



**Dr. David Stukus:** Hello and welcome to Conversations From the World of Allergy, a podcast produced by the American Academy of Allergy, Asthma & Immunology. I'm your host, Dave Stukus, I'm a board certified allergist and immunologist and serve as the Social Media Medical Editor for the Academy. Our podcast series will use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The Find an Allergist <http://allergist.aaaai.org/find/> search engine on the academy website is a useful tool to locate a listing of board-certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allergy, Asthma & Immunology terms of use agreement which you can find at <http://www.AAAAI.org>. Today's edition of our Conversations from the World of Allergy podcast series has been accredited for continuing medical education credit. The American Academy of Allergy, Asthma & Immunology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Information about credit claiming for this and other episodes can be found at <https://education.aaaai.org/podcasts/podcasts>. Credit claiming will be available for one year from the episode's original release date. We also encourage all listeners to visit the website to see additional resources and provide feedback. We are pleased to welcome William Silvers who will discuss the hot topic surrounding marijuana and how it affect asthma and allergic conditions. Dr. Silvers is a clinical professor of medicine at the University of Colorado School of Medicine and has over 30 years of clinical experience as an allergist in private practice in Denver, Colorado. Dr. Silvers has been an active member of the American Academy of Allergy, Asthma & Immunology and served as a founding member and former chair of the original complementary alternative medicine committee. Dr. Silvers has led a distinguished career devoted to advocacy and bioethics with clinic interests in publications related to personalized integrative allergy care and most recently his experiences with allergic reactions to marijuana. Neither Dr. Silvers nor I have any relevant relationships to disclose. Dr. Silvers, thank you so much for taking the time to join us today and welcome to the show.

**Dr. William Silvers:** Thank you very much for inviting me and for broaching this topic.

**Dr. David Stukus:** And I think it's a fascinating topic and as you know, this tends to generate a lot of interest particularly given the widespread adoption of complementary and alternative medicine approaches for treating various medical conditions. Before we discuss specifics related to marijuana, can you describe how the terms complementary medicine, alternative medicine and integrative medicine differ from one another?

**Dr. William Silvers:** David, thank you. I think that the semantics are important, CAM or complementary alternative medicine encompasses complementary modalities that complement traditional medicine, that are used in addition to the orthodox treatments, for example, yoga type breathing for asthma using

eucalyptus in a steam shower in addition to the environmental medications that we may recommend, while alternative medicine are those modalities that are used in place of traditional medicine, for example acupuncture, chiropractic for asthma, homeopathic medicines rather than the pharmaceutical medications that have been tested for safety and efficacy. So I relate to the approach of integrative medicine which is those modalities that have evidence-bases integrated with the time tested treatment for which we have the studies. As an example probiotics that we give now in pregnancy and vitamin D supplementation potentially because after enough evidence for safety and efficacy has accumulated then these complementary modalities can transition into mainstream therapy. So an integrative approach takes into consideration the environment, the nutrition, the diet, exercise, sleep and stress management for the patient in addition to them discussing the medicine's immunotherapy that the patients may need. And I think that medical cannabis when well studied can be considered at presently a complementary modality for certain conditions, we're starting to see it used now in seizure disorders, movement disorders, cancer, pain, HIV/AIDS but we need more research to know exactly how to administer, how much, what adverse effects, interactions it may have. So medical cannabis needs to be placed into our armamentarium after we have addressed the traditional approaches, in addition to that with due consideration, we can consider it a complementary approach presently because it does have certain evidence that's being accumulated for certain conditions and that's why you have certain legal indications in states that have medical marijuana legalized but it's not yet in our pharmacopeia and our standard approach.

**Dr. David Stukus:** That's a great introduction. Do you find that there's a lot of confusion or misuse of the terms complementary and alternative medicine from the patients that you discuss with or even in media reports that you read about?

