Transcript of Cerebrum Podcast—Naltrexone: A History and Future Directions

Guest: **Thomas R. Insel**, M.D., is an adjunct professor in the Department of Psychiatry at Washington University and an active member of the advisory council at the Washington University School of Medicine's Public Health Institute. Gold was a professor, eminent scholar, distinguished professor, distinguished alumni professor, chairman, and emeritus eminent scholar during his 25 years at the University of Florida. He is the author of *Wonder Drugs: How They Work* (Simon & Schuster, 1986), and he and co-workers have won a number of awards, including the Foundations Fund Prize (APA). Gold has been recognized by the Drug Enforcement Administration for 30 Years of Service, the National Association of Treatment Professionals for Lifetime Achievement, ASAM's McGovern Award for Lifetime Achievement, National Leadership Award, DARE Lifetime Achievement Award, and PRIDE awards for his career in research and prevention, and the PATH Foundation's Lifetime Achievement Award.

Host: **Bill Glovin** serves as editor of *Cerebrum* and also executive editor of the Dana Foundation. He was senior editor of *Rutgers Magazine* and served as managing editor of *New Jersey Success*, editor of *New Jersey Business* magazine, and as a staff writer at *The Record* newspaper in Hackensack, NJ. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

Bill Glovin: In the next seven years or so, about half a million people are expected to die from opioid overdose. This forecast is overwhelming, troubling, disturbing. Pick your adjective. The causes of what has been labeled an epidemic are many. But I think we can all agree that opioids are simply not going to disappear overnight. So the next best thing is coming up ways to treat it. To help sort through all of it in this next Cerebrum podcast is Dr. Mark Gold, who has been on the front line of drugs to treat addiction since the late 70s and has seen and hear it all.

He co-wrote our most recent *Cerebrum* article, "Naltrexone: A History and Future Directions." You can find the article by going to dana.org. So what is naltrexone? As Mark explains, it's a bit of a wonder drug in that it blocks the effects of opioids like oxycontin, morphine, and heroin. As Mark's article points out, it was also recently approved by the FDA to treat alcoholism. A little more about Dr. Mark Gold, who will be on the phone with us in a minute. Mark is now an adjunct professor at Wash U in St. Louis, but has spent most of his career at the University of Florida School of Medicine, where he was chair of the Department of Psychiatry.

In 1986, he wrote *Wonder Drugs: How They Work*, published by Simon and Schuster, and has authored at least seven other books on various types of addiction that are available on Amazon. I've got to say upfront that this podcast is more dramatic than most. I think that's because opioids are a public health emergency. Mark addresses issues like how effective are naltrexone and other

treatment drugs? Are we spending enough money on the opioid crisis? With the money we are spending, are we spending it properly or most effectively? Does socio economic status factor into addiction? Is naltrexone affordable? How does AA feel about naltrexone? Can marijuana help stem opioid addiction? But enough from me, let's hear from Mark. Welcome to the podcast Mark.

Mark Gold: Thanks very much. It's really great to be here.

Bill Glovin: You've got a fascinating Wikipedia page. It references you studying opium in Afghanistan. And then studying physicians and healthcare professionals who have had their own addiction problems. I know you're living in Florida but are you still teaching and doing research, or are you playing golf and dodging alligators?

Mark Gold: No. I wish I could even play golf. I'm here in Florida today, but I go for this week to teach and mentor at Washington University in Saint Louis. So, I'll be in Saint Louis this week.

Bill Glovin: Can you tell us how you first got into research for naltrexone and other drugs that deal with opioid addiction?

Mark Gold: Sure. So I started as a basic scientist and working in neuro anatomy. And my interest was where in the brain do opioids act? And that work really started, believe it or not, in the 1970s, around 1973 and 4. I moved from The University of Florida to Yale, and I was really fortunate to have basic science mentor George Aghajanian at Yale, and a clinical science mentor Herbert Kleber, also at Yale, who is recently deceased, and non-human primate research mentor Eugene Redmond. And so, with the three mentors, I was able to conceptualize a project that went from rats to non-human primates to people. And that was a project to help to find the neuro anatomy of opioid action, the neuro anatomy of opioid withdrawal, and how to reverse opioid withdrawal.

Mark Gold: That may seem like it was overly complicated. But up until that time, any drug that reversed opioid withdrawal, heroine, morphine, methadone withdrawal, was considered an opioid. We really didn't have a good understanding of how opioids work. We didn't know very much about opioid receptors. So when we said we could identify where in the brain opioid action occurred, where in the brain opioid withdrawal occurred, and that we could turn off opioid withdrawal by giving a drug like methadone, but also turn off opioid withdrawal by giving an anti hypertensive of medicine that could lower blood pressure that's not an opioid, a medicine like clonidine or lofexidine, then we really had something.

