

40+ Years of Addiction Research, Dr. Mark Gold

DEA Museum Lecture Series, June 6, 2014

SF: Not a bad crowd for a Friday morning. Ladies and gentlemen, good morning and welcome. *My name is Sean Fearn, and behalf of all of us and the DEA Museum staff, we want to* welcome you this morning to the continuation of the DEA museum's Spring Lecture Series. Just a quick side note, as a courtesy, both to your fellow audience members as well as to our guest speaker, if you could silence your electronic devices, we would appreciate it. Here at DEA Museum, we focus on presenting history, facts, and science. The history of drugs in this country, the history of DEA, the facts about how drugs affect society and what DEA is doing about it. The science, how science has and should always inform drug policy. How science tells us what drugs do to the brain and the body, and how science is helping us understand and treat addiction.

SF: Today we have a very special guest speaker with some very special socks from the University of Florida. Someone who has a long history with DEA but an even longer history on this topic, Dr. Mark Gold. It would take hours, literally hours to tell you all of Dr. Gold's accomplishments in work. Dr. Gold if you will indulge me, I'm going to go with a Cliff Notes version of that. First and foremost, Dr. Gold is a researcher and a mentor. He began his career at the University of Florida back in 1970. He has authored over 900 medical articles, chapters and abstracts. He has 40 years of successfully mentoring young addiction researchers, teachers and clinicians. He has been a leader at the university level, the state level, the national level and the international level in drug abuse prevention treatment and research. He's been a contributor to national drug strategy. He is been an advisor and a participant in consensus panels and worked at the national institutes. He has pioneered work on brain systems, underlying the effects of opiate drugs that has led to a dramatic change, in the way opiate action is understood. And certainly we know, Dr. Gold from his work in the 1980's, developing a new theory for cocaine action, cocaine dependence and cocaine withdrawal in the dopamine rich areas of the brain. Dr. Gold is the Donald Disney eminent scholar, a distinguished professor, a distinguished alumni professor, the chairman of the Department of Psychiatry. All of that at the University of Florida. And while there, he has been a distinguished professor in the departments, plural of psychiatry, neuroscience anaesthesiology and community health and family medicine. Please welcome to the stage, Dr. Mark Gold.

MG: Thank you very much. That's a great introduction and it'll be hard to follow. I'll do my best. You know, when I was invited to speak at this series, I was given a choice of dates. And I took the one with the best weather. So I was, I was right that the weather would be great. And I'm grateful for all of you that have come out because you could have equally have chosen to be at the beach or the shore. So hopefully we'll have some really good lessons for everybody and some good sharing.

MG: So, that's where I work at the McKnight Brain Institute which is a really unique University of Florida, kind of cross discipline, research, enterprise with neurology, neurosurgery, psychiatry, neuroscience and addiction. All sharing space and trying to figure out what drugs do in the brain? Could constituents of food have drug-like qualities? Is smoke in cigarette smoke the same as nicotine? Is smoke and cannabis smoke the same as THC? What choice will animals make when they find that they like drugs? And well, how much pain and suffering does that cause them in terms of survival. So, we have a lot of really

exciting work we're very proud of, and I'm grateful to have the chance to share some of that with you. I also do talks at the University of Florida alumni clubs and my joke to my Dean is often that when the football team is bad, they celebrate the academics. And I go to Gator Clubs and everywhere and speak about the academic mission and about the things that we're trying to achieve at the University of Florida and I'm very proud to do that.

MG: I thought that I would show you some person that you cannot possibly recognize, and that's me. But the person that you can recognize is here in the front, Jack Lawn, who worked closely with me when we were trying to figure out how people could possibly be getting addicted to a drug that was called the champagne of drugs, non addicting cocaine. And you know sterling in a lane and so many of the people here are such a big part of my career that... They are all... Your pictures and these remembrances are all part of my office at the brain institute and very important. Because it's one thing to do research that leads to greater understanding. This is just some of my body of patent work where there would be inventions and relate to new treatments.

MG: So, the first on the list is the use of clonidine or catechists. And that treatment discovery followed a whole reawakening in neuroscience like, where does opiates... Where do they go in the brain? What do they do in the brain? How do people get withdrawal? Why do they get withdrawal? Is withdrawal central to the disease of addiction? These are all projects that we worked on. Herb Cleaver, who you also know and Yale inventors. And that led to this new treatment for opiate withdrawal which was really the first proof of concept that translational research, research based on rodents, then non-human primates, then humans could become new treatments. And so, clonidine now is still used for neonatal withdrawal, and we have a new epidemic of the mothers taking pain medicine, babies born addicted. It's still used as an analgesic potentiator and it's still used as non-opiate treatment for opiate withdrawal. And that all started there. And that kind of defined me as a drug abuse researcher. Before that, I thought of myself as a pleasure researcher. Now, that sounds like a good field to be in, but it's very hard to explain what it is. But that was really the focus of my work before.

MG: So when I was doing neuroscience at the University of Florida, I was looking at ways of understanding pleasure. And one way might be to give drugs, so we gave amphetamines, We gave... and looked at the effects. And I'll tell you a funny story because it came up yesterday in Baltimore. Was one of the first findings that we had was giving amphetamines and trying to test the theory that amphetamines would help you learn. And this is really early science and many of my mentees don't even find these articles because they're not on public. And sometimes I get to review a paper and I'll say, I reported that in 1973. And they'll write back, how do you find that? Do you have to go to the national library? I mean, so we gave amphetamine and we found one thing very interesting. Which is that your maximum learning ability, learning and recall, occurs in a straight state but if you're on amphetamine, you can get maximum recall if you're at about the same amphetamine level during learning and recoil. But if you're at a different level, there's a mismatch. The memories are still in your brain but you can't get to them as well. So you sometimes see yourself hitting yourself, trying to rouse yourself, do something to get access to these memories that are trapped there.

MG: So state dependency of memory became very important to me and was a very early paper of mine in the 70's, as I said. And it's been used to explain things like why mothers remember child birth when they're in it again. If they remembered it all the time, maybe you'd only have one baby. But, and you see that, you're going into labor. Oh no, what have I

done? I have to do that again? And why depressed people commit or attempt suicide when they're depressed again. Because they can't go through this again. They're spared access, maximal access, when the chemical states are different. But when they align that's when they have full recall. And that's also what we see in addiction. Why one slip so often turns into a full blown relapse. All of those drug related memories are coded with the drug state and maximum recall occurs in the identical drug state.