**Dr. William Silvers:** Oh very much and so that's why in those patients who have chronic illness, chronic sinusitis, chronic asthma and they've been on the usual medications and they become more desperate in search for something that will help them will go to other practitioners, alternative practitioners that may be using modalities that have no substantiation and so that's why I think that it's important for we as allergists with our patients, for primary physicians to be open about a patient's personality, a patient's needs and address them in the context that the patient will be cared for well with what the tools that we have and then if they wish to explore beyond that, they know what they're getting into, they know what techniques there are and that they feel they can come back to their allergist, their primary physician with where they have been exploring. Because all too often patients will go out and not tell their primary doc, they'll be ashamed to discuss that they have been to wherever they've been and they've had blood tests for food allergies for example that really have no established clinical relevance. And so we know from previous work that we've done quite frankly that two-thirds of our patients in the allergist's office would like to address complementary approaches within the traditional model rather than having to go outside of it. So that's why I think that every good physician practices in a holistic fashion but those who practice so called holistic medicine you have to be very careful about.

**Dr. David Stukus:** I'm so glad that you brought up that important aspect of our patients, we know that they are investigating and interested in these complementary therapies but we also know that many physicians are ill equipped to really discuss them. And along those lines, can you provide some talking points for our colleagues, specifically when patients ask about complementary approaches to treating

their allergic conditions and do you have any take home messages surrounding the quality and amount of evidence that's either for or against?

**Dr. William Silvers:** I think a few things, number one we need to be open and nonjudgmental when caring for our patients. And number two, we need to be able to know the resources that are available to us in terms of what complementary or alternative things that the patients may be thinking about or doing. So for example, the NIH, the National Institutes of Health has an institute previously called the National Center for Complementary Alternative Medicine which is now called the National Institutes of Complementary Integrative Health, that one can search on their website and have patient derived information and so allergists can address that also as to what the references, the evidence-bases is. In addition, we have certain well vetted resources such as the Natural Medicines Comprehensive Database, natural medicines which is provided by the Pharmacists' Newsletter, it's very well a resource. And in fact the Academy, the American Academy of Allergy, Asthma & Immunology for which we're doing this now provides this resource as a benefit to its membership which I hope the membership will take advantage of because it will be able to educate us as to what supplements people are using, what the adverse reactions may be and what the interactions may be with traditional medications. We in fact wrote a paper in the Annals of Allergy, Asthma and Clinical Immunology in 2014 on an integrative approach to allergy and asthma using complementary alternative medicine. Gailen Marshall is the editor and he's interested in the stress component of allergic disease. What we really came up with is that lifestyle is important, patient's diet, not only avoidance of highly processed foods, et cetera but enhancement of fruits and vegetables and coldwater fish like salmon are important to address, biologically based therapies like herbs, vitamins, minerals, supplements can be resourced. And there's a value to exercise and as an important role of stress management because even meditation has been shown in one of the studies that Gailen Marshall was involved with in decreasing skin test reactivity therefore potentially decreasing allergic reactivity. So I think that allergists in addition to what we traditionally recommend in terms of environmental precautions, medications, allergy immunotherapy, potentially allergy injections, allergy shots, the biologic therapies that are emerging, I think we need to be very attentive to the art as well as the science of our patient care and address the patient with mind, body and spirit and even in the best of the scientific hands.

**Dr. David Stukus:** There's a lot to unpack there and that's wonderful and we're going to make sure that we provide the links to those resources that you mentioned on the website and I think we're going to have you back on if you're willing to really take a deep dive into all these issues because there's a lot of great information there. But alas, let's get back to the topic at hand. And as you know, you live in Colorado which is one of the first two states to legalize recreational use of cannabis in 2012. Can you give our listeners some information about the current state of marijuana legalization in the United States?

**Dr. William Silvers:** Be happy to. It's interesting, medical marijuana is now legal in 33 states and recreational marijuana is now legal in 10 states plus the District of Columbia. California was the first state with medical marijuana, Colorado was first out of the gate with recreational marijuana legalization, same time as the State of Washington legalized it by ballot, but Colorado was able to put it into effect in 2014. And different states have various indications for medical marijuana for different conditions, in Colorado for example, the indications, the legal indications to have a medical marijuana license are cancer, glaucoma,

HIV or AIDS, cachexia or wasting syndrome, persistent muscle spasms, seizures, severe nausea, severe pain, PTSD, post traumatic stress disorder and more recently added on autism spectrum disorder. We actually found in Colorado when it was first legalized that we had a lot of patients, families, especially with seizure disorders coming in, moving to the state so they could have easier access to the availability of recreational marijuana. And variously in other states, you have indications where there has been evidence for Parkinson's, inflammatory bowel disease, multiple sclerosis, ALS, et cetera, it's been used in the elderly and the senior population because they have the tremulousness, the movement disorders, depression, they found that the elderly with small doses of both inhaled and oral do better. So with more legalization we know that more research needs to be done. And since it's still a Class 1 FDA federally therefore illegal drug, this needs to change to really be able to do the population research we need to do.

