are now seven different approved sources nationally. So there's a greater diversity of supply. So that's a good thing. But you still have to, if you wanted to do medical marijuana research, you still have to get your products from one of these approved sources. So the irony of it is that, you know, I can recommend these medical marijuana products to my patients, but I can't actually do any research on the actual products that are available in New York State. Nonetheless, there's lots of different clinical trials, ongoing in lots of different indications. You can see that currently, if you do a search in clinical trials.gov, there are 167 different studies, different clinical trials pertinent to cannabis ongoing with a lot of different different conditions that they're studying, including inflammatory conditions, HIV associated neuropathies, pain, and all sorts of different psychiatric conditions as well. So what what do we know about what medical marijuana might be good for? This is a very, very comprehensive monograph that was published in 2017 by the National Academies of Science, Engineering and medicine, and they basically reviewed all all the literature up until that time of what the health effects of cannabis and cannabinoids were. And this was their sort of executive summary from this whole monograph which is quite lengthy. They said and an adults with chemotherapy induced nausea and vomiting oral cannabinoids are affected antiemetics. In adults with chronic pain patients who were treated with cannabis or cannabinoids are more likely to experience a significant reduction in pain. In adults with MS related spasticity, the use of oral cannabinoids improves their self reported spasticity. And then for for all of these indications, the effects are modest. And for most other conditions, there's not adequate information. So as you can see, in this graph down below from PubMed, the rate of publication on cannabinoids continues to rise. And so there's significant amount of new studies that have come out between 2017 and 2023.

38:01

Probably, well, what I'll say is that the research here is based on commercially available products, and cannabis itself. So there's like quite a variety of different cannabinoid related research. So here is a more recent systematic review from 2022. So it included the documents from before 2017, and then the ones that were more recent. So the ones that the conditions that were added that that got sort of better data in the last five years, particularly epilepsy, CBD having a significant therapeutic effect on epilepsy Parkinsonism chronic pain, we sort of already had Tourette syndrome, and then chronic pain and spasticity were already in the 2017 version, and then sleep was added as an indication in this systematic review. Let's look at a few studies in particular, and I've chosen these ones. The first two because they're among the strongest and most hope high profile studies involving cannabinoids and then some of the other ones I've chosen because they're more HIV specific. Um, so these were two studies that came out very, very close to one another in 2017 and 2018, in the New England Journal, and then in Lancet, and they were both using the Epidiolex products. These were the pivotal studies that led to its approval. The New England Journal Article study Dravet Syndrome, which is an epilepsy syndrome and then Lancet study Linux gusto, which is another epilepsy syndrome. These were both add on studies. So it's not ethical to do placebo like purely placebo controlled epilepsy studies because we have effective anti epileptics so in all epilepsy studies that patients are left on their staple drugs that they were taking already. And then we do an add on kind of study to see if the the addition of a drug versus placebo changes the seizure rate. And so what you can see is that when they had add on cannabidiol versus add on placebo, then the rate of seizures dropped significantly. And then the same was true in the New England Journal article. In terms of specifically, with regards to people living with HIV, there was a systematic review performed in 2012, that I that sought to look at any studies that have looked at any kind of cannabis products for any indication and people living with HIV. At that time, eight randomized control studies were included in in this meta analysis. And they had lots of different outcome measures, some were more focused on changes of weight, appetite, nausea, vomiting, performance, status, and mood. So here are some examples of two studies that were focused on HIV associated neuropathic pain. So these were both kind of similar designs, and they looked at smoked cannabis. So research involving smoked cannabis is still pretty limited, because you can't just sort of send someone out with the canvas and say, you know, take this three times a day, and you know, report on your outcomes, it has to be done under observation and controlled, and uncontrolled environment. And so you might imagine that this is pretty laborious and cost and costly. So these were studies in which the participants were given a cannabis versus a placebo cigarette to smoke three times a day, for five days. And so they were looking at acute reductions in in pain related to HIV neuropathy. And both of those studies had a positive outcome, smoke cannabis reduced daily pain by 34%, as opposed to 17% in the placebo cigarettes. And they also use the sort of dichotomous outcome of a 30% reduction in pain, which is considered clinically significant. And that was reported by 52% of patients in the active group versus the placebo, which was 24%. And the second study, which was done by a different group was was substantially similar. There have also been studies looking focused on kexi and HIV, these were mostly older studies, I think that Texia is probably less of a concern for most of our patients these days, and we, perhaps, if anything, worry too much about weight gain. But there were a significant number of studies with both smoked marijuana, Andrew and Abin offer kexi and HIV. And these data were summarized nicely in a systematic review published in 2016. There's also been some research in what patients report is their reason for