MG: Okay, so what would be like our take home messages? There're a lot of them but research over the past four decades has shown that, what is a drug of abuse is answered now by a compound that stimulates its own taking. And sometime, I think it's in June, I have an Academy of Sciences panel on whether food or constituents of food have drug-like qualities to the point that we could consider food an addiction. And certainly gambling has been redefined as an addiction even though it's not. But let's say that binges, loss of control, tolerance, cross sensitization, craving, wanting, changes in the brain. Changes in the brain rewards threshold, now this is an arcane but interesting concept which means that if you're all born with how much environmental stimulation it would take to make you feel good, to give you pleasure, drugs change the brain's reward threshold so it becomes harder for you to appreciate pleasure to the same degree. And that maybe the association with extreme sports and other extreme activities because the brain reward threshold has changed. And there are other changes that make future use more likely.

MG: So in animal experiment it's pretty straight forward. You stick an animal in an experiment, it's not a good or bad rat. It's just trapped in a bad experiment. And you give it a telegraph key and you hook that telegraph key up into an IV. And if you put cocaine in that IV, the animal doesn't know, it just is curious. There's a whole book series on curious animals, because they are, and so, after a while the animal hits the lever, it's not been... These are just regular animals. Its identical twin animals in a different cage, minding its own business. But its lever gets cocaine. So, you say to yourself, isn't that... That is so compelling that drugs stimulate their own taking, cause loss of control, cause continued compulsive use despite consequences, cause changes in reinforcement to the point that rather than thinking of eating, the animal's thinking about hitting the league. And in the case of cocaine, the drugs itself administered often to the point of an epileptic seizure, the dire consequence heart attack, so forth.

MG: This has been done for all drugs of abuse and so you can safely say that all drugs of abuse stimulate their own taking can cause all these things we've just described. Now they have, they're different in the end stage, and that's worth considering, and they have different consequences during the use. One scientist did an experiment where they gave a hundred animals, and divided them up fifty and fifty and gave fifty unlimited access to cocaine and 50 unlimited access to heroine or morphine and the same kind of experiment. And what you might guess happens at the end of the experiment, most if not all the cocaine animals are severely disable or dead. And the opiate animals have put themselves on a maintenance program. Hit the lever, not off. Hit the, not of. So, in a very interesting way you can see drug effects, all right.

MG: Drugs abuse a certain doses, duration by roots cause changes the brain that is structural. This is very important. So what we say is that smoking is injecting without a needle. So that's the pharmacology. If you look at the brain, it's so fast to the brain it's about equal, and smoking is injecting without a needle. Now, in binges, you can show structural changes and you showed structural changes depending on the age of the animal or the age of the person.

So, it wouldn't be the same for me at 65 as it is for Jack Lawn at 26. You're not 26, are you? All right, so, and that's because of what Nora Volkow has shown in other people that if the substrate for drug feeling states, anticipation and pleasure is dopamine. One thing's for sure, as you age you have less and less dopamine. So the peak dopamine would probably be at puberty or around in your teenage times and it would decrease.

MG: And recently, I was with Nora and we were talking about my own pleasure cells, and she actually said to me that I didn't have any, because in the last study she did counting dopamine cells, she had a graph where they decline and decline and decline, and then the graph ended, like, I think it was even before sixty. So I said to her, I mean, "How could that be that I still feel a lot of pleasure. I love mentoring, I love my research and prevention work. How do I still feel pleasure at my age. According to you, I don't have any pleasure cells." And she said, "Mark," I can't imitate her accent", but she said, "Mark, It's euphoric replay. I am replaying memory circuits that have accumulated in the 40+ years of positive work in interactions and living on them" This is just her way of looking at it, very interesting.

MG: So, what is addiction? It's what I just said, you get binging, you get withdrawal, you get craving, you get cross-sensitization. You have drive to use the drug, there's a motor component to it, anticipation, increased consumption, loss of control, tolerance, and lo and behold, you get what neither has shown very dramatically, D2 down regulation, common to all drugs of abuse. And as Shawn described in 1984 and '85, we worked on this problem as a mind experiment and figured out that all of the pharmacological theories and data at the time, which said that cocaine in chronic use would not be addicting and would not cause any structural dopamine changes and certainly wouldn't cause a decrease, we suggested the opposite and said that cocaine, by stimulating dopamine, would tell the brain it didn't need as many dopamine receptors or as much dopamine as in the past and it'd stop making it.

MG: And that's the same, whether it's cocaine, methamphetamine, heroin, alcohol or even food. In obesity, the obesity brain looks pretty much identical to the alcohol brain. All drugs, again, aren't the same, this is a paper that we did based on our UF studies, which show that methamphetamine in binges wasn't very forgiving, and that the effects were quite similar to a concussion, and I think that's very important. We've also worked on what's recovery. We do know that addiction is a disease, a disease of the brain that can be successfully treated, and recovery is being reported as an outcome and drug-free recovery being reported as an outcome.

[drunken sandals video]

MG: So, we are on a college campus, of course we have alcohol and we have problems related to alcohol. Let's see if I can get this to work. One of the big problems that we have and everyone has is when you see alcohol abuse and when you see alcohol impairment, very few people go up and say, "There's hope, there's treatment available, you should get help." The only help that he's going to get is in finding his sneak - his sandal. And really, we have good intervention, good brief treatment and good treatment that we could offer. Everyone that's walking by certainly would know that he's impaired. So this is a lot more than just the drug's effect on the brain's dopamine system, it's the drug's generalizable effect. Tonight, NIAAA have interests in alcohol across the lifespan from a prenatal exposure which is so important throughout family interactions, teenage times and they support research in this area just because it's so pervasive and so very important. But with that, did that go anywhere?

MG: Well, if I lost that one, I'll describe it even though the video is much better, which is in St. Kit's... the island of St. Kit's. They have Green Vervet monkeys, and these monkeys basically find and ingest fermented sugarcane, and there, they've been used as living models for alcoholism and alcohol dependence, and they've even tested new treatments on them, like injectable naltrexone, which reduces the amount of drinking by interfering with alcohol's free access to the brain's reinforcement sites. That's how far research has gone since my work in '71, that you could give someone a medicine, and that medicine just changes the relationship between alcohol and the person's brain.