Mark Gold: And what we had was a way to successfully detox people without giving them opioids. And that then opened the door to what's next. Because, as we know, detoxification is not treatment. Mark Twain said it best when he said giving up smoking was easy, he'd done it thousands of times. I mean, clearly, detox isn't treatment. But we could detoxify people from Methadone and from heroin. And

we showed in 1978 at Yale again that you could detox people and offer them maltrexone. And naltrexone, as you mentioned, is a wonder drug. It's like narcan and naloxone, but longer acting. And really, we, at that time, thought we had a cure for opioid addiction, for heroin addiction, because we could detoxify people with Clonidine, and we could give them naltrexone, a drug that made them immune to overdose and relapse at that time. Low and behold, we found that no one really would take it.

Mark Gold: So even though Naltrexone is close to the perfect medication ... And I say it's perfect because you could give it orally. It was cheap, maybe a couple of dollars per dose. It was rapid in onset. It lasted a long time. Literally, you could give somebody a dose and it would last a day. It was safe. It had few if any side effects. People who took it couldn't really tell the difference between naltrexone and water. It completely blocked the effects of heroin so that if a person was on naltrexone, you could inject them with heroin and inject them with a placebo, and they couldn't tell the difference, really remarkable. It's non - addicting, meaning you could stop it and had no consequences. You didn't have tolerance. The same dose that you started with was the dose you'd be taking for a long time. No tolerance, no dependence, no withdrawal. It's totally perfect.

Mark Gold: So I made the mistake of saying in 1978 ... at that time, it was to the local Yale newspaper, *The Register*, that we had invented a cure for opioid addiction. And boy, was I wrong. Because subsequent with follow up studies, we found that almost everyone who was detoxed relapsed. And that is the nuanced approach that I've developed over the last 45 years from literally learning that treatment is much more than detox, and treatment is much more than blocking the effects of opioids.

Bill Glovin: Well, your article points out that addiction is a chronic disease. And when most people think of chronic diseases, they tend to associate the term with arthritis or asthma. Why should we think of addiction as chronic?

Mark Gold: So, we've learned a lot about where drugs go in the brain, kind of rodent neuro biology neuroscience. The neuroscience of drugs of abuse is quite elegant. We know that animals and self-administered drugs, we know where they go, we know where withdrawal occurs. We have a pretty good idea where the fatal attraction occurs, where the animal changes and craves and wants drugs despite numerous and adverse consequences. We know all those things. But what we haven't been able to figure out is how to totally reverse that. So there's an AA saying that you can turn a cucumber into a pickle quite easily, but no one has figured out how to turn it back. So that the switch process of experimentation and use ... Well, that becomes dependence or addiction.

That process, once it occurs, is like a development of a acquired drive state. So even if you talk to someone, and as you mentioned I've worked with impaired health professionals, some of whom have 25 years of sobriety and continued work, those unimpaired professionals will tell you that they can still from time

to time vividly remember drugs, from time to time have provoked craving and drive for drugs, and they need to keep their addiction current by either going to meetings or remembering how fast it is for a slip to become an overdose or complete relapse. So I think it's pretty clear that we've been great at developing treatments for rodents and non-human primates. But in the human condition, what often drives success is much more complicated and involves a physician/patient relationship, involves a 12-step program relationship, involves an employer, involves successful case manager, in addition to MATs and therapy.

Bill Glovin: So, can somebody ween themselves off of Naltrexone?

Mark Gold: One dose. That's the easiest part. And that's turned out to be, ironically, one of the challenges. So naltrexone, when we gave it, was oral. You basically took it every day or every other day. But then, it's been developed into a depo, an injection, which lasts a month. The reason for that is that it was so easy to stop that patients often thought that they were cured or they wouldn't relapse or didn't need any additional treatment and just stopped. So compared to other treatments that we have for addiction, like opioid use disorders, like methadone or buprenorphine or suboxone, naltrexone can be easily stopped because you're not addicted to the treatment.

Bill Glovin: You read my mind. That was going to be the next question. What are the differences?

Mark Gold: So, there are really differences. And they're all very valuable. There's really no doubt that medication assisted treatment is quite helpful in response to the opioid use disorder epidemic, in response to the opioid overdose epidemic, and that any kind of treatment that you currently have, whether it be Narcotics Anonymous or community-based treatment like they have in West Virginia ... It's called COPE. It's a use of community resources. They committed an MAT to that, and treatment only becomes more successful.

So we do have a lot of good treatments now available, much more than we would have if we were in the middle of a cocaine or methamphetamine epidemic, and comparable to the kinds of treatments that we have for cigarette smoking disorders. The treatments aren't the problem. The problem is really encouraging adherence to the treatment, helping the person if they have disorders, which often occurs. Like people who use intravenous drugs often have cardiovascular disease or liver disease or infectious diseases that have not been diagnosed for treatment.

People who use drugs of abuse and who are dependent commonly have psychiatric disease like depression and suicidal thinking or anxiety. So really, the approach to the whole person helps make treatment the most successful.