**Dr. David Stukus:** Have you always been interested in marijuana or did it really grow after legalization in the state where you reside?

**Dr. William Silvers:** Well I can tell you, my personal experience and my involvement with it began when I started seeing patients in the office, when it was legalized medically in 2010 in Colorado and then we saw a number of patients that especially those who were working in the industry, who were the growers, the bud tenders, those who had exposure and we saw classic allergic reactivity, I mean asthma, allergic rhinitis and especially a lot of dermatitis and contact urticaria. But then when it was legalized recreationally or what's now called adult use, then I saw a lot more patients coming to the practice as did the other allergists in Colorado. But I think that some people, a lot of patients are reluctant to talk about it because it's stigmatized and was illegal and I think a number of docs are not comfortable in asking about it and dealing with it. So that's why I started to pay more attention to it. And then quite frankly in 2015, there was a paper that came out in the Annals, a review article by Thad Ocampo who was a fellow at Wilfred Hall Air Force Base in their fellowship program and his research project he did a paper "Cannabis Sativa: The Unusual Weed," it was a very highly accessed reference paper and so they asked for there to be a commentary on it and a number of people were reluctant to give commentary and I said that, "I have a--" I was on the Board of Regents at that time, I said, "I have a number of patients who have had reactions and these are the kinds of reactions." You get your five minutes of Andy Warhol fame. And then there was a American Thoracic Society meeting in Colorado that had for the first time a session on cannabis respiratory reactions and Don Tashkin from UCLA who's kind of the grandfather or allergy pulmonary reactions to cannabis was speaking and then the Colorado law required that there be some tax money devoted to research, it was the first time in the world that we know of that there was government sponsored research, so a number of researchers in the university applied for grants and they had to present their results publically and so there was even a presentation at National Jewish Hospital, National Jewish Health by these researchers and I happen to have been the only allergist in the audience then because I had been asked to give a talk elsewhere. And so it led to, I said, "Somebody needs to lead the charge here," and so I felt that being a clinical professor at the University of Colorado and being in practice for a long time myself that I had a track record that I could speak out on this. And that's how I got involved with it. And since then, now we have just sort of in the last year we've now put together a cannabis allergy discussion group at the Academy and the college, part of the Integrative Medicine Committees whereby a number of people who are interested, United States, Canada and also Europe at

the last Academy meeting, we had about 35 people that were in round table discussions, so everybody's needing to pay attention to it now.

**Dr. David Stukus:** Oh certainly, especially as you mentioned with the widespread legalization in various forms and things like that. But thank you for the fascinating historical background and it's truly interesting to see how you've been involved and also how this has gained attention from the professional organizations and at the meetings and things like that. You've mentioned a couple of different terms and I wonder if we can pause for a second and have you go back and really describe the differences between terms such as cannabis, marijuana and I'm going to throw in CBD oil which is quite popular these days but can you describe how those are the same and/or different?

**Dr. William Silvers:** Yes. Actually there's a lot of confusion in the people who are working with it, but basically I like to view it as medical cannabis when it's used for a medical purpose. And I can tell you that hemp and marijuana are simply broad classifications of cannabis that cannabis sativa, the cannabis indica plants that were adopted into our culture. Hemp is a term used to classify varieties of cannabis that contain less than 0.3 percent THC, delta-9- tetrahydrocannabinol which is the psychotropic, the one that causes you the high. Marijuana is a term used to classify varieties of cannabis that contain more than 0.3 percent THC by dry weight and can induce the euphoric effects on the user. So I like to use the term medical cannabis because that's really what it is and it has been, marijuana was a term used to describe the influx of this plant from Mexico in the early 1900s, mid 1900s with a negative stigmatization connotation by the government especially when they made it illegal. It's really the cannabis plant used medically or recreationally and hemp derived CBD is the term used when the THC content is less than 0.3 percent, so that's the important semantics description I think.

**Dr. David Stukus:** So CBD oil should not give anybody the euphoric high that they would get from consuming marijuana in other forms, is that correct?