MG: Similarly, Knight is working on vaccines. How could they have a vaccine, you might say, because we actually know where drugs of abuse go in the brain, how they access the brain's reinforcement system and we could block that. Now this all suggests that people would take the vaccine, and that's a challenge, and... but research has been quite remarkable. Anybody here would be happy to share with Shawn the alcoholic monkeys. But another thing came up in this which was about only fifteen percent of the monkeys lost control over alcohol and became kind of alcoholic monkeys, and others found tourists on the island and stole their alcohol and would raid the bar for their alcohol, but there were still many of the monkeys that appeared to not like alcohol, just like we have in our population, there are many people who don't like alcohol. Those monkeys like soft drinks and that has been the bridge model between some of the manufactured foods, and saying constituents of foods could be reinforcing like alcohol and studied like that.

MG: Our lab at the University of Florida has been doing this kind of work and we're very interested in that. We've also done interesting work on our... one of my new friends in the back said that he was at the swamp when Florida State played Florida, and we were interested in our college and universities and how night game versus day game, and you could guess, director, whether there's more drinking at night game or day game, you pick night. How about the time of kickoff? The most impaired students and people come the closest to kickoff. They don't want to waste a minute. And Lisa Merlo has done this work.

MG: So, starting early is where it all happens. So, we know that if we start smoking cigarettes early at 12, you end up having the most intense relationship with tobacco of any person and it's much harder for you to stop. If you start drinking and binge drinking as a young person, same thing. And when we get to cannabis, it will be the same. Early onset when the brain's developing, the brain doesn't know the difference between the chemical changes of puberty and the drug environment. And it kind of gets confused thinking that, well, maybe this is just part of development and makes permanent accommodation to drugs and drug pleasure.

MG: So, this is Dr. Merlot's summary of what we do, we try to understand how this could turn into this. How is that possible? And then, from an AA point of view, once a cucumber becomes a pickle, can you ever go back? Now, as many of you... many of you know here, I stay connected to the modern age by having grandsons, and... you know, these celebrities who are in one way or another describing drug use and taking have become part of our culture, and we have to deal with that. So, while some of the celebrities have said that detox was treatment, Mark Twain, who might have been a better expert, said that detox is not treatment. It's just detox. And I think as we go on, you'll understand this. So, smoking is like injecting without a needle and detox can't be treatment because Mark Twain said it was the easiest thing to do to stop, but it's the hardest thing to do to stay stopped, and the reason for that may be as simple as the withdrawal center of the brain is very low. And the "I want this

drug, I need this drug, I love this drug," the relationship between you and the drug is very high, and really like a bad lover, like a fatal attraction, whereas withdrawal is very primitive in the lower part of the brain.

MG: This is a young guy working with Herb Kleber at walk-in street level clinics, where we use to evaluate people, and we'll offer them methadone or detoxification, and I learned another important fact, which is, if you have two open windows in a maintenance clinic and one window is detox and the other window is retox, there is no one at the detox window. And even when they come to the detox window and you try to work with them, it's very hard for them to be in that environment. So, we had to separate detox trials from the maintenance programs which we did, and that's the... that's kind of, again, this young guy... well, the first administrator that I worked with here at the DEA was Bud Mullen, and he loved Connecticut. And that leads back to my earliest days.

MG: So, we developed a theory for how opiates worked in the brain, how they intoxicated you, what withdrawal was, how you could replace that with an alternative safer, longer-term, longer acting form, and that's on the one side. And on the other side, we could offer detox and then prevention of relapse, so as early as 19... I can't remember exactly, but I'll guess it's 1978, we reported in doctors detoxifying them with clonidine and putting them on naltrexone, which makes them immune to opiates. So, here you could think you had a cure for opiate addiction. You detox them and you put them on naltrexone, they can't even feel an opiate. You can inject them with heroin and inject them with saline, they can never tell the difference if they're on naltrexone, because you block the opiate receptors where the opiates land. No, it wasn't a cure because they didn't want to take it. They said they were cured when you detox them, they said they were cured shortly after. So it's very, very difficult, except it mandated administration with urine testing to use this new treatment.

MG: And so, as I said, our understanding now is that higher in the brain is addiction and lower in the brain is withdrawal. And that's the APA Foundation's prize for the top research in 1980. That's a young Herb Kleber and a younger me. So these problems haven't gone away even though our brain science has advanced. We now know that the brain has endorphins and all kinds of and all kinds of receptors. We understand where drugs go in the brain. The science is quite excellent, but it hasn't prevented people from harming themselves and that's because these are powerful drugs that induce a state where reason is quite difficult at times and judgment is affected, decision-making, risk-benefit.

MG: One of the main targets for drugs is the kind of risk-benefit center and how can you assess risk and benefit if that's impaired. And we've had tragic losses of really talented and great people from drugs. And, again, kind of tragic performances like the student, where anyone could tell there's a level of impairment that's dramatic, and where an intervention could be lifesaving and where long-term treatment was the answer because of early onset and chronic exposure. But she couldn't remember her own songs and literally was dead shortly thereafter, but mostly was scratching and under the influence.

MG: And so this is a really important part of everyone's work, I've taught this at the university to medical students, if you see a person smoking, tell them there's hope, they can stop. There's treatment, there's new understanding. If you see a person intoxicated, in need of help, addicted, please try to get them to a meeting. Try to help them. That's really what we're trying to do in our work. But it really was very, very sad, as you can see. And very, very sad when her death followed.

MG: So, now we have a pain medicine to heroin crisis. And it's been a crisis in women. 48,000 women died of prescription overdoses in a very short period of time. 400,000... 400% increase in women, compared to 200 to men and 30, in addition to those who die, go to emergency departments. And, look, every three minutes a woman goes to the emergency department for a prescription pain killer misuse or abuse. In Florida, we see this with many of the older, widowed women living in communities of older people taking multiple medications that interfere with each other and this is a very difficult thing, but it's also difficult to see it in our celebrities and see this reported. The combination of alcohol and heroin can be deadly.

MG: So, the profession, addiction medicine, has said for a long time and reported in this Columbia University panel that I've worked on for ten years, that we have a tremendous shortage of addiction professionals, compared to the number of people who need addiction evaluation and treatment, and the training gap is what's keeping us from closing the gap between great science, new treatments, hope and help and actually helping people. And one of the panels that I served on with Bob Dupont, it was estimated that we wouldn't... we would need 700 times the number of practicing addiction doctors to just satisfy the need today, before parity and before ObamaCare was taken into consideration. We certainly are not there. So, the number of people now, moving from opiates, prescription opiates to heroine is increasing and increasing. Again, 80% of people who use heroin had previously used prescription painkillers. Again, a training gap in physician education about prescription painkillers, about what is malignant pain, about what circumstances should prescription opiates be prescribed.