using cannabis. This was a study in 2005. And the authors surveyed 523 HIV positive people attending a large clinic system. And 27% of those surveyed are the or those who responded reported using cannabis for treating various symptoms. And these are the symptoms that the patients reported that they used it for. poor appetite being number one, obviously, these are not mutually exclusive categories. So lots of people use different appetite for pain, nausea, anxiety, nerve pain, in particular mood symptoms, and then paraesthesia, which presumably is related to peripheral neuropathy. And then 47% of those patients reported some sorts of memory issues that they attributed to their cannabis use. So there are more studies and more longer term studies using the products that are not smoked. So no Biggie Smalls is that plant derived product that is half CBD, half THC that is available in Europe. And so there are quite a number of pain studies that looked at the use of Nabiximols. So for example, and five week duration was sort of the the duration used by most of them with this other one being being longer. So this is an example of 66 patients who had pain related to Ms. This study showed a reduction in the mean intensity of pain and better sleep as well. This was a study in neuropathic pain, which was also positive. This was a study that was negative. This This was a sort of a more treatment resistant group of patients. These were 263 patients who had cancer related pain that was already being being treated by opioids. So they were a pretty tough to treat group. And then this last one was also neuropathic pain associated with allodynia and had a positive outcome. So we talked a bit about what the potential uses for medical marijuana are and what its benefits might be. This same monograph, which I mentioned a little while earlier, also talked about the potential risks. So they evaluated risks in 10 domains, and you can see those listed up at the top of the screen. And unfortunately, they found that data was insufficient In many areas, but they did find evidence in for an association between cannabis use for different symptoms. And then they also found significant evidence against an association between cannabis use and some other indications. Excuse me. So some of these are things that you might expect. So if there's if the cannabis is being administrated administered in a smoked form, then chronic cough and phlegm production might happen, lower birth weight and pregnancies, some exacerbation of pre existing psychiatric symptoms can be an issue. And then they identified here at the bottom different risk factors for developing problematic use, and you can see what those might be there. These are sort of epidemiologic type associations. So it's not 100% clear that there are causal. But, you know, they these were identified as being associated anyway, with increased risk for problematic use. There are also potential for some drug drug interactions based on the hepatic metabolism. And you can see those,

46:14
those potentials here. So one

46:20
particular risk that I'll call attention to is this idea of cannabinoid induced psychosis. So some patients will develop psychotic symptoms when exposed to cannabinoids and particularly with with THC. Probably, for the most part, these are patients with some kind of predisposition to psychosis already, either those with family history or, or some isolated psychotic symptoms in certain conditions. Certain states like for example, with altered mood. This, I don't personally view as a complete contraindication to medical marijuana, I have recommended it once to a patient who had a diagnosis of schizophrenia. I'm a little hesitant about it. But in this particular