**Dr. William Silvers:** Exactly right, providing it was produced by reliable growers, distributors, et cetera, CBD itself is purported to have an anti-inflammatory, an immunologic effect, the degree of which it has this effect without the THC is subject to question because a lot of the studies are showing that it's a THC CBD relationship. Mind you, the cannabis plant has over 60 cannabinoids in it, CBD, CRG, CBN, et cetera, it's the THC that is the psychoactive one, it's the one that causes the high and then it's other parts of the plant also, the flavonoids, the terpenes that may be playing a role. So there are some researchers who are working with cannabinoids in terms of the receptors, the CB1, CB2 receptors in the endocannabinoid system, we have an endogenous cannabinoid production and there are others who are plant biologists who feel that it's really the complex of the whole plant with the THC, the CBD and all of the other cannabinoids and terpenes and flavonoids that make a difference. So that may be a long answer but the science of it and the psychopharmacology of it and the medical effects of it because there may be different strains that are valuable for different disease processes, so that's all still needing to be worked out. We know though that patients improve or at least a lot of patients improve with the specific disease processes such as I had mentioned where a lot of states have different legal indications for it. So it's a patient driven sort of a need for further research.

**Dr. David Stukus:** Boy that's just a lot to also unpack there as well and it is complicated and as you mentioned multiple different levels to it. I can see why this would be rife for confusion among patients and providers as well as an area that's really rich where people can take advantage and apply their own pseudoscientific spin and things along those lines, so thank you for that introduction. Now we're going to talk in a second about IgE-mediated hypersensitivity reactions to marijuana and derivatives. But before we get there, can we talk in a more general sense about some of the health risks that can occur for somebody who has asthma for instance whether if they directly inhale marijuana, what can happen to them?

**Dr. William Silvers:** A lot.

**Dr. William Silvers:** Potentially a lot. And I'll tell you, it's been a subject that the allergy and the pulmonary community has been aware of for a number of years. Just by background, marijuana or cannabis and we'll use those terms kind of interchangeably and hemp derived CBD we might use that term specifically, can be consumed by several routes of administration, smoking, vaping, oils, topicals, capsules, they're putting especially CBD since it's now become legal in everything and it's not being well tested in a lot of, in food products for example and the positive and the adverse reactions can be different depending upon how it's consumed. We know respiratory wise that smoking marijuana can cause a chronic bronchitis with an irritant cough reaction and sputum production and you can have wheezing with it. We know that the same carcinogens are seen marijuana as in tobacco smoke and we see premalignant lesions in the airways. But interestingly there's no substantiation of lung cancer, in fact there may be an antitumorigenic effect of marijuana which is why it's being used in a number of cases with cancer in addition to its treatment for the nausea, vomiting that can be seen with the chemotherapy, by the same token, interestingly there's no solid evidence for emphysema or COPD. So marijuana is an acute bronchodilator and it also has a relaxation generalized anti anxiety effect so some asthmatics may feel an improvement with marijuana depending upon the method of consumption. But interestingly heavy use can cause airflow obstruction so it's not generally recommended for asthma and while I say that, as you know every patient is different, the heterogeneity, the difference in patients' presentations and so we need to pay attention to the individual patient but there are adverse health effects, allergy, respiratory wise, et cetera. Interestingly I can tell you inhaling cannabis has a much faster onset of action than other routes, edibles have a slower onset of action, et cetera but inhaled, while there are now computerized meter dose inhalers that are being developed to give you a certain number of milligrams of cannabis, they call it titrating or dosing, the effects and the adverse effects are such that it still needs to be worked out.

**Dr. David Stukus:** And to be clear, as we mentioned at the beginning of this show, we are not advocating that any patient with asthma self medicates with the use of marijuana for the purpose of improving their asthma, would you agree with that?

