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CLINICAL APPROACHES TO MEDICAL CANNABIS

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[video transcript]

00:08
So Dr. Slawek is an Assistant Professor in the Division of General Internal Medicine. She is board certified in Infectious Diseases and Internal Medicine, and provides HIV and AIDS care, Hepatitis C treatment, as well as General Medicine care at Montefiore Medical Center where she also helps to lead the Montefiore Medical Cannabis Program. Dr. Slawek's research focuses on improving outcomes in people living with HIV. She is currently studying how medical cannabis affects pain in people living with HIV. Dr. Slawek is the recipient of a K23 Award from the National Institute on Drug Abuse to test how different formulations of medical cannabis affect pain and inflammation in people living with HIV in an innovative quasi-experimental study. So thanks again for being here, and I will turn it over to you.

00:59
Thank you very much. I'm really excited to be here and talk for the next hour about medical cannabis with all of you. So, just some learning objectives for the next hour. By the end of this, I'm hoping you'll be able to discuss how the historical and cultural context of cannabis regulation in the US has impacted current policy and practice patterns. And you should be able to demonstrate an understanding of the risks and benefits of using medical cannabis, and describe harm reduction principles to patients who use cannabis in clinical practice. This is just a brief outline of the talk today, we're going to start off talking about medical cannabis in New York State and then move on to cannabis pharmacology and the endocannabinoid system, therapeutic uses of cannabis, formulations and administration methods that patients use, and finally closed with assessing patients and initiating them on medical cannabis, and monitoring them. And hopefully we'll have enough time at the end for questions too. So starting off with just a polling question, so of the people who've joined, how many of your patients are currently using medical cannabis? Alright, so it's a pretty good distribution, either looks like we have about half of everybody has basically no patients or maybe just a couple, and then a few of us have over 10. So pretty good panel of patients using medical cannabis. So let me just get myself oriented here.

02:32
So why is this topic important? And I think all of you are here because, in some respect, you think that this topic is important. But over the past 25 years, we've really seen this vast increase in cannabis legalization in the United States. So starting in 1996 with California, over the past 25 years we've seen more and more states enact laws that legalized medical cannabis use. And so up until yesterday, actually this number should say 38 because Mississippi joined the group. But we now have well over half of our states with medical cannabis laws. And 18 states that have passed legalized adult use cannabis, meaning recreational use or non medical cannabis. So there's certainly an increase in interest in medical cannabis. And here in New York state, our medical cannabis law was passed in 2014 and enacted in 2015. So here in New York State, we started seeing patients for medical cannabis certifications around the end of 2015. And in the first two years, so following it out to 2018, there were nearly 100,000 patients who had received certification for medical cannabis, and over 1,700 providers who completed the training required to become registered practitioners to assess patients for medical cannabis use. And if you

follow that out to just recently, so I just checked this last week, there are now over 3,500 registered practitioners and over 150,000 certified patients. So even for those of us who don't have any patients who are using medical cannabis, that we know of, many of them are accessing it through means that are not necessarily their primary care doctors. And patients are really interested in this and seeking it out.

04:29
And beyond that, in March of 2021, New York State took extra steps. So New York State passed the marijuana Regulation and Taxation Act at the end of March. And this act did a lot of things but the most important things or the high points of it, I would say, are that it legalized adult use or recreational use of cannabis. And the plan is to operationalize a way for recreational cannabis to be sold legally in New York State. And it also expanded a lot of the certifying conditions for medical cannabis, meaning that people can seek out medical cannabis for more symptoms than they could before. And so there are lots of other aspects of it, but this is just to say that there is broadening of these laws consistently. And in the first few months of this law being enacted, of it being passed, not much movement was made on it. But when Governor Hochul came into office, she has really been pushing for the MRTA, or the Marijuana Regulation and Taxation Act, to become a reality. So she made appointments to the Office of Cannabis Management Board. And it seems as though there's really going to be all of these big changes happening with the medical cannabis and cannabis programs here in New York state.

05:55
So it's important to really put all of this into the historical context in the United States and in our culture to understand why this is so revolutionary and crazy, and why us as providers really don't know that much about cannabis often. So back at the end of the 19th century and at the beginning of the 20th century, cannabis was used widely. So it was recommended by healthcare providers, it was accessed by the population through dispensaries with or without the involvement of their doctors or their physicians. And so it was sold as things like tinctures and fluids, it was accessible that way. And then between that time and the 1930s, the US saw a whole lot of cultural shifts. So during that time, one of the things that happened was that the Mexican American revolution occurred in 1910. And following that, there was quite a bit of immigration from Mexico into the US and the population in the US, as though it had not already been changing quite a bit with Europeans coming here, but it changed even more for those who were living here. On top of that, in the 1910s and teens, there was a movement toward prohibition, primarily of alcohol is what we all know it as, but it was a really a sentiment about any intoxicating substance. On top of that, there were then big changes that occurred in pharmaceuticals, there were things made available like other pain medications, antibiotics. And on top of that all, in 1930, what did we see? We saw the Great Depression, so we saw huge economic instability.

