Q&A: Expert discusses the science and safety of recreational marijuana

July 10 2023, by Emily Gaines Buchler

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In 1951, the Boggs Act signed into law by President Harry S. Truman meant that anyone caught with cannabis received a prison sentence of two to 20 years, on top of a $2,000 fine. Today, however, adults in Maryland can consume cannabis with no penalty, thanks to legislation enacted on July 1, 2023, making the former Schedule I drug legal to use

and possess statewide.

Maryland joins 23 other states, plus the District of Columbia, Guam, and the Northern Mariana Islands, in permitting anyone 21 and older to buy and use cannabis for both recreational and medicinal purposes. But as more states make cannabis legal, what are policymakers and government agencies doing to ensure its safety? What does the latest research on cannabis indicate that can help the public make informed decisions?

For answers, The Hub at Johns Hopkins University recently sat down with Ryan Vandrey, an experimental psychologist in the Department of Psychiatry and Behavioral Sciences at the Johns Hopkins School of Medicine, who works with an interdisciplinary team in the Cannabis Science Laboratory. There, he investigates the effects and pharmacokinetics (how the drug moves through the body) of cannabis on humans. He also tests products and tracks trends in the burgeoning retail cannabis market, seeking to understand how alterations in dose, chemical components, and methods of use can affect the user experience.

Vandrey has spent more than two decades studying cannabis and can rattle off with ease long lists of new cannabinoid isomers on the market, from delta-10-THC to delta-6a(7)-THC. Below, he breaks down the science of cannabis and the unsettling need for more education, research, and testing to ensure the safety of the products now available at the roughly 102 licensed dispensaries in Maryland—and thousands more nationwide.

What follows is an edited version of the conversation.

As someone who spends day in and day out studying cannabis, what does the legalization in Maryland mean to you?

People get harmed by drugs all the time, even prescription drugs, and cannabis is no exception. But if there wasn't good reason to believe that some value would come from legalization, it wouldn't have happened. On the benefits side, there's been a clear demonstration that the long-lasting war on drugs has been largely ineffective and has marginalized subgroups of individuals. There's also clear evidence that making cannabis illegal hasn't stopped people from accessing it. This isn't my area of expertise, but from a criminal justice perspective, it makes sense to try to establish quality control for this commodity and to pull manufacturing and revenue out of the hands of drug dealers and into the hands of responsible businesses.

But there's always risk and some level of concern when you grant open access to the public of a substance that can produce intoxication and impairment. My biggest worry is with public education and the information about the risks and potential harms of using cannabis that might get lost in the excitement of legalization.

What important research findings do you think are getting left out of the public conversation about cannabis?

[As a society,] we need an open dialogue and increased education about the risks and how to minimize the likelihood of harm for individual users. There just isn't enough discussion currently. For example, research tells us that there are subgroups of people with certain health conditions who should not use products with high tetrahydrocannabinol (THC), the psychoactive component that produces the "high" in cannabis. These include individuals with a personal or family history of psychosis, who can end up in an acute psychotic state that lasts hours or days. Likewise, individuals with heart conditions or even asymptomatic cardiovascular disease can end up having a heart attack or heart failure, despite

exhibiting no previous signs of trouble.

Then there's the risk of accidents that can happen as a result of impairment from intoxication. THC does, in fact, impair a person's ability to drive—and impair plenty of other things, such as decision-making and sense of time. There's also the potential for interaction between cannabis products and medications people take—interactions that many physicians are unaware of. CBD, for instance, inhibits the metabolism of a wide range of prescription drugs, but few people realize this.

Broadly speaking, cannabis containing THC is a drug of abuse. Users can become dependent on it, which means that addiction is another concern—the science is very strong on that, despite many proponents of cannabis use stating otherwise. There's an abundance of evidence showing that the earlier in life someone begins using cannabis—for example, in early or late adolescence—the more likely they are to use cannabis heavily over the long-run. With long-term, heavy use comes the risk of long-term negative health outcomes. The research on that is also clear. All of this said, I want to point out that the science on this is specific to the non-medical use of cannabis that contains THC and is typically inhaled. The risk of abuse for other types of cannabis, other routes of administration, or solely for medical purposes remains to be determined.

Popular messaging suggests that since cannabis is natural, it must be healthy and good for you. On the flip side, there's an outspoken group of people who view cannabis as terrible, as a gateway to misery, despair, and more drug use. So, cannabis tends to be polarizing, much like gun control and abortion, with camps at both extremes.

The truth, if you take all the evidence, is in the middle—cannabis can be both beneficial and harmful. Whether it's beneficial or harmful depends

on an individual's genetics and disposition, what product they use, how they use it, how frequently they use it, and at what dose. It's nuanced.

A wide range of cannabis products exists on the market. What concerns do you have about the safety and regulation of these products?