**Dr. William Silvers:** I agree with that totally but I will also say that not to be surprised if some patients come in and they say that when they inhale marijuana they feel better, why, because we know that it's an immediate bronchodilator and we know that it has an anti-anxiety or a relaxation effect so people may feel better with their asthma but it's not something that we can recommend because we really need to study it and that's why I bring up the heterogeneity of patients, it may be just individual patients may have a

greater response than others. I'll say this, I have been involved recently with Joanna Zeiger, who's an Olympian, an Iron Woman champion, lives now in Boulder, Colorado, she's actually the daughter of Robert Zeiger, one of our colleagues who's an eminent MD/PhD allergist in Southern California and Joanna who ran in the first triathlon in the Sydney Olympics and came in fourth actually had an accident, a biking accident, pain which was not well controlled with conventional medications and you know we have this whole opioid epidemic that we as a society and the government is trying to address now. And there's a thought that cannabis may be a step down, that it may be one of the approaches to getting down off the opioids. But in Joanna's case as an example, her personal case and she in fact has started this group called Canna Research Group, [www.cannaresearchgroup.net](http://www.cannaresearchgroup.net) which is trying to do observational studies for improvement adverse affects of medical cannabis with her father and I'm involved with them also. And she has spoken at the Academy meeting for example last year on exercise induced bronchospasm in elite athletes. And what she has said is that she cannot smoke it in any capacity because it's a huge irritant but there's some vape pens that she can use without incident, she has to know how to regulate how deeply she inhales and why vape at all when you have asthma but the question is with chronic pain, sometimes you need a quick onset of action and can't wait for the 45 to 60 minutes for an edible to kick in. So sometimes, and there are a number of athletes in Boulder actually which will sound familiar that will sometimes take an edible and a vape so they get the immediate relief from the vape and then over time, in an hour the edible will kick in and wears off longer. So there's an evolving use for it medically and as I think we get more-- as pharma meets weed, as the pharmaceutical industry addresses medical cannabis, we're going to be seeing hopefully more effect with less adverse effects but as allergists and pulmonologists, we need to pay attention to it a lot.

**Dr. David Stukus:** To go back to what you just mentioned, do we have actual evidence yet that demonstrates one form of inhalation is more risky or safer compared to another?

**Dr. William Silvers:** No, and I can say this that as much as an example, e-cigarettes or the vapes are being touted as healthy, there's nothing healthy about them, they may be a healthier alternative than smoking cigarettes as an example, healthier alternative but there's nothing safe about them, and in fact the concentration of the oils, the cannabis in them may be greater than that of just smoking a joint let's say or a pipe. But there's been no studies that I'm aware of that show-- only anecdotes and as they say the plural of anecdote is anecdotes, it's not evidence, so patients need to try and see what works. If there's a need, especially if there's a patient with pain that has asthma and that has found that cannabis is helpful for the pain and they need immediate onset, perhaps there's a role for using a vape that they can tolerate and I'm not advocating it necessarily other than in states where it's medically legal perhaps and to see. But there's also a concept, not to get too detailed of micro dosing, of using-- because now we can measure the number of milligrams that cannabis is being produced in flower, in vape, in oil, et cetera, to micro dosed, what they call start low and increase slow to where you take a little bit in whatever fashion, vaping, edible, oil, et cetera and just increase slowly to see what your therapeutic effect is so that you don't get a lot of side effects. For example, you want to have an effect for pain relief but you don't want to have the high and you find that you need a little THC in addition to the CBD to really have the effect. Quite frankly, a study that had been done by Joanna Zeiger and the Canna Research Group in terms of elite athletes with pain, showed that it's the combination of THC and CBD that makes the biggest

difference, not the CBD itself. So there's a lot that we have learned and there's more that we really still need to learn.

**Dr. David Stukus:** And I think you really summarized this quite well, but at this point in time and we're recording this and we'll launch it in the summer of 2019, it seems like we're just lacking in evidence that can really help healthcare providers determine the safest form and that amount that patients should be using while at the same time we want to encourage open conversations between medical providers and patients in regards to the use of these products because we know that they are being widely consumed.

**Dr. William Silvers:** Well said, well said.

**Dr. David Stukus:** Well thanks. So let's move on to the allergic reactions because that's something that you've really been one of the pioneers in describing, so let's go back to that and can you describe the types of allergic reactions that can occur to marijuana and how that might differ from symptoms that occur with other forms of exposure for instance?