MG: This is a statistic that the CDC has that's really quite wonderful. The US has 4% of the world's population and we consume 80% of the world's oxycodone and 99% of the world's hydrocodone. So, it's not ridiculous to say that a lot of our problems starts here. They're very addictive. You get started, you hit the lever; you hit it again, you lose control, your judgment goes. You hit it again and you're likely to... any number of things can happen, from overdose to dependence and, again, there, our drug poisoning rate. More people dying every year from drug overdoses for... this is a first time, than for car crashes, and it's just remarkable.

MG: So, you know, in AA, we always talk about, you know, your own moral inventory, so for me, my drug of choice is caffeine. I love caffeine and, in fact, Shawn will attest that he's already had to make me a cup of coffee today. And so, because of that, I, with two MD, PhD students from UF, showed a quite interesting finding, which was that decaffeinated coffee had caffeine in it. And it was... this study was published, but before it was published, it was published on the prestigious medical journal, CNN, and where they were incredulous. How could it be that decaffeinated coffee had caffeine? Well, you've ever gone into Starbucks? You wait in line for 12 minutes. Then, people order decaf, and then what does it cost for a cup? Like ten dollars? Okay, so like, you're in the drug... you work with drug addicts all the time. What drug addict is going to wait in line, that's... that goes without saying. They don't want to wait in line. But they'll wait in line for decaf, right? Pay ten dollars and then get placebo? So I figured there had to be caffeine in decaf or else they couldn't sell it, and that turned out to be the case.

MG: So, there is something about understanding self-administration that helps you understand how the brain works. And of course, caffeine is a drug, and people have known this for a long time. That's a historic ad. I thought I... then move on to talk a little bit about

doctors, because I've worked on a number of Board of Medicine projects in a variety of states and the university has an addiction treatment program... evaluation treatment program for impaired doctors for Florida recovery center. But it starts early with doctors. The first drug epidemic, the nicotine epidemic, that left us with 440,000 smoking deaths a year, started with physicians who said drugs like smoking were safe, and then even went further and endorsed them in advertisements. People knew that smoke had to be scary, but it helped them to say, "Well, it may be scary, but then why is my doctor smoking camels?" And they even had an ad campaign... I didn't bring all these historic ads, but they're easily available, where doctors recommended mentholated cigarettes if you had a cough. So, you know, president Reagan endorsed Chesterfield's. And there, you had all these things, it's hard to imagine now that we have 400,000 deaths a year, but that's how it starts.

MG: This is the history of Johns Hopkins Hospital, and it started with morphine addicts and cocaine addicts. So, Sean likes David Musto's work, and people have always commented, like, "How could that be?" And it was very interesting. Same as the animal experiments. The cocaine addict founder needed to take long absences from his work at Hopkins, where the morphine addict founder could go on a maintenance program and stay at work almost till the end. Even recently, alcohol's been out there as a problem among surgeons and maybe they think it's because it's medical wine and I don't know what. Our group has studied prescription misuse among doctors and it's very interesting. Doctors have a really incredibly low cigarette-smoking rate, much, much lower than the average. In some samples like, you know, less than 5%, and in one sample 1% cigarette-smoking, but many times more or equal to the public and prescription misuse.

MG: Why do doctors misuse prescription drugs? And this is from Lisa Merlots study, but basically, they have all these different things. They have access to it, they can order it, they can get it from pets, they can get it from abroad, they can get it on the internet, and sometimes they just steal it. Or they ask their patients if it doesn't work, to bring it back, and they'll destroy it. This is a real doctor who said, "I would have patients bring their prescriptions to the office, and I'd say, "Oh, I didn't mean to give you that one, I meant to give you another one. Give me this one, I'll give you a new prescription."" "So, I called in prescriptions and patients names to pharmacies, memorize their addresses, their birthday, their wife's name and I picked them up myself," said this doctor. "I kept the prescription, starting using it, and I never stopped." Of course, drugs stimulate their own taking. "I had pain. I have pain management," said this doctor. "I had an endless supply. They gave me patches, lollypops, and then you crave it, then you're addicted to it." "I used it because I had a cold morbid." Doctors... Physicians are very bad at getting help. They don't want to hear about it, they don't go to psychiatrists, they could have depression and go to a pain clinic and get treated with fentanyl. They use it for stress, so in most of the physician studies, the opiate-addicted doctors tend to be anesthesiologists, the opiate-abusing doctors tend to be anesthesiologist, surgeons and some other doctors out there.

MG: And then there's recreational use. We have ongoing studies now with some medical students and it may be that, if you think about the kinds of issues that you have in the field now, like, many... some of those people have been able to maintain themselves in high school and college and will be applying to medical school, and that's a challenge as well. They take the drugs to prevent withdrawals. So, we started talking about this in 2004, so it's only 10 years ago, but it's very important. And so, you have this doctor saying, "You have a lot of boring health issues, so I'm gonna prescribe medical marijuana for myself because, you

know, he's boring." And we're working now to understand this among students, the kind of new scorch.

MG: And I'll get back to marijuana in a second, I wanted to thank everybody that helped this work in Afghanistan, because it was a smoking study. We basically showed that children exposed to smoking fathers, mothers exposed had opiates in their breast milk and the baby had opiate levels that made it almost impossible for them to learn. And I think that's really a remarkable study. Because it was secondhand, through the air, skin, hands, head and we all know that because we know that from cigarettes. You know, they have signs that say 'No Smoking'. There's now data that says that if one person smokes a cigarette in the hotel, everyone has some detectable nicotine byproduct in them. And we showed about the same thing in Afghanistan. If somebody's smoking opium, everyone's smoking opium, so stay away from smoke and that's been an advice of mine for a long time.

[BEGIN VIDEO TRANSCRIPT]

Cannabis triggered a house fire in San Diego. When fire fighters put out the flames, they discovered an elaborate pot-growing operation there, in the garage. Fire fighters say some of those marijuana plants did burn, and they also say one person was treated for smoking elation.

I inhaled so much smoke.