07:44
So with that came a great amount of xenophobia, and finger pointing, and general upset with the world. And there really came with that lots of desire to blame the situation on somebody. And so around this time, we started to see that cannabis was rebranded as marijuana. It was really a concerted effort. It wasn't just like, you know, some people sort of like, 'oh, maybe we'll

call it marijuana, or maybe we'll call it cannabis,' it was more like, 'no, we should make this a word that sounds more foreign, and that we are more capable of associating with Mexican immigrants.' And not surprisingly, this was really an example of early systemic racism in this country. The narrative was changed on purpose so that we can say that marijuana was responsible for all the societal ills, whether it was wild parties or all of the reckless things that humans just do on a regular basis. So around this time, we started to see that there was increased taxation of healthcare providers who were interested in providing cannabis. So the Marijuana Taxation Act was passed in the late 1930s. And that along with all these other medical advances that were happening at the time, resulted in cannabis falling out of the Pharmacopoeia in around 1942. Following that, we started to see that though it was not necessarily recommended by physicians, cannabis entered the conversation as more of a substance that was used by subcultures, such as beatniks, hippies, the anti-war movement, and others. And so it was very publicly used by people. I mean, Allen Ginsberg holding a sign up that says 'pot is a reality kick.' It was a large part of the hippie movement. And it was a large part of this idea that it was that cannabis can be used to expand your mind and your experience. This was met in 1970 by President Nixon signing the Controlled Substances Act. And the Controlled Substances Act was responsible for developing a system for having punishment for possessing, or selling, or using drugs. So it was a large part of why we see the current drug war and a lot of the drug war that we all experienced in the 1980s, 90s, and 2010s. So the Controlled Substances Act created a schedule of controlled substances. And as of around 1973, cannabis was scheduled as a Schedule One Substance. Between the years of 1970 and 1973, what happened during that time? Well, there was a lot of debate over whether cannabis should be included as a scheduled substance at all.

10:49
So at this time, there were a lot of people who came up and said, 'you know, I don't really think that cannabis should be controlled. We don't know anything about it, you know, people are using it, but we don't know anything about whether it meets a definition of having a high potential for abuse, or whether there's really no accepted medical use and treatment, or there's lack of accepted safety for it. We can't really say these things about it.' So a commission was created, that was created by Congress, it was bipartisan. And it was a group of experts who assessed what we know about cannabis at that time. They looked at the data that we had, and said, 'we don't know anything about this. And we don't think it should be controlled at all.' And recommended actually, that we do more research to understand what cannabis does, what the risks are, what the potential benefits are. Unfortunately, President Nixon's response to that was to say, 'well, I kind of think it should be Schedule One.' And so since then, cannabis has been categorized as a Schedule One Substance, along with other substances like LSD, MDMA, and heroin.

12:00
So what has really been the impact of this? John Ehrlichman was President Nixon's Chief of Staff. And he later on noted in this memoir that was published, that 'we knew we couldn't make it illegal to be either against the war or Black, but getting the public to associate the hippies with marijuana and Blacks with heroin, and then criminalizing both heavily, we could disrupt those communities.' And that's exactly what they did. So we saw that starting in 1970, so this graph

right here, so 1970 starts right here. That the US prison population, both state and federal, just exploded after the Controlled Substances Act was passed. And we've seen a real impact of this even to present day. So as recently as 2018, arrest rates for Black people were 3.6 times higher than for white people. And this is despite the fact that consistently survey data that's nationally done has shown that there are nearly identical rates of cannabis use among Black and white people. So I think it's really important to keep all of this history in mind when we think about not only why we are where we are with cannabis, but also why do our patients have the responses that they have when we talk to them about cannabis? And why do our colleagues even have the responses that they do? Because this is almost 100 years now of the narrative of cannabis being changed. And you'll notice that I refer to cannabis as cannabis and I try to avoid calling it marijuana, and that's a conscientious decision, because I find this to be a scientific discussion that should be medicalized. And I prefer to use the term cannabis in that context.

13:46
So let's talk about cannabis pharmacology and the endocannabinoid system. So let's start off with a polling question. So which plant based cannabinoid causes euphoria, anandamide, tetrahydrocannabinol-9 also known as THC, limonene, or cannabidiol also known as CBD. Alright, so let me just say that 94% of you identify THC as a euphoric plant based cannabinoid, so great job.