**Dr. William Silvers:** Yeah. Well as I had said, we have to remember that marijuana cannabis is a weed and just like other weeds or even just like other pollens, trees, grass, it can cause similar reactions upon exposure whereas I saw a few patients from 2010 to 2014 when medical marijuana was legalized. After 2014 with recreational marijuana legalized, we saw a lot more and different presentations. So I had written that up, "A Colorado Allergist's Experience with Marijuana Legalization" where we saw a lot especially those working in the industry and having a lot of contact with their skin, dermatitis, hives, itching and nasal allergic rhinitis. If you're growing plants in your home, it may be causing you the difficulties, not just elsewhere. Lungs, asthma, cough and there's reported anaphylaxis on ingestion of hemp and hemp seed although I personally have not seen any anaphylaxis with ingestion. I will say this for the allergy community that we did a study in our office that reported in 2017 actually, the "Spectrum and Prevalence of Reactions to Marijuana in a Colorado Allergy Practice," I can just speak to our own practice. It showed, and this is what's really important for the allergists to be aware of, that of our patients that had no previous exposure at all, had never smoked marijuana, et cetera, only 12 percent of them had any kind of an adverse reaction upon passive exposure. Of our patients who had previously smoke marijuana but not presently, 26 percent of them had some kind of adverse reactions. But of our patients, and these are still small numbers, just about 130 patients, of our patients that continued to use marijuana, half of them, 50 percent of them had experienced an adverse reaction. So we know that the more exposure the more reaction, so we as allergists need to advise our allergic patients to be more careful than the general population. And it may not be just due to the pollen or the protein, it may be due to other factors in the production, the mold, like Aspergillus, the pesticides that-- that's why you have to be very careful about who the providers, the growers are, there may be dust mite in there. So that's, it's something that we as allergists really need to pay attention to.

**Dr. David Stukus:** That's just so fascinating to me. Now in addition to taking a detailed clinical history of the typically symptoms that would occur with an IgE reaction, as you mentioned hives and dermatitis, coughing, rhinitis, upper, lower respiratory symptoms and with exposure, is there a skin or a blood test that allergists can use to help confirm whether somebody has a marijuana allergy?



**Dr. William Silvers:** Not commercially available. I think the most important is the history, just like with any other evaluation, a nonjudgmental history of the patient's exposure and usage and quite frankly, not just personal usage but maybe even secondary, second hand smoke as you may be interested in that other people smoking in the vicinity and so you have passive inhalation just like you have with cigarettes. In fact, the National Jewish, Nathan Rabinovitch and colleagues are studying the second hand exposure also as they're studying pollution, air pollution. And now just recently there's being described, we just went to this Institute of Cannabis Research sponsored by Colorado State University in the State of Colorado in Pueblo third hand exposure going into laboratories, going into workplaces, going into homes where marijuana cannabis has been used but it's not presently for second hand exposure, just going into those environments, you can have third hand exposure, it's just like cat and dog dander, right, when you go into a room that the cat had been in and you get reactions because there's a second and third hand exposure to it. So I think that firstly, in the evaluation is the history of not only the person but the environment. Secondly, what we did quite frankly is just do a skin test with the raw substance, had the patients bring in the marijuana, hopefully the grass from the dispensary where they got it and like the old mortar and pestle the allergists use to do, it gets grounded up and made our own skin test and have actives and have controls and so we tested patients themselves and also staff in our office. And I got to tell you, it's very interesting, for example we had some young medical assistant students that were training in our office and they lit up like lamps with the skin tests that we did, and fortunately a number of our medical assistants and nurses were negative and the patients were positive or negative depending, but you can do your own skin test. Now here's where it gets a little bit immunologically challenging for the allergist, obviously with a Class 1 FDA federally illegal, we're not going to get any commercially available extracts any time soon. You can do a puddle test, you know, that the patient can bring in their own, et cetera, et cetera. Cannabis allergy has been mainly attributed to the Cannabis 3 segment, the nonspecific lipid transfer protein of cannabis sativa. So you have to look at both the-- it's an interesting thing, they're developing just for research use only extracts for in vitro blood testing but there's nothing available now but we know that it's an immunologic imperative.

Q Do you recommend using a presumably non-sensitized control when you do these sort of homemade skin tests, just since we don't really understand the false positives, negatives, things along those lines?