Twenty years ago, cannabis gummies and vaporizers didn't exist. If you used cannabis, everyone could smell it, and the products inhaled through a joint or bong were generally chemically the same. Now, we have a range of different methods of administration, different doses, and different chemical compositions that make products substantially different from the naturally occurring chemical components of the cannabis plant. Manufacturers are doing selective breeding by extracting and reconstituting plant constituents in unnatural ratios, or they're making the predominant chemical not THC or CBD but THCV [delta 9 tetrahydrocannabivarin], CBG [cannabigerol], and HHC [hexahydrocannabinol]. We don't really have safety data on these chemicals. They may be very innocuous, or inert, or unsafe—we just don't know. For instance, with CBG, we're only halfway through the first human experiment on the chemical, and I could probably name 20 other compounds being added to products in high amounts for which we have zero human data.

This is an example of where the readily available products in the marketplace have little—if any—science that's been done on safety toxicology and things like that. There's a push for cannabis businesses to differentiate themselves and create new products. Market competition, instead of safety, is driving a lot of this.

Some of your research looks specifically at edibles. What have you discovered?

The big takeaway from the research on edibles is that there's a lot of variability in drug absorption and the magnitude of drug effects. Unlike alcohol on an empty stomach, which can cause more impairment, edibles taken on an empty stomach are poorly absorbed. When taken with food, however, edibles produce a higher drug effect. The more fat in the food a person eats, the faster and more [potently] the drug gets absorbed.

It's important, then, that people taking edibles consider their gastric contents and how quickly the product might get absorbed. Someone might take an edible, wait 20 minutes, feel nothing, and decide to take another one. Then they get twice as much THC as they need for an effect and have a terrible experience.

The effects of taking an edible also last longer than when cannabis is inhaled. This may be beneficial for someone trying to manage symptoms of a chronic health condition, but at the same time, can put someone at greater risk if they try to drive home, say, from a friend's house or party.

The other main finding we have discovered is that edibles containing CBD can interact with many prescription medications and increase the likelihood of side effects. Edibles with high amounts of both THC and CBD can have stronger effects than edibles with just THC.

What adverse reactions can people experience, presumably from too much THC?

When people get too much THC, they can have a couple of different types of experiences. One is the impairment of functioning—impaired psychomotor ability, attention, and higher-order cognitive abilities like judgment, planning, and prioritizing. People can also get what's called orthostatic hypotension, meaning they get dizzy when they go from

sitting to standing.

Another experience involves nausea. In our laboratory studies, it is not uncommon for healthy adults to feel nauseated or even vomit when they get high doses of THC. Others can get really anxious and paranoid—and start to question, for instance, whether they're ever going to come down. Anxiety, nervousness, and paranoia can occur in social settings or even when people are alone. Typically, these symptoms resolve with time and rarely require any kind of medical intervention. But to the extent possible, we encourage people to have a confidant nearby to help them get into a comfortable, supporting environment as they ride out any uncomfortable drug effect.

Of course, there are individual circumstances that can warrant medical attention. If the user has a personal or familial history of psychosis and starts to experience psychotic thoughts or behavior, then absolutely, go to a hospital. The same holds true for cardiac events. THC increases heart rate, and there's growing recognition of risk for cardiovascular events—of people, for instance, having a myocardial infarction right after using cannabis. In many cases, these are younger individuals with no telltale signs of cardiovascular disease. But if someone uses cannabis and notices symptoms along these lines—tightening or pressure in the chest, heartburn, shortness of breath—then they'll want to get to a hospital.

Again, it's important for people to understand their family history and genetics and carefully weigh the risks and benefits of deciding to use cannabis.

According to your research, how much THC is too much? And how can users avoid these unwanted effects?

The common adage is to start low and go slow. This way, people can carefully work their way up and find out how they're going to react to a certain dose.

Our research has shown that healthy adults can typically tolerate up to 10 milligrams of THC fairly well, but for some individuals, 10 milligrams can produce a very strong drug effect and lead to an adverse reaction. That's why, for those who choose to use cannabis, we recommend starting at 2.5 milligrams, and then, if desired, working up to five milligrams of THC. If someone can handle five milligrams, then they might consider 10, but they should know that at 10 milligrams of THC and higher is where unwanted consequences like vomiting, anxiety, and paranoia can start happening.

When it comes to edibles, the largest unit dose of THC in Maryland is supposed to be 10 milligrams. But that's too much for many people, so it's important to understand that the edible needs to be broken up into smaller portions. In some cases, that means eating only a quarter of a gummy bear.

Medical emergencies involving vapes continue to make headlines. What have you learned, whether in your own research or elsewhere, about the safety—or lack thereof—of cannabis vaping?