14:19
The other cannabinoid that is plant based of these is cannabidiol. Anandamide is an endogenous cannabinoid, and limonene is a terpene. So I'll tell you about what all those things are. So let's start off with what is cannabis? So cannabis is not one thing. It has been cultivated and used for recreational and medicinal purposes for centuries now. And the term cannabis broadly defines products derived from the cannabis plant. And there are subspecies of cannabis plants, including cannabis sativa which is generally taller, skinnier and has thinner leaves, and also tends to have higher THC content. And then there's cannabis indica, which is a plant that tends to be shorter, more shrubby, and has leaves that are thicker, and cannabis indica tends to have more CBD in it. Now, I think a lot of us and I think in the population of people who think about cannabis, many people like to say like, 'oh, there's cannabis sativa and it has these effects and cannabis indica has these other effects.' However, there's not a whole lot of pure cannabis sativa or cannabis indica in existence any longer. Most of them are hybrids of the two. So what's seen is really hybrids of cannabis sativa and indica to have varying concentrations of THC and CBD.

15:47
Within cannabis there are greater than 100 biologically active chemicals, including cannabinoids, which I just mentioned are THC and CBD, the most well known of which are THC and CBD, and these contribute to the therapeutic and euphoric effects of cannabis. Terpenes, such as limonene which I mentioned earlier, affect the smell, taste and appearance of the plants.

16:22

Alright, so let's talk a little bit about THC and CBD. So THC is the most well known and best studied of the cannabinoids, it was identified in 1964. And it's known to have psychoactive and intoxicating effects. It also has effects on pain, muscle spasms, nausea, appetite, and stimulation. And plants are often bred to have high THC content, particularly unregulated cannabis that is used for the intent of intoxication. CBD on the other hand, was identified around the same time that THC was, it's thought of as being psychoactive and not intoxicating. So it's used often as an anxiolytic and is thought to have anxiolytic properties. It also has antioxidant properties, anti inflammatory properties, and it's used as an anti convulsant. It might have some anti tumor properties, but that's still definitely in the animal model phase of things. Plants that are bred to be high in CBD are often used for fiber, such as hemp. And the interesting thing about cannabinoids in general, and the endocannabinoid system, is that THC and CBD might have their individual effects, but when they're used together, you tend to have a different impact. And so that is often explained by saying that CBD potentiates the action of THC. So for example, if you were to use THC or CBD for pain, each of them might have an impact on pain. But when you use them together, they tend to have more of an effect or at least a different effect on pain than either given alone.

18:05
And so these cannabinoids work within the endocannabinoid system. And so the endocannabinoid system exists within all of us, and it interacts both with THC and CBD, as well as endogenous cannabinoids. So to our right is a figure that shows where CB1 and CB2 receptors are, these receptors were relatively recently discovered like in the 90s, early 90s and late 90s. And so here in this diagram, the light blue dots represent CB1 receptors. CB1 receptors tend to be present in the CNS and system. So the brain, the spinal cord, peripheral nerves, and is also present in some other organs such as the liver and reproductive organs. The CB1 receptor is the most abundant G coupled receptor in the CNS, and it's involved in the experience of pain, stress, and anxiety. CB2 receptors are represented here with the red dots and they have really high density in the immune system, particularly macrophages. So they do have some CNS expression, but they're primarily in that immune system and are involved in inflammation. So THC binds primarily to CB1 receptors, so the light blue dots remember. And so that's thought to be why it has effects, why it has psychoactive effects, and how it creates analgesia or pain relief. It also has some binding to CB2 receptors, leading to an anti inflammatory response with THC. CBD or cannabidiol binds primarily to CB2 receptors, and that's why we often see anti inflammatory effects with CBD. It also has some binding the CB1 receptors in the CNS, and that's responsible for its anti anxiety properties. Endogenous cannabinoids interact with both CB1 and CB2. And just some examples of those are anandamide, like I mentioned in the polling question. And 2-Arachidonoylglycerol, also known as 2-AG which is much easier to say. So that's generally how cannabinoids interact with our endocannabinoid system. It's actually a quite complex system, and we're still learning quite a bit about it every day, it's not well understood.