**Dr. William Silvers:** David, absolutely it's imperative that you have your positive and negative controls, positive controls so that you know that you're getting an immunologic reaction with your own extract. There is a protocol, Gordie Sussman in Toronto and colleagues including colleagues from NIOSH because the National Institutes of Occupational Safety and Health have been concerned about the occupational safety of workers in the industry because of the increase in, in part allergic and respiratory reactions. So they have put together a protocol that has been published for how to put an extract together. But without getting into the details because it's not a standardized, it's just their suggestion, you have to have a positive and negative control to know that you're doing a good skin test just like a fresh food extract. So yeah, so the technique is important and without positive and negative controls you may be seeing an irritant reaction or you may not have the potency of the extract that you're putting together that you really need.

**Dr. David Stukus:** Now once you sort of go through the evaluation and you identify somebody who likely has an IgE hypersensitivity to marijuana's derivatives, those patients need to strictly avoid exposure, are there other treatments that they can try first? I can only imagine that a lot of folks would be resistant to strict avoidance so any recommendations on how to talk to those individuals?

**Dr. William Silvers:** I have to tell you David, I'm smiling because how to approach this in terms of assessment and recommendations and patient education is part of the art given the science that we have. So now environmental avoidance is a natural response but for those that are as you say resistant to the suggestion of avoidance, perhaps suggestions as vaping may be better than smoking but not necessarily healthier, perhaps the newer now available sublingual sprays, oils, maybe-- I know that for example in Israel where medical marijuana was first legalized in the early 1990s because they found that the AIDS patients who were smoking grass were healthier and had greater longevity, better qualities of life than those who weren't smoking grass, why, because it stimulated the appetite, maybe it had other effects. And so they now have medical marijuana both inhaled and by oil and it's a patient preference. I think that while there may be a role for inhaled because allergists, pulmonologists need to be especially careful with that, the oils may be the way to go but the inhaled has a faster onset of action. So there are allergic reactions and the avoidance or the minimization is important but also the newer forms of delivery, patients just have to kind of experiment but again, it's the theme that is now being given in all the literature in the states that it's legal you start low, you increase slow, you start low and you go slow and then you treat the patients as we treat any other allergic reactivity.

**Dr. David Stukus:** This whole conversation is really, sews up this theme of individualized approaches, open conversations, shared medical decision making, understanding of education, risks and benefits and I think more than anything that this whole topic really, that all those things need to be taken into consideration.

**Dr. David Stukus:** The harms and benefits relationship, the safety efficacy is ultimately important for us as physicians and for us to impress upon the patients but also the need to be very sensitive to the patient's personality, their needs, their wishes and to see what might be available that the patients can follow with, yeah, you're absolutely right, this is where the art and science and medicine of being a good holistic compassionate physician is front and center.

**Dr. David Stukus:** Well as we wind down to the end of our conversation here today, I'd like to touch upon CBD oil, as you know, this is one of the most popular trends that we're seeing and it's being marketed as a treatment for just about every type of symptom or medical condition that you can imagine. Can you discuss any evidence that demonstrates benefit of using CBD oil specifically for asthma or allergic conditions?

**Dr. William Silvers:** In a word, no, not well.

**Dr. David Stukus:** Okay.

**Dr. William Silvers:** The world of CBD has blown up, you know, you've got CBD being put in all kinds of foods as a marketing stunt, the growth of CBD infused products is undeniable, Colorado as an example is a micro brew capital also, we've got the Great American Beer Fest and several years ago there was a cannabeer that had CBD showing up in drinks, salves, touted as the next best thing but it's really just too early to know the true medical impact. One of the factors is dosing, how much is a therapeutic dose, is it 5 milligrams, 500 milligrams, 1,000 milligrams. And there's no regulation on the testing of the CBD products now, it's not only the Wild West but it's the Wild East, North and South. So I think the best advice is to be an informed consumer, do homework on the products that you may be purchasing and to assure that there's a certificate of analysis that it's been independently tested by a state regulated lab, that's important.

**Dr. David Stukus:** What about any risks that have been recognized from using CBD oil for somebody who has asthma or allergic conditions?

**Dr. William Silvers:** You know, we're doing a study here on dermatitis because there's a lot of literature in this area in terms of the lotions and oils and salves that are being produced and reactions to it. We know that from patients' histories that there is a risk in adverse reaction, we just don't know the nature and why and how much, et cetera, it's all open right now.