In our laboratory, we've found that vaporization tends to produce a stronger drug effect than smoking due to the combustion of material that happens during smoking, which probably destroys some of the drug. So, if you put the same amount of cannabis in a pipe or joint that you put in a vape, then the vape will produce the stronger effect. Compared to edibles, vaping again produces a stronger effect, but the timing is different. By inhaling the drug through a vape, the peak effect of the

drug happens almost immediately and then reduces fairly linearly over time, whereas an edible involves a much slower onset, a longer peak effect, and a slower return back to no drug effect.

Less harmful byproducts are inhaled with vaping, compared to smoking. But research indicates that vaping devices can introduce other harmful substances that wouldn't be introduced, when say, smoking cannabis in a pipe or eating an edible. For example, a lot of vaporization devices have heating coils made of a certain type of metal, or coated in a certain metal, that can break down and get inhaled. So, it really depends on how the device is manufactured. It also depends on the voltage of the battery because the higher the voltage, the higher the heat—and the more THC (and perhaps metal) getting inhaled.

Right now, there are a lot of unknowns about the long-term health effects of using vape cartridges that contain things like vegetable glycerin or other kinds of vehicles for the drug. Research coming out on e-cigarettes shows that propylene glycol and vegetable glycerin [two chemical compounds present in most e-cigarettes and vaping products], are harmful to a person's pulmonary health in the long term. I would predict that being the case for cannabis vaporizers, too.

Based on that research, I expect the safest method of consumption would be to use the raw botanical flower—the dried flowers, [which are the actual green buds of the plants]—and a vaporizer that doesn't involve putting the cannabis into any kind of liquid or cartridge or anything like that. But again, users need to weigh the risks and benefits, while keeping in mind that everyone reacts differently to THC.

It's important to know, too, that some cannabis extract products like "wax" and "shatter" may contain up to four times the THC than the naturally occurring flower. The use of these products, then, can make it more difficult to titrate the inhaled THC dose with extracts. So, high

THC extracts may raise the risk of someone inhaling too much THC and having an adverse reaction.

You've alluded, throughout our conversation, to gaps in knowledge and a need for more research. Are scientists only beginning to scratch the surface on cannabis research? From your perspective, are more policies and regulation needed on things like marketing and advertising?

Most certainly, there's a need for more research. In fact, we have lifetimes of science to try to catch up with where the market is now. I believe strongly that the onus is on the state to invest funding to evaluate the public health impact of these changes in regulation and laws around cannabis. I'd like to see legislators and policymakers do far more, not only with the rollout of the medical cannabis program but also now, with the adult recreational program. Colorado, California, and Michigan have invested millions of dollars into research on the public health impact of cannabis legalization and on laboratory science to better understand the therapeutic and non-therapeutic effects of cannabis. But Maryland lags behind in that area.

It's easy for scientists and policymakers to lose sight of the medical program versus the non-medical program, but these are separate and distinct programs that need to be looked at through different lenses. For example, what is the rate of misuse of cannabis among those who are using for medicinal versus non-medicinal purposes? What is the public health burden associated with adult non-medical cannabis use, and how does that compare with alcohol, tobacco, or other drug use? Will cannabis legalization result in meaningful changes in the public health burden of other drugs or of criminal justice impacts on marginalized communities? I would like to see the investment of resources to

understand the impact of policy change on these areas. Data needs to be collected at the state, community, and even individual level.

We also need evidence-based regulations on packaging, labeling, and advertising. There's huge concern—and rightly so—about the accidental ingestion of edibles by both children and adults (particularly adults impaired by intoxication). And if we're going to make a drug like cannabis and THC available to the public, then we need to make it distinguishable from non-drug containing food products. There's no reason, for instance, that cannabis needs to be put into a gummy bear, cookie, or brownie for it to work and do what it's intended to do for the end user, whether therapeutic or not. What about the impact of flavors and other formulations of products that are designed to draw in younger users? Right now, regulations around product specifications, packaging, and advertising are poorly developed, and there's a need for research on these topics.

Another piece is education. Adults using cannabis products need to keep them locked up and completely out of reach and sight of kids. Likewise, would-be consumers need to know what an appropriate starting dose of cannabis might be. They need to know the differences between THC, CBD, and other cannabinoids, and how drug effects differ based on whether the drug is inhaled, swallowed, or topically applied to the skin. People need to discuss use with their doctors to determine if there might be interactions with medications they are taking. For example, we recently completed a study showing that oral CBD can significantly inhibit the metabolism of many prescription medications and can increase the potency of oral THC. That's a significant finding that could affect millions of people.

In general, there just needs to be more of an open conversation about cannabis and the potential risks that come with using. Education and dialogue are key to empowering people to make informed decisions and

avoid risky use patterns.

Provided by Johns Hopkins University