[END VIDEO TRANSCRIPT]

MG: What a career. So, why should it be a surprise that exhale drug vapors could intoxicate you. The secondhand smoke is firsthand smoke for the non-smoker. It's just involuntary. The child didn't ask to smoke the parents' cigarette, but it does if it's in a car or in an environment with a smoke. So, we have smoking models now to compare tobacco and nicotine, and compare cannabis to THC. THC has its own receptor system, it's quite diffuse around the brain and parts of it are in areas that wouldn't be particularly good, you'd suspect, for driving, like a bag with cerebellum is like, you know, floating, moving, timelessness and motor coordination, motor memory, driving, and others you can see in pain areas. And you'd suspect that some cannabinoid constituents would have an important role as a pain treatment. And then others in the higher part... Highest parts of the brain affect judgment.

MG: So, one thing that's been going on is that the marijuana's getting stronger. That's important because when Jack Warner and I were talking about cocaine, it may have been \$150 a gram, and it was very hard to get. In 1980, someone told me that it only was delivered to certain places like a day or two a week and has no shelf life, so it's hard to show a cocaine addict at the time. You need a lot of money and you need to have access. And so, Woodstock One, if the average marijuana cigarette at Woodstock One was 0.5% THC, inhaling that cigarette would not give the levels of THC that you could get today. So, now we're... we would be 18 or more cigarettes at once, if you inhaled the same number. And this is, you know, one of my readings so... I read all the medical journals and so, this is the 2014, 15 strains over 23% THC. That's 46 Woodstock One equivalents. So, Nora just had in yesterdays New England Journal of Medicine review of this and basically she did take the same data, which was that, as the potency of THC has gone up, you would suspect the emergency room visits have gone up, and as people in treatment like us, the number of treatment episodes of

gone up and the number of adolescents asking for treatment has gone up, and it sounds like cocaine with a comment to treatment and go, "Tak, you're not going to believe this. I am addicted to marijuana, but it's not addicting."

MG: And it was the same thing when the cocaine crisis started, people said, "I don't know how this could be, but for some reason I'm addicted to the champagne, the safe drug." And so, Nora listed these impairments, and I think in the New England Journal, these are very reliable. She... impaired short-term memory. We know that because cannabinoids have as a primary job in the brain to wash out this... the short-term memory when you're sleeping. Impaired motor coordination and driving problems in roadside checks where the officer finds a person that looks like they're driving under the influence and they have negative breathalyzers and then they test them, a high percentage of those people are impaired. It's just hard to go through all that time to do it.

MG: Altered judgment and altered risk-taking and sexual risk-taking, and in higher doses or if you're sensitive, paranoia and psychosis. But for people in addiction like me, is addiction, would be number one, animal self-administered THC. We have a smoking model, THC and marijuana smoke can cause continued compulsive use and the risk would be addiction. Nora said 9% of users overall would be expected to be addicted and we don't have the treatment capacity right now for the drugs that we have. That's the challenge. Altered brain development, schizophrenia risk, and these are adolescent. The interaction between puberty, brain pruning, development and cognition. In some studies, there have been increased risk. So, what did she say in the New England Journal was the confidence... the highest confidence that marijuana is addictive. Medium confidence that it would give you abnormal brain development, that it would progress to other drugs, that you could get schizophrenia or depression or anxiety, that you'd have diminished lifetime achievement high, that you'd have motor vehicle accidents high, that you'd have chronic bronchitis and lung... But cancer is a question.

MG: So, we have the secondhand effects, in this case might be accidents, roadside accident. So, we've gone from the biblical plagues to the modern plagues, and this is even recognized in the April High Times, five signs you smoking too much marijuana: you're not taking care of your responsibilities. Maybe they... This is an addiction rating scale. You have wheezing, you got residue, well you can't get that high anymore and you're thinking about smoking. Sometimes there are cannabis driving accidents, this was a famous one in Gainesville, where this man left his marijuana cigarette lit and drove right into the US attorney's front window. So it's not that difficult a prosecution. But, the 28% of drivers who died in an accident, tested positive for non-alcohol drugs, most commonly marijuana. But this is my definition, people ask me all the time, about what's the difference between marijuana and alcohol, and so I take, you know, as a New York, Jewish person, I have the New York Jewish person's point of view and view of the world which is, when Willie Nelson was pulled over for driving under the influence of cannabis, he had nothing bad to say about the Jewish people. Okay, back to this. Sorry. So, cannabis is the most prevalent in a list of drug identified in drivers and we now have cannabis smoking doctors.

[BEGIN VIDEO TRANSCRIPT]

Well, you operated on my kid last week.

I don't remember that.

[END VIDEO TRANSCRIPT]

MG: This is a really important and emerging issue, which again is, you know, our physicians, health and safety workers, should they be like police officers and bus drivers and people who work at nuclear power plants, and should their patients have the right to know. We treat impaired doctors all the time and many times they come into treatment because of a mistake. Sometimes they come into treatment because of an accident where they fell down or something. But there are plenty of them with mistakes. So what do we know again? All drugs of abuse are self-administered, they hijack the brain, they increase dopamine, gives you a high. The faster it gets to the brain, the more likely it is to catch your attention, smoking and ejection are the same, and you then, have the great equalizer, so in our treatment program, we can have a neurosurgeon and a high school dropout, and if I don't identify which is which to you, you will not know.

MG: So, a lot of the humanity and the differences among us are brought together as we turn ourselves into a self-administration model. And all you can think about is drugs, and the next drug, and no wonder that the patient is shorted on fentanyl or pain medicine, and no wonder we've have to set up these elaborate checks and still are failing. I can't cover all the drugs, of course is methamphetamine, but I kind of like to think about the young. So we have... we understand critical periods. Anyone who's a parent is faced with this like, at what age should you teach a child to play piano? When's the best age? How about learning another language? And we know the brain learns better when its young, and it learns bad lessons better when its young too. So, most of prevention activities have been based on waiting until the brain's developed. And you might ask, when is the brain developed? Good question. I wish I knew.

MG: So for females, normally the answer that neuroscientists give is the brain is fully developed at 21, that seems to be a good age. For males there has been much debate in the field and actual arguments, and some people have said never. But the consensus is between 25 and 28. So, you have this interesting fact and if you go back into the cigarette literature, it makes some sense, early on when cigarettes were 27 cents a pack and almost free at the VA, young soldiers were given tobacco. Pershin actually said he didn't need more bullets, give him more tobacco. And they got started early, and if you get started early, you smoke forever and well, unless you have a great intervention and treatment. And so the average person who started smoking as a teen, smoke, when cigarettes were cheap, three packs a day. And the average person who started smoking at 35 smoked two or three cigarettes a day. Just less substrate, less excitement, more fully formed brain.