20:41
So now that we've covered kind of historical context, and cannabis in New York state, as well as the pharmacology, let's talk about the therapeutic uses of cannabis. In New York State, all right, as of January 24th, so literally this week, I said the stuff is changing very quickly. The

indications for medical cannabis in New York State are now pretty broad. So these indications were specified in the MRTA back in March of 2021, but they were just implemented this week. And so now patients can receive certification for medical cannabis for any of these indications, including chronic pain, PTSD, even substance use disorders, neuropathies, and other things like seizure disorders, Alzheimer's, dystonia, HIV, Parkinson's, multiple sclerosis, I'm not going to read all of them out loud even though I just read most of them out loud. In addition to that though, providers can identify any other condition that they feel a patient might benefit from cannabis for. The only caveat is that it must be specified in the patient's chart. And I would hope that the provider would also have reasoning for why they would think that cannabis would be helpful in that medical situation as well. So another polling question. What do you guys think the most common indication for medical cannabis certification is? Insomnia, PTSD, pain, or inflammatory bowel disease? Right, all right, yeah. So 74% of you guys said pain. Good number said PTSD and insomnia. No one said IBD, that's interesting.

22:59
So this is data that's a little bit old. So data from 2018 looking at certifying conditions for medical cannabis in New York State. And this was looking at certifications from New York state over the course of three years, closer to two years but still, so this is the early days of the medical cannabis program here in New York State. 73% of certifications were for severe or chronic pain, then an additional 13% were for severe or persistent muscle spasms. And then there were other patients who were receiving it for things like nausea or seizure or cachexia, but it really was predominantly people seeking out pain relief. And this is actually a pattern that's been seen not only in New York State, but throughout the country. Patients are really looking for pain relief these days. And I think there's a lot of different reasons for that, but I think it's important to understand that. And so a lot of my talk, when I'm talking about therapeutic uses of cannabis, is going to center on pain, specifically because that's really what patients are looking to use it for, looking to use cannabis for. So before I get into that, where the evidence stands, there's a lot of barriers for any evidence to exist about cannabis. And so those barriers exist at many different levels, and they really start at the federal level. And these barriers were created mainly by the Controlled Substances Act, that there are many, many hoops that someone who wants to do research on cannabis has to jump through in order to do so successfully. So investigators need to obtain investigational new drug approval, in addition to that they must get a letter of approval from NIDA because NIDA has to provide cannabis product if you're planning on doing randomized controlled trials.

25:00
Investigators also have to get a DEA Schedule One license, as well as receive funding, usually from a federal funder. And that federal funder, which is usually NIDA, or in the National Institute on Drug Abuse, needs to think that cannabis research is a priority. And then as I mentioned before, that study drug must come from a NIDA supplier. The state, on top of that, that the investigator is researching in might also have to provide their own approvals. And sometimes each state has different rules about this. So if you're working in say Connecticut versus New York State, those researchers might experience very different things in terms of what licenses, certificates, or approvals they might have to get from their state. Then because of all of that, institutions are often really wary of doing cannabis research. So you might see increased

scrutiny from your IRB, institutions then have to have all these resources available to keep this Schedule One substance on their campuses. So they might have to have specific storage, security to comply with DEA regulations, which is very expensive. And there's a lot of fear from institutions that federal funding will be made vulnerable if they proceed with something like cannabis research. And there's a lot of fear also that there will be increased scrutiny from the press if they proceed with it. This all lands on the investigator who then has to be fearful of this lengthy approval process. They have pressures to be productive, published papers, get grants, and promotions. And all of these external factors or internal factors that we all deal with right in our careers, and these investigators need resources and support that might not be there. And on top of that, they're looking at these products that NIDA is sending patients to us for their research and noticing that they have literally nothing to do with the products that our patients are using in medical cannabis programs.

27:01
So that NIDA cannabis that's used for cannabis studies is primarily all smoked cannabis, there's going to be an increase in other formulations of cannabis that are available. But up until very, very recently, it was all smoked cannabis. It arrived to facilities as plant material, and it didn't bear any resemblance to what patients were using at dispensaries. So the research community and investigators have found themselves in a real catch 22, they're being told that they can't research medical cannabis because there's no medical use, but they can't research whether or not there's a medical use because of the regulations. So that being said, in 2017 the National Academies of Sciences, Engineering, and Medicine published a large report that was a comprehensive review of what evidence that exists, that was put together by the experts and then peer reviewed. They really attempted to look at every possible indication for the use of cannabis. And it's long, it's like over 400 pages long, it has extensive review of all the studies that had been done to that time.

28:15
So related to chronic or severe pain, this report found conclusive or substantial evidence that cannabis is effective for the treatment of chronic pain in adults. Cannabis or cannabinoid treated patients were more likely to have clinically significant reduction in pain symptoms compared with placebo. And they noted in this report that while the use of cannabis for the treatment of pain is supported by well controlled clinical trials, very little is known about the efficacy, dose, routes of administration, or side effects of commonly used and commercially available cannabis products in the US, which kind of echoes what I was just saying about the products that are made available for these trials.