Bill Glovin: I guess it's a no brainer to say that many drug and alcohol abusers are also suffering from depression. If someone is suffering from depression, can they take anti-depressants at the same time as naltrexone?

Mark Gold: Yes. And there's pretty good evidence that depression is commonly co-morbid, or occurs at the same time, with opioid use disorder and other drugs of abuse. Now, why this occurs is only being understood. So there's Ed Canton, a great researcher at Harvard, who's researched the notion that pre-existing psychiatric disease is a risk factor for drug initiation and drug use. In his work, it's called self -medication. In his work, people might have had depressive disorder, then developed into addictive disorder, and then have double trouble or both at the same time.

My own work has been looking at it from the other way around, which is drugs of abuse target the brain's reinforcement sites. Drugs of abuse produce Euphoria and a positive mood state. Drugs of abuse do not have an exact fit within the brain and at the pleasure system, and thereby, over time, compromise that system and make depression more likely. Both self-medication and neurotoxicity add together to make depression a likely consequence of any disorder. Anti-depressants have been used, and really in Methadone programs are quite commonly used. And National Institute of Drug Abuse has a new group studying transcranial magnetic stimulation in ... or TMS, in dual disorders and in addictive comorbidities. I think you're going to see a lot more in that area, because it's so very important.

Bill Glovin: How good are physicians at determining which drug to prescribe for addiction since it seems like there's four or five of them out there?

Mark Gold: Things have gotten a lot better since I entered this field in the 70s. So, when I was at the University of Florida, I was the founding chief of addiction. And we had an addiction medicine training program. I think we trained 80 physicians to be board certified in addiction. Right now, the addiction medicine as a discipline is quite different than it was in the 1970s. I often joke that when the American Society of Addiction Medicine was in its infancy and had its first official textbook, I think I had to write seven chapters because there were so few people in the field.

Right now, I think it's well over 5,000 trained addiction medicine specialists. And in addition, there's addiction psychiatry specialists. So, these are all board -certified physicians, who, in addition to training in boards in another medical discipline, took an addiction fellowship or had a sufficient addiction clerkship to be able to pass their boards. And they would be experts in all of these treatment modalities. For the listeners, I worked for many years with Joe Califano and Heb Kleber's group at Columbia University called Casa, C-A-S-A. And there's a Casa addiction medicine state of the art report. And in it, Suzanne Foster and the CASA staff figured out that addiction medicine was under-staffed and we

needed more training programs that supported those programs. And that's been initiated.

But the biggest problem hasn't been the lack of physicians, but it's been the support for the people who are delivering the treatment where the rubber meets the road, the counselors, nurses and so forth, and that there was a lot of turnover, a lot of burn out, it's really tough work. And I'm hopeful that we're making progress in that regard too. There's also been some controversy overall within the field debate about the role of MATs. Because historically, rehabs like Betty Ford, which would be the best known rehab, was designed to treat alcoholism, maybe alcohol with pill dependence, but not intravenous opioid use or post opioid overdose. In that model, Mrs. Ford identified successful treatment intervention, successful treatment outcomes. And for the most part, in the early days, that was treatment that did not include MATs.

Now, we didn't have [inaudible 00:18:32] really. But they didn't include it. And then, many of those rehabs that were modeled on the Betty Ford model, the 28 day/12 step model, were not adopting MATs until quite recently. So I do think things have changed. And MATs and access to MATs are being solved as a problem. Almost every day, there's an improvement.

Bill Glovin: I just wanna point out here before we go on to the next question that MATs is an acronym for Medicated Assisted Treatment. Your article points out that naltrexone is now used to also fight alcohol addiction. How does AA feel about it?

Mark Gold: So, I mean, I can't speak for AA. I can say that Naltrexone, and especially injectable where you're sure that the person has month by month coverage ... And I was really interested to learn that, at Yale, it's used often times in the homeless population because they can't come to clinic all the time to get Suboxone or Buprenorphine or Methadone. And in addition, it covers both opioid drugs and alcohol. I think for AA, abstinence is the goal of alcoholism treatment. And naltrexone, as you suggest in your question, reduces drinking. It doesn't eliminate it. It's not antabuse, which makes you sick if you drink. It just blocks the free access of alcohol to the brain's reinforcement sites, making alcohol less pleasurable, less reinforcing, so it reduces binge drinking and total amount of drinking, and is a harm reduction or risk reduction strategy for alcohol.

So I'd say there's a role for all of these treatment approaches in the current ... you know, we have so many problems. To say one treatment is best for all is just not going to be logical. I'll give you another example. In our physician addict population ... And Bob DuPont and Tom McClellan really pioneered the study of physician addiction and physician addiction treatment throughout the United States. We did a study in Florida that helped get this going by showing that physicians identified at the level of the Board of Medicine or the Physician Health Programs, and given an evaluation, and