MG: And you know when you go to London, and you go to hospice, they give people in hospice Brockman Cocktail, which has a whole cocktail of dangerous and addicting drugs. It's not quite the problem that a 60+-year-old person has, who's dying of cancer. So, we have to keep the critical periods in mind and focus on our work on preventing first use, preventing use in young people. Preventing easy access like we allowed for cigarettes, low-cost, high-smokable, low-cost, easy access vending machines. I remember growing up, vending machines. You didn't have to ask your mother if you could smoke cigarettes, you just went in the diner, Harrogate... you know, you would like, think about around Yankee Stadium. You basically... you go in and get cigarettes anytime. And we have now reinvented the vending machine for other smokables. So, while we have tremendous progress, and we're all proud in neuroscience that we know where every drug of abuse goes in the brain, we have animal self-administering, we can make vaccines and antidotes, we can treat overdose if we get to the

person in time. We have all of this great advance, but none of that can turn a pickle back into a cucumber. And that's why your work is so very important.

MG: Freud, as we know, was very interested in cocaine as a treatment, and it shouldn't alarm us that drugs are treatments. There are... cocaine still used as a way to reduce blood flow in laryngeal surgery, it's used in some nasal surgeries, but again, what Freud did was give cocaine to try to help morphine addicts, and he inadvertently became, known on Saturday Night Live as the father of the speedball. So yes it's true, it starts like this. It's a go-to medicine, it's safe, it's non-addicting, doctors use it, doctors say it's safe. Don't worry. It was... It's used in Peruvian... and then you have one problem after another that targets the brain. The brain doesn't forget. The brain is unprepared by evolution for the intensity of the drug experience. And it's also unprepared to have that kind of pleasure disconnected from work.

MG: So, if you take me, I could work a year. I worked longer on one of my books, but you know, you work for a year, it comes out, they review it in JAMA, they love my book, five people buy it, and you know, I still like... I feel good, I'm an academic, that's what we do. But for a person who's changed their brain reward threshold, would it be reinforcing to work for a year and have five people buy your book? No, not possible. So, we know a lot. Neurobiology is well understood but that is not where the rubber meets the road. The rubber meets the road in preventing people from becoming users and addicts. Preventing secondhand effects, accidents and suicides, and enabling the earliest intervention and treatment, because treatment really does work. In our impaired doctor studies, which we reported with Bob Dupont and Tom McClellan, who you know from the White House and... We showed 80% of doctors in a five-year treatment program had negative urines and could return to work. That's very good. But why isn't the same treatment applied to everyone? That's the question.

MG: So we have... The last thing I wanted to mention was just that... Just like our methamphetamine work, show that some people don't recover quickly. The same thing as now being shown for cocaine. So, how long is the question. How long do I need to be in treatment? How long do I have to go to meetings? When would my brain return to the way it was before? Those are really questions still out there and probably the answers are: forever. And we don't know and they'll be individual differences, but we hope that you get full recovery. And I'm just showing you progress in our field, which is monumental. We didn't even know that these brain systems existed. Billy Alden told me to not be too technical, but he told me that last night in Baltimore but I forgot, I'd left to slide it.

MG: But we also have addictive-like behaviors that are produced by non-addicting drugs and drugs taken as medicines for diseases like Parkinson's disease. So that is another kind of dopamine fact for you, that if, you're an old guy, and they give you a medicine for Parkinson's disease, it is true that a certain percent of people will develop brand-new pornography addictions, overeating and gambling. And there's a big, big series from Mayo Clinic that has shown just that. So that's kind of the... You remember this TV commercial: don't mess with Mother Nature. And that's kind of the dopamine thing. We use it to anticipate and to learn about our environment and to seek novelty and reward for a job well done. But if a job well done is just puffing on a cigarette that hijacks and disrupts and diverts the system, and makes it less likely that you'll seek reinforcement in the other ways that your brain was set up for. So, most people say drugs of abuse hijack the brain, meaning that they replace the reinforcement that would normally happen, they compete with the brain events that are a logical and that are related to species survival; food, water and sex, and subvert them all. So

when you see someone in the street, they aren't thinking about their next meal, they're thinking about their next fix. So, thank you all for all that you do and I appreciate you inviting me here.

SF: Amazing. Before we end the webcast, I'd like to invite the Deputy Administrator of the Drug Enforcement Administration, Mr. Tom Harrigan to come forward for a special presentation to Dr. Gold.

TH: Thanks Sean, what, no applause folks? Wow. Doc, how are you doing?

MG: I'm good.

TH: Yeah, it's... it is... it's great to be here and it's great to see you and Jack and the Junior Jack. This is the house that Jack built, DEA headquarters, so anytime you and your lovely wife, Virginia here, we really appreciate you being here. Now, one of the questions, I got a text on your presentation, do we get three or six credits for sitting through this? We just... We just wanted to make...

MG: You can only get one.

TH: Okay, just one credit, but, you know, Billy Alden had a question during the presentation since the University of Florida, he asked, "Did you have anything to do with the creation of Gatorade?"

MG: No.

TH: No, nothing?

MG: But I knew the man who did.

TH: Okay, you see that, Billy? But anyway, Doc, if we can step here maybe, again as... So, again, do we get a check for this showing?

MG: I got a thirty-year pen.

TH: Do you have the seventy-year pen? Thank you very much.

MG: Thank you.

TH: Thank you for your lecture. Can we get a picture? Yeah?

SF: This concludes the portion of the webcast. Thanks for those who were watching online. And now we are going to open it up for Q&A. Dr. Gold has agreed to stay on for a bit, and all we ask is, Vince, if you can stand up over on that isle, and we got Catie on this aisle. Please just raise your hand, we'll pass you a microphone, that way everybody in the audience has a chance to hear your question. It's rare that we have the honor of someone as brilliant and experienced as Dr. Gold speaking us on these topics. Please feel free to ask questions.

MG: Well, this is the way that we can talk without slides, and I remember sitting in Jack Lawn's office and we used to call them briefings. But I never... It was great. So, you got the first question.

Q: Thank you very much Dr. Gold for all you've done over the years. My question is, is there such a thing as medical marijuana?

MG: So, there is such a thing people... Literally, I got a call from an academic colleague who said that a patient... "What would you do if a patient came in and they had medical marijuana but they're an inpatient, and the person who's in the room with them is coughing?" And these are the kinds of questions that are coming up all the time, because somehow or another, smoking marijuana has been considered by some to be equivalent to a prescription medicine. So, cannabis is this smokable plant, like tobacco. THC is a psychoactive principal ingredient. It would be conceivable that you could use a THC product that's been tested for a specific purpose, like nausea, a new one like pain, it would never surprise me that a nasal spray, that a pill would... a derivative would be viewed safe and effective and approve for use. What's going on is probably more like what we saw with medicinal alcohol.