28:50
So there has been about six meta analyses of randomized controlled trials looking at whether cannabinoids treat pain, and I'm not going to go through all of them, but each of them looked at pain in different ways. So they may have looked at plant based cannabinoids, smoked, inhaled, pills, synthetic cannabinoids such as Dronabinol, or other preparations, it's kind of all over the place. The one thing that's consistent though is that all of their results showed a reduction in pain in those subjects who were in the randomized control trials that they studied. So I'm going to talk more specifically about one specific meta analysis published by Penny Whiting et al in

JAMA in 2017. And so they looked at 79 total randomized control trials for a number of indications, most of them we're looking at the question of chronic pain. And most of those studies tested Nabiximols, which is THC and CBD. It's usually administered with a spray in the mouth. Synthetic THC. They also looked at NIDA supplied cannabis, but none of them has looked at cannabis products currently available in medical or adult use markets. And so they found that there was moderate quality evidence of moderate effect on pain with cannabinoids. And this meta analysis also tried to answer the question of whether there are adverse effects with cannabis use or medical cannabis. And they found that there was an increased risk of short term adverse events. So looking at the question specifically of pain, these are the studies that Whiting and colleagues looked at in their meta analysis. And so they found that the odds indicated there's a 30% or greater improvement in pain with cannabinoids compared with placebo. And so they were really looking for a clinically significant reduction in pain, and that's really defined as at least 30% reduction on a numeric rating scale. So for example, if someone usually lives at a 10 with their chronic pain, we're hoping a clinically significant reduction would be to reduce them down to about a 7. So that's considered clinically significant, and this is what Whiting and colleagues were looking for with their meta analysis. So this study, this meta analysis, is kind of landmark in some ways. I think many of the people who are doing medical cannabis have read this study, there are criticisms of it that I think are valid, you know, because a lot of these findings are nearing a level of insignificance. Right, they're significant, but it's not as if it's like obviously significant. And additionally, most of these studies didn't have very large sample sizes. And so the evidence is what it is because of the quality of the research that we looked at.

32:14

So just zeroing in on a couple of randomized control trials of smoked cannabis for pain. This is a prospective, blinded, placebo, randomized controlled trial published in 2007 by Don Abrams. And his group was really looking specifically at people living with HIV. They randomized participants, 55 participants, to either smoked cannabis that was 4% THC, they use that three times per day, versus placebo cigarettes smoked three times per day. And the primary outcome was daily pain, a daily pain diary, and a visual analog scale. And participants were evaluated for eight days preceding their first study day, they completed surveys before they started the cannabis or placebo and then followed for 12 days after that. So they found that in the cannabis group, which is represented here with the lines connected by squares, so this one right here, that there was a 34% reduction in pain in those who received cannabis versus a 17% reduction in pain in those who received placebo. And when comparing these two groups, it was a statistically significant difference. Another RCT, this is a prospective, blinded, crossover trial published by Ellis in 2009, also specifically in people living with HIV. And so in this one, this is a crossover trial, so participants either started with placebo or smoked cannabis. They use that for five days, and then they had a two week washout period with no placebo or cannabis use. And then they switched to the other product for an additional five days after that. And these researchers looked at pain severity scores, that was their primary outcome. So they found that there was greater pain reduction with cannabis when participants were using cannabis compared with placebo.

34:18

Okay, another way to think about this is whether there are changes in medications after starting medical cannabis. So many patients, especially with chronic pain, are taking a whole slew of medications for their pain relief. And so this study published in 2016 by Boehenke and colleagues looked at self reported online questionnaires of patients who visited cannabis dispensaries in Michigan between November 2013 and February 2015. And they asked the question of 'how has your opioid prescription drug use changed since you started using cannabis?' So they found that respondents basically said that before starting medical cannabis they were using about 65% of their prescription, of their allotted prescription doses, and after starting medical cannabis that dropped to around 18%. There was a similar pattern seen for other medications, so anti inflammatories like NSAIDs and antidepressants in this study survey. Another study which is relatively small, published by Vigil and colleagues in 2017, looked at patients who were in a chronic pain clinic that also provided medical cannabis certification. And so they looked at 37 patients who were prescribed opioids and who were also certified for medical cannabis, and then followed them over 21 months. And then they compared them to a group of 29 patients who were on opioids for chronic pain, but who were not certified for medical cannabis. And so when they compared them, so the group that received medical cannabis is represented with the green line here, and the group that did not receive medical cannabis is represented by the orange line here. They saw that over the 21 month observational period, 41% of medical cannabis patients stopped opioid prescription versus 3% of the comparison group. And 84% of medical cannabis patients reduced their opioid dose versus 45% of the group that did not receive medical cannabis. So these two studies really seem to indicate that patients sometimes do substitute their medical cannabis for their other pain medications. It's not clear until we do more studies that are high quality randomized control trials, we're not really going to know the details of that, but they're really promising that people are actually getting a lot of pain relief with their medical cannabis.