**Dr. David Stukus:** Okay, well as we kind of wind things down, I have one final question for you if that's okay and then I'll allow you to obviously any comments you'd like to convey. But this was a fascinating conversation, it's complicated and I'm sure this is going to evolve over the next several years as well but as we see legalization and use becoming more widespread, do you have any talking points or anticipatory guidance that you can lend to allergists and other physicians when they discuss this topic with their patients?

**Dr. William Silvers:** Well number one, I appreciate your invitation to speak on this because I think that it's important to be open to what's happening in our society and to address that, the history with our patients, you've got to ask. We know from a previous Academy survey that was published that allergists are excellent at asking their patients about smoking cigarettes, but do we ask our patients each time about any marijuana or cannabis use? Because if we don't, I think that now we should and not just personal use but exposure to second hand smoke and perhaps even third hand exposure. And next just to recognize that marijuana is a weed, cannabis sativa, cannabis indica which can act like an allergen like any other tree, grass or weed allergen. And in addition to the pollen, the IgE known reactivity which is why you have skin test positivity, there may be other factors, they may be IgE negative but it may be the moles or pesticides. And I think that another point that's very important for allergists to know is the cross reactivity with foods, we know that there's a pollen food cross reactivity, ragweed, chamomile, melons, et cetera and it also has been described, a cannabis fruit vegetable syndrome, not only is it the Bet v 1 as in oral allergy syndrome with birch, tree pollen and certain foods but now there's a group especially from Belgium, Didier Ebo and his colleagues that has identified a nonspecific lipid transfer protein seen in certain fruits and vegetables included pitted fruits like peaches, what they call stoned fruits so to speak, not to be too humorous about it, that cross reacts, no seriously, they published this, that cross reacts with the cannabis flower itself. So we may be seeing more cross reactivity with foods and pollen as we do with

latex and foods like kiwi and bananas. And that's part of the reason that we started this cannabis allergy discussion group with the allergy community at the Academy to address this and our experiences in North America as well as internationally. Just to go back David, I think that it's important to recognize the history of the development of this, cannabis has been in the literature for thousands of years, 5,000 years ago in China, 3,000 years ago in the Middle East, Persia and Egypt as a treatment for headaches, arthritis, menstrual periods. And that's why an Israeli plant biologist in the '60s, Raphael Mechoulam started studying the plant cannabaceae getting it from police busts and he first identified delta-9-THC in 1964 and he in fact is in his '80s now and is still at the Hadassah School of Pharmacy every day and his laboratory is studying the endocannabinoid system which is a natural system in our bodies, we have CB1, cannabinoid 1, cannabinoid 2 receptors so it's a natural chemical. And in fact cannabis was in the U.S. Pharmacopeia in the early 1900s produced by pharmaceutical companies like Lilly and Merck until 1937 with the Marijuana Tax Act when the government made it illegal. So we know that it's been in the ancient literature, we know that patients get better, how and why, et cetera we don't know yet but now is the time that this bench research that plant biologists and chemists have been doing can be translated to the bedside, I kind of call it pharma meets weed, you know, for benefit, harm, safety, efficacy for our patients' benefits. And I think that medical cannabis, medical marijuana can develop from a complementary add-on to a pharmaceutical with our openness and good pharmaceutical research and societal and governmental acceptance of it and people like yourself who are doing podcasts, you know, for educating our own allergy community of which I'm very appreciative.

**Dr. David Stukus:** Oh, thank you, I really can't thank you enough for being with us today, it's a captivating story, one that has not been completed as of yet and I for one am interested to see what the next chapter brings us. And thank you again, this is extremely helpful, I learned a lot by talking with you and I look forward to having you back on in the future as we learn more about this. Is there anything else you'd like to add?

**Dr. William Silvers:** David, I thank you and the Academy for all of your educational efforts and for bringing the older guys like myself into the world of social media.

**Dr. David Stukus:** Was this your first podcast as a guest?

**Dr. William Silvers:** Yes, absolutely, first podcast as a guest or as any part of a podcast.

**Dr. David Stukus:** Wow, I'm honored and you nailed it, so thank you.

**Dr. William Silvers:** All right David, thank you very much and Laura, thank you very much.

**Dr. David Stukus:** We hope you enjoyed listening to today's episode, please visit <http://www.AAAAI.org> for show notes and any pertinent links from today's conversation. If you like the show, please take a moment to subscribe to our podcast through iTunes or Google Play so you can receive new episodes in the future. Thank you again for listening.