case, you know, oftentimes the patients who asked me as I had mentioned before already, marijuana experienced. So in this particular case, it seems it seems like a harm reduction. Intervention, if they can get their marijuana from the program instead or from the street, then at least you know that it's not going to contain other kinds of contaminants, but it is just something to be aware of. And they also don't feel, you know, aside from the psychosis, which is kind of the main thing that that sticks out in my mind, you know, I'm not comfortable relabeled subscribing to patients who are pregnant either doesn't seem like a good idea to me. Okay, so we're getting near the end, and I want to leave a couple minutes for questions. So just to summarize, cannabis is one of the oldest cultivated plants it's been used as a medicine for 1000s of years. Despite certain regulatory barriers, there is significant research which demonstrates its effect on epilepsy, and that's cannabidiol or CBD only. And then other indications, including chronic pain, anorexia as an antiemetic. And for spasticity and multiple sclerosis. There's also mounting evidence in Parkinson's disease, and also in Tourette Syndrome. Although overall, the evidence for other indications is weaker. The safety profile is in general favorable, but we are cautious and tend to avoid and patients with pre existing psychotic symptoms and then also in pregnancy because of the risk of lower birth weights. The caveat to all of this is that the specific preparations available in New York state and other states that have legalized are not subject to research because we this is currently illegal under the schedule one controlled substance designation. The New York State products are derivatives of the cannabis plant itself, so they're all natural, naturally derived entities. The plant derived products usually have two main components the THC and the CBD. But they're also likely to have many of these entourage compounds, which may be may have active properties but are much less well studied. THC is the psychoactive component it and this occurs based on its interactions with the CB one receptor which is broadly represented in the brain. And should one want to become a registered provider. It is pretty straightforward to do so it's all online based and registering patients is also pretty simple to do. But prescribing should be done as part of a normal therapeutic relationships with regular follow up similar to any other medication that you would provide for your patients. So with that, I will stop. Our first

49:42
question is I'm wondering about using HIV AIDS as a qualifying condition. The existence of the diagnosis itself is simply appropriate or should there be some implication that there is pain to out of to be HIV or something? So not sure what that question perfectly but

50:03
secondary to view it. Yeah. So yeah, that's a good question. So it used to be the case that you had to indicate both a diagnosis and a symptom. So you used to have to say, for example, like neuropathy and pain, or HIV and paint or something like that. And they've loosened it up so much, which I think is because we have recreational available now anyway. So even if you didn't certify them, they could go and get it on their own from the recreational dispensaries. So you know, you can do what you feel most comfortable with. I agree with the sort of spirit of it that like, obviously, like cannabinoids don't treat HIV itself. So like, that's kind of a weird indication, right? You're, and perhaps you would worry that you were inadvertently implying that you're treating HIV with marijuana, which wouldn't make sense. But it doesn't show up on the card or

anything. So it's like not, it's more of like, kind of a logistical issue. I typically just don't put that because I prefer to put something more neutral.

51:05
Okay. And then we have a second question. How can CBD products assist patients? with Parkinson's, with Parkinson's?

51:16
So I think CBD alone is there isn't the greatest evidence of assisting with Parkinson's and then the literature on Parkinson's overall, is pretty mixed. The mechanism, I think, understanding what the mechanism of it is, would be even a bit more confusing. I think in general, some of the thoughts are that it's an anti inflammatory mechanism in some neurologic conditions. And there's a little bit of data of that it might improve some of the symptoms like particularly the tremor kind of symptoms, the positive symptoms of Parkinson's disease, it may treat some of the sort of ancillary symptoms like you know, mood symptoms, or insomnia, which can be really common. Again, it's not going to be like treating them with an actual pharmaceutical agent for Parkinson's disease like cinnamon, like you give some person with Parkinson's disease, cinnamon, they're, you know, markedly better you can see like the difference in their walking and you know, their tremor, and it's definitely not going to be something like that. But patients may find it subjectively helpful for some of the symptoms.

52:24
We do have another question here. Is there a cost difference between medical and recreational THC? That's a

52:31
really good question. I don't know the answer to that. I don't know what the recreational cost is. I'm I would guess that it might be a little cheaper, but I have I really am not sure about that.

52:47
And I have does insurance cover the cost of appointments? Oh, that's

52:52
a good question. insurance can cover the cost of appointments. Usually, if it was just for the medical marijuana registration, I'm not sure about that. I've never done it that way. Because it's I only do it for patients that I'm seeing usually as part of like a more general relationship in which case you just felt like a normal visit. If it was only for the medical marijuana alone. I think that might be a little bit more dubious,

53:19
I'll say, okay, great. Thank you and have.

[End Transcript]