37:00

So what about other non pain conditions? So severe and persistent muscle spasms have been studied primarily among people living with multiple sclerosis. The studies that exist have looked at THC and CBD together compared with placebo, and they found that there is improved patient reported spasticity in these patients. For PTSD, it's not well studied, it's primarily been studied in combat veterans and the sample sizes have been incredibly small. However, in those small sample sizes, people have reported improved sleep quality and reduced intensity of nightmares. For nausea, synthetic THC also known as Dronabinol, has been compared with placebo and found to be effective for chemotherapy induced nausea. And CBD has been studied in animal models and improves nausea, but it has not really been studied in human models yet. For cachexia and wasting, there's some evidence that in AIDS wasting syndrome and cancer associated weight loss that medical cannabis is effective, but there's high risk of bias in the existing studies that have been done and those studies additionally have very small sample sizes. And then finally for seizures, CBD is the only plant based cannabinoid that has any FDA approval at this time and was FDA approved in 2017 specifically for the management of intractable seizures in children with Dravet Syndrome and Lennox-Gastaut Syndrome, which are very, very specific syndromes. High dose CBD is being studied for seizure reduction in adults. However, those studies that have been published have very small sample sizes, and the

doses that are being used are nowhere near as high doses that are available usually in medical cannabis dispensaries.

38:59
So how are patients using their medical cannabis? What do the formulations and administration methods look like? So, in order to really conceptualize this, it's important to think about unregulated versus regulated cannabis. So unregulated cannabis I think is what many of us had our initial introduction to cannabis with, right? So it's not sold by regulated dispensaries. It's not recommended by clinicians usually, and it's just generally bred to have high THC content. This is cannabis that's sold on the street or accessed there. It tends to have unknown or untested doses of cannabinoids, as well as unknown content of pesticides and other things like tar, heavy metals, and other contaminants including other drugs like K2 or spice, which are synthetic cannabinoids, and cocaine. And there might be availability of different routes of administration, but it's very inconsistent and people are really at the mercy of whomever they purchase their unregulated cannabis from, in terms of what types of cannabis they are able to access. This is in comparison to regulated cannabis which is sold in regulated markets such as the New York State Medical Cannabis program. And even in regulated adult use or recreational markets too in other states, ours has not been set up yet, but hopefully this will be the case for ours whenever it is in effect according to the current law. So there's a variety of cannabinoid ratios available. It's not all super high THC, you might be able to access high THC, or equal parts THC and CBD, or even high CBD products. Patients and providers tend to know exactly what the cannabinoid dosing is, and that's usually confirmed by the state laboratory where they're able to say like, 'Okay, you say that this is five milligrams, we're checking it out and making sure that it actually is.' Those same state laboratories are testing regulated products for pesticides and other contaminants that I already mentioned, like heavy metals and tar, and other drugs. And if they have those things, then they're removed from the market. And in most states, including New York state, there are many different routes of administration available, including tinctures, edibles, and other non smoked options. In New York state right now, patients can purchase a 60 day supply of medical cannabis products. They cannot grow their own cannabis plants in their homes yet, although that's part of the MRTA, but patients are able to purchase things like chewable gels and gummies, tinctures and this is usually a dropper where you drop oils under the tongue, oral sprays, ground flower, this is intended to be used in a vaporizer like a tabletop vaporizer device, or oils that are vaporized too. And just recently, whole flower was made available in New York state medical cannabis dispensaries as well.

42:16
So what does all this mean? This is a really busy slide, but I'm going to walk us through it. And I think it's one of those important things to counsel patients on when you talk to them. So I'm going to try to go through this somewhat quickly, but not too quickly. So dabbing, also known as wax, is a very, very concentrated form of cannabis that individuals have used solvents to concentrate it down to really, really high concentrates of THC. It's utilized by putting that wax in a hot platform and inhaling it, and it has an almost immediate onset of action, the duration is about two hours. People like it because it has a quick onset of action, but those solvents that are used to create the wax have a potential for causing lung injury and you have real risk of a lot of intoxication with this because of the really high THC dose in it. So people can experience