MG: So, if you just do a quick history of alcohol, I think Kennedy's own Dewers, and they got it originally around the restrictions by saying it was medicinal Dewers whiskey. And that's a pretty good idea. So, in a way, there... that lowered the barriers and then people said this and that. But my short answer is no, that this note, there's a... there's no smokable medicine that I can think of at all. There's digitalis for heart disease but digitalis comes from foxglove, but it would be crazy for a doctor to prescribe smoking foxglove. So, and in Nora's paper in New England Journal, she went into some of the things that have been claims, you know, like cannabis... medical marijuana for glaucoma. No, can't be, because there would be so many better medicines that worked around-the-clock. Even a person that works hard at smoking has to sleep. So, there'd be so many better medicines, there would never be approval for that.

MG: How about for nausea? Yes, that's a possibility. AIDS wasting? No, that's not a possibility. In fact, even if it's stimulating your appetite over the short term, it would probably interfere with your immune system. So, it's really hard to answer because the normal process of going through the FDA and saying the drug or medicine is dangerous until proven safe has been reversed, and it's now safe, and they dare you to prove it's dangerous, which is a really difficult burden of proof. So, you have all of the single case studies now being reported. Even in the New York Times, Maureen Dowd had toxic marijuana syndrome and in today's follow-up, it was, do you think the state of Colorado should help people understand how much cannabis to eat? So, it's like a user problem, her problem. So, my short answer is, no.

MG: The long answer is you have to expect that brain system like the cannabinoids access, like marijuana accesses, will have important medical uses, and that over time, someone will come up with a pill, one constituent. Nose spray, one constituent. Something that could be tested and compared to the standard treatment of the day. But for right now, this is what we're stuck with. You know, what we see in treatment centers are mostly kids. So they can apparently get medicinal marijuana in some places for menstrual cramps, headache, irritable bowel syndrome, pain and its creating... if Nora's right, then 7 to 10% of the users will have a treatment episode. We can't treat the number of people we have right now, and if you are young, it's a lifelong chronic relapsing illness, you'll have more than one treatment episode. So, we are focused on the addiction and treatments on it. You know, then I think that people

who are driving cars should be considered. There's no way that cannabis-related driving is gonna be not a public health issue that we'll need to take into consideration. It's a longer answer, but the answer I could've just said no, but then, I missed the reason that we're doing this is just a briefing. So I can just brief.

Q: Dr. Gold, I understand that different people have a different brain chemistry.

MG: Yes.

Q: Is it possible that some people are more likely to end up having addiction issues than others based on their unique brain chemistry?

MG: That's a really excellent question. So nobody knows that in advance. Some people who have a family member who was an alcoholic, for example, on the basis of having that, the other people in the family don't drink, and in a way that fooled scientists early on into thinking that alcoholism skipped a generation. It didn't skip a generation; it was just that that generation that lived with that wild alcoholic didn't drink. So, do I think there will be a blood test for alcoholism risk? Yes. But, it's a trick question. So, when I looked at this... every... NIAAA uses, like, Irish families in Ireland for the genetic studies, and so I had to take a trip to Ireland to see for myself. And one thing I learned was that it was a habit among the pregnant women to drink Guinness when they were pregnant. And it was a source of iron and it was sold, really, as a supplement for women. So, in a way it's not the genes that the fault, it's the early exposure. So, in that sense, the genes aren't the cause, it's that... the mothers drinking during pregnancy. The baby has like... now have alcohol exposure-related gene changes, what we call gene expression changes. And so, when it's born, it likes alcohol more than it should.

MG: The same thing occurs for cigarette smoking mothers and their offspring. They're the highest group for cigarette smoking, and it's not genes or brain, it's that the gene expression cause the brain to be different at the time of the drug challenge. So I'm... I would say you're correct. There are differences between people, but you have to always factor in prenatal exposure, early childhood exposure and then early use. Because by getting into the brain and causing this hijack experience, it causes changes in the brain so that the brain of the baby is unlike the brain it should have based on genes alone. It's very complicated, that I do it right? But it's really, again, why it's so important to think about prevention. Because what we used to think was that genes were destiny. Well, you can't change your eye color, but believe me almost everything else changes.

MG: My mother is a Juilliard trained concert pianist, gave piano lessons when I was growing up and she objected to her mother bringing her up and forcing her to play the piano at a very young age. So, she told me that I didn't have to play piano until I was 16. But I sang A cappella choir, some people say I have perfect pitch, my mother's certainly quite talented. At 16, I couldn't learn. I just couldn't learn to play at the level that she wanted. She kept saying like, you know, that's not... 'cause she's so fluid. It was a language for her that she didn't need to think about. And I think that's really... We forget how plastic-malleable the brain is and how environment plays such a critical role. If you were born in South Central LA, or with a bunch of trauma, you've seen somebody killed, you worried for your life, your brain changes to allow you to live, but it can't really change back, and it's a risk that you'll carry with you.

MG: The same with the soldiers, the younger the worse. In a way, we should have soldiers who are 30 because their brain is fully formed. And women... Women have more resilience and a shorter window where they could get PTSD than men. Because, again, I just told you, the male brain develops too slow and so that... however unusual it is to say, when the war is over, they'll probably show that women have less PTSD than men, that women would be the ideal soldier for that reason, for submissions that we wouldn't think of because of physical strength. But emotional strength go heavily to the women.

I thank you for your talk. As a DA pharmacologist, I really enjoyed your presentation and...

MG: Thank you.

Q: I completely agree with your discussion of of medical marijuana and whether that existed or not. Now, I haven't quite kept up recently with the research on treatment.

MG: Yes.

Q: And you touched on in a couple of slides on vaccines and you mentioned that patients weren't willing to keep up with naltrexone once they were detoxed. Now, what is the latest on vaccines and have they started trying the extended relieves and subcutaneous things with naltrexone.