psychosis or hallucinations. Dabbing and wax products are not available in New York State dispensaries. This is really only seen in the unregulated market in New York State. Smoked flower is what we typically think of with cannabis and what most of our patients have the most experience with. It's dried cannabis flower administered in a cigarette style device, like a joint or a blunt, sometimes mixed with nicotine or tobacco, and sometimes administered in pipes as well. It's combusted, which generates smoke, and then that's inhaled and the onset of action is around three minutes, usually lasts around two hours. People tend to like that they can titrate their dose with smoked flower. However, that smoke that's inhaled tends to be a very high temperature and that high temperature has the risk of causing chronic bronchitis over the long term. In addition to that, when people are inhaling these smokes, they tend to lose a lot of their dose with sidestream smoke, meaning some of that smoke does not get inhaled and so people might not be getting as consistent a dose with smoked products. This is a similar thing with vaporized products, they essentially have the exact same issues. The main difference is that in order to create that vapor or smoked, usually a battery operated device keeps the cannabis or oil and creates a vapor that's inhaled that's, generally speaking, a lower temperature. So in that respect, it's a little bit safer than smoked flower that's combusted. Unregulated vaped products runs the risk of having other additives in it that could cause vaping lung injury. Tinctures or sprays are oils, they're administered sublingually under the tongue or sprayed in the mouth and absorbed directly into the blood stream through mucous membranes. Onset of action is around 10 minutes, they generally last around 10 hours, has a relatively quick onset of action, not as fast as smoked, but it's much faster than the other products that I'll be talking about after this. A benefit is that you have consistent dosing with it, so you know the exact dose that you're receiving of THC and CBD. However, patients tend to not really like the taste of it. Some patients do, some people don't. And there's potential for user error in that people might accidentally swallow it, effectively making it ingested product then and not sublingual. Suppositories are not well studied, I very, very rarely ever recommend them to patients. However, they are administered as a suppository, they are able to avoid a first pass effect, so their onset of action is about 30 minutes to an hour. It isn't a desirable dosing method, and there's not very much supporting data for it, but some patients might actually benefit from it. You know, people who might have end of life care or those who cannot tolerate something that's sublingual or smoked. And then finally, ingested products usually look like capsules, edibles, gummies, candies, things like that. They must be processed by the liver first, so that can take one to two hours before someone feels an effect, and they can last up to 25 hours. That's a slow onset and duration of action. For some people that's a good thing, if they have chronic symptoms. Some benefits are that you don't have any dose loss, you know exactly the dose that you're getting. However, it can be difficult to titrate for people because they don't tend to understand that they need to wait to know what the effect is before they take another dose. So it requires really careful counseling on the clinicians part, to tell people to wait, to not dose stack or take multiple doses if they don't have an effect within 15 or 30 minutes.

47:03

So when we assess patients for medical cannabis use, our assessment is very similar to a primary care visit. We really want to know what people's motivations are for using medical cannabis. We talk to them extensively about their prior and current experiences with cannabis and get an extensive medical and psychiatric history. We speak with them about the relative

risks and benefits of using cannabis, and we also talk with them about determining a therapeutic potential for their cannabis use. We also review the New York State prescription monitoring program just like we would for any other controlled substance, cannabis products are reported there as well. There are special considerations when assessing patients. Conditions that require caution include psychosis, because THC can worsen psychosis. Arrhythmia, again THC can lead to tachycardia, so that can make arrhythmia worse. And the same logic is used for proceeding with caution with coronary artery disease. And in pregnancy and breastfeeding, cannabinoids do cross placenta and can lead to low birth weight. There's also the potential for drug drug interactions, THC and CBD are metabolized by the CYP P450 system, so you have to be very careful about the potential for interactions within that same system. And the other thing that's important in this assessment is that when you are assessing specific symptoms, to the best of our ability, we should use standardized tools such as DSM 5 criteria if you're using cannabis to manage something like PTSD, or the PEG scale if you're managing pain with medical cannabis.

48:43
When we initiate patients, I just wanted to talk about this clinical scenario. So say you have a 45 year old male with a history of chronic pain secondary to multiple prior MVAs or motor vehicle accidents. They smoke unregulated cannabis three to four times per day for pain relief, and they come to you looking for a safer alternative to unregulated cannabis. So as the audience, what would you do in this situation? We tell them to stop using all cannabis immediately, advise on regulated cannabis use, prescribe opioids, or refer to pain management? Alright, so the majority of people want to advise a regulated cannabis use and about a quarter want to refer to pain management. I don't think that there's any right answer here. You know, it's not easy to encounter patients in this type of a situation. The thing to keep in mind though is that regulated cannabis is safer than unregulated cannabis, hands down, we know exactly what's in it. We know whether or not there are contaminants in it, and we can advise patients on that fact at least. So if I were seeing this patient, I would advise them on using regulated cannabis and I would probably certify them for medical cannabis. When we're initiating patients on medical cannabis, we tend to take a lot of things into consideration, which I've already mentioned, like other medications that they're taking and their comorbidities. Another thing that we do is we give counseling on how they start their medical cannabis. In patients who are cannabis naive, meaning they're not currently using cannabis, we start them on the lowest possible dose of THC, around 2.5 milligrams, and tell them that they should increase the dose incrementally every two to three days until they start feeling symptom relief. If they have any side effects, they should back off, either backup or stop and reach out to us so that we can give them advice on what they should do next.

50:42
For those who are cannabis experienced, we try to estimate their current THC intake, I'm not going to go into that in detail because I'm kind of running out of time. But we start them around 5 to 10 milligrams of THC. However, in people who are using much higher dosage doses of THC than that, we might start them at a higher dose in order to avoid any type of THC withdrawal. All in all though, whether they're naive or experienced, we really recommend to start low at a low

dose and slowly increase their dose, never to rapidly increase. And we also advise people to start their doses in a safe place before bed and at home.

51:26
Precautions and adverse effects, we counsel people on the potential for feeling high, experiencing dizziness or the inability to concentrate. They might also in some cases experience anxiety, paranoia, panic attacks, particularly with high THC doses, and euphoria. Patients should also be very mindful the fact that they can have driving impairment if they're exposed to THC. And we counsel patients extensively about not operating motor vehicles when they're under the influence. Rarely, patients might experience nausea, vomiting or abdominal pain. We also counsel patients on keeping their products in a safe place, not crossing state lines with their cannabis products, and not mixing their products with other substances.

52:16
So I already reviewed all of this, patients also have to register their certification with New York State to confirm that they are actually residents of New York State. That's the purpose of it. We generally counsel patients on how to do that, talk to them about location of dispensaries. And we talk them a lot about cost because another ramification of the Controlled Substances Act and the Schedule One status of cannabis is that it's not covered by insurance. So patients are paying out of pocket for the cannabis products. We've signed a treatment agreement like we would with any other controlled substances and counsel on risks. Aside from that, we have a two week follow up either with the certifying provider or with the dispensary pharmacist to discuss dosing and evaluate for side effects. And we try to have follow up with patients every three to six months to assess for side effects and monitor for cannabis use disorder, and we usually use the CUDIT-R for that.

53:13
So I want to talk about the Montefiore Medical Cannabis Program, but maybe I'll do that after I've answered some questions. Just want to summarize by saying that the historical context of cannabis in the US includes a long history of systemic racism and that shapes the way we view it now. Patients are using cannabis to manage symptoms and need evidence based advice from clinicians, and there are symptoms and conditions that may benefit from management of cannabis. Clinicians can promote harm reduction by counseling patients that regulated cannabis is safer. Avoid smoking cannabis, if possible, and be aware how varying routes differ from each other, and start low and go slow. So I'll take questions now, and if we have time I can talk about our experience at Monte.

53:56
Thanks so much. That was fantastic. We do have a few questions hopefully we could get to all of them. So the first one is can you explain the definition of hemp?

54:07
So hemp is high CBD, so according to the US government it's a cannabis product that has less than 0.3% THC in it. So it's predominantly CBD cannabis products, whether it's fiber or other products.

54:28
Awesome. Thank you. The next question is can you please speak to the timeline from legalization to adult recreational access to cannabis? When can we expect that?

54:40
So I read an interview with the person who's running the Office of Cannabis Management relatively recently in Gothamist, I believe, and they said that they expect to see recreational or adult use cannabis available in 2023, around April 2023. So we'll see what happens though.

54:59
Awesome, thanks. So in the q&a chat we have, what is the data behind using cannabis for anxiety and other mental health disorders?

55:10
So that could be an entire talk, I could say that there's not a ton of data behind it at this time. There's some evidence that you know, utilizing cannabis that doesn't have an excess of THC, so a good balance of THC and CBD, may be helpful for the management of anxiety.

55:33
The next question is what do patients share in terms of a cost difference for regulated medical cannabis versus unregulated cannabis?

55:42
So we tend to see that there's quite a bit of variability, some of our patients are seeing that they are paying around the same amount for regulated as unregulated, depending on the quality that they get. So if they're getting something, usually unregulated, that doesn't have a lot of THC in it, they might be paying much less. And some of our patients actually can't afford regulated cannabis and end up just switching back to unregulated because they just can't do it. So despite the fact that they want to use regulated, they go back to unregulated.

56:15
So the last question that we'll get to is for practitioners that want to register patients, I believe the requirements are medical license, DEA license, and at least a two hour training course. Is this correct? And which training courses do you recommend?

56:31
That is correct. The training courses, so when I took the training courses probably about five years ago, there were two available at the time, I think it was TheAnswerPage.com. The state has a list of available resources that you can use for them. I thought that that course was just fine. I have not actually gone through and looked at each of the courses because they're not all available to me without paying for them. But you know, I think all of them have been vetted by the state and they should be worthwhile.

57:00

Great. Thank you. Well, thank you so much again for being with us today. This was fantastic.

[End]