MG: So, you know, it's more than one question. Isn't it? I'll try to remember though. So, the injectable naltrexone... So we've been able to give that to anesthesiologists in recovery as part of their mandated court-ordered or board of medicine-ordered treatment. In that setting, it works like a gem. Spectacular. Without... People always say treatment's a carrot in a stick, without a stick, the carrot can't compare to fentanyl. So, that's the reason drug court works a lot better than any other treatment in my mind. So, mandated treatment is very important. We have leverage with the doctors, that's very important. The two vaccines, is one vaccine for cigarette smoking, that's in late stages, and another one for cocaine and another one for cocaine overdose, a treatment for overdose. The challenges for that are methamphetamine is sufficiently different from cocaine that the cocaine vaccine won't protect the person, and that seems like a really easy work around, so I'm not that hopeful. And then the second catch in all of this was that the vaccines probably will not be approved for women of childbearing age. So, they've... it becomes the minimus, you know, it's an unlikely treatment approach, but injectable naltrexone has been used successfully in alcohol and opiates as long as you have the mandated treatments. And in physician health treatment, you do have five years. Regular treatment, you got to name that too. "Cause I can treat that person in four days." "No, no, no, no. I can treat that person in three days." "I can treat that person at home." And the insurance industry has supported detox-only as a treatment, and most of the detox treatments that have been studied show 100% relapse within the first few months. So, I think there's a lot of waste on that side, and I agree with you that injectable naltrexone, it's impossible to get around. You are a fentanyl addict anesthesiologists, good luck, you know, trying to find a little window in between your fentanyl dose in your day, if you're on naltrexone. But you have to get somebody to take it, and love won't do it, carrots won't do it. You need a stick. That's really where law enforcement can help us the best.

Q: Dr. Gold, thank you for your time and your expertise today. My question is about our international counterparts. As you know, many of the countries with whom we work are considering legalization of Marijuana and we've seen that unfold in Uruguay. They are

looking to Washington and Colorado as examples that they like to follow. What pieces of research do you recommend that we share with our international counterparts to better educate them?

MG: So, you know, I mean, in many ways the movement has nothing to do with facts. It has to do with choices. So the facts are... And Sean has the New England Journal of Medicine Article. You have the director of NIDA, in a time of medicalization, who has a lead article in the number one journal in the world that says it doesn't make any sense. So, but I do think there should be concern about secondhand effects, effects on children, effects on numbers of addicts, driving and the like. And they're summarized nicely with references, but I'm not sure that science wins the day. So, it's not an argument that scientists are having, whether THC's self-administered by lab animals, whether THC gives you continued, compulsive use despite consequences, whether marijuana-smoking animals have lost their control and addiction, it's not the scientists that are arguing about this, it's the politicians and the advocates for smoking and, really, the high times of peace points out how important doses, and Kevin Sabet has tried to bring this out, which is, if you're in the business of selling cannabis, you don't want Woodstock One cannabis, 0.5% THC, you want a lot of THC, because you want addiction, you want the cigarette addicts and the return business. That's where it pays. So, you know, where does it end?

MG: I think there'll be a THC concentration that makes a lot of people psychotic and they'll have to be... some limit, maybe it's 25%, who knows what the number is, but I would just really worry. We have... we had in our treatment program in Gainesville Florida, two people from Colorado. It's just a shortage of treatment available for kids, and they're almost embarrassed to say they're addicted to a drug that all these other kids are smoking. I've also published some on this, and I don't know if this will turn out to be the case, but we did an early paper on whether learning to smoke is the gateway event. So, learning to inhale a drug vapor, I remember when President Clinton said he didn't inhale and everyone was laughing, and I actually did laugh because you have to learn how to inhale. It's a special skill to inhale a drug. You have to suck it in and inhibit the cough reflex. It's a new brain learning and it requires a little practice. Maybe it's easy, but, I mean sex is pretty easy too, it requires a little practice to be good at it, but nevertheless, you can do it. So I think the learning to smoke side, Nora mentioned this a little, and it was my idea, is serious. So, if you learn how to inhale drug vapors, you can smoke crack, you can smoke cigarettes, and that... In one of our studies, we showed that students who smoke cannabis often smoke cigarettes in the morning on their way to class because they had to get awake, and they often ask for amphetamines at exam time to help them stay up and concentrate. So I do think this gateway idea that has had... people have picked on Bob DuPont for, has something to it in learning how to inhale a drug vapor and in cannabis, you see a lot of poly-substance abuse. Is that okay? I don't have a great answer other than "don't blame the scientists."

Q: Dr. Gold, last question. Can you talk for just a couple seconds about what the next ten years look like in this field and in the work that's gonna be coming along the pipeline.

MG: That's bad. Well I'm 65, so I'll be like, fishing? But... I'll be with my grandchildren, but we're doing an experiment now on cannabis like we did on cocaine. So, you should expect it to be the same, large numbers of people becoming dependent, many people having accidents or problems that they can't really work their way out of, and being vulnerable to a chronic, relapsing disease, I think that's going right now. we have an absence of drug education and drug role models. So that, if kids want to grow up to be Charlie Sheen rather than Jack Lawn,

we have a big problem. And we have... So the balance has switched from drugs are dangerous until proven safe, to safe until proven dangerous and so, emergency rooms and addiction doctors have... they'll just get more and more evidence together and over a period of time, people will understand that this was a difficult choice that was made. Maybe there'll be drug-free states, maybe there'll be drug-free doctors, and I do think it does start with doctors. There's a lot of... There's even one study that I saw that doctor drug addicts prescribed more opiates. Doctors that use drugs prescribed more drugs. So, if schools would start doing drug testing, that would be helpful. We are going to report at UF one of these days the medical student use in the state of Florida and it will not be a pretty sight. We have... Because there's been this controversy, like, do people go into anesthesiology because they love drugs, or do they love drugs after being an anesthesiologist, and I actually think some of them... love drugs, pain doctors and others, and having drug testing would help everybody identify people who've identified with drug solutions first rather than meditation, mindfulness, alternative treatments, and I'm... As you know, my wife has three discs and goes to exercise every day, she's got pain, and you try to go as long as you can and still function, but our culture's not based on that anymore.

SF: Thank you very much, Dr. Gold. One final housekeeping item before you leave, just the way the dates worked and Dr. Gold's incredibly tight schedule and availability, our final lecture in the Spring Series is actually next Tuesday, June 10th, right here in the auditorium, 11 AM. We have retired special agents, Fred Gregory and Harold Patin, coming in to talk about the operations back in the 60s and 70s and 80s to go after clandestine drug labs right here in the US. We hope you'll come back and, again, who'd like to come up to talk with Dr. Gold, he's got a few minutes before he heads to Dallas to catch a flight to God knows where.

It's good. Thank you.

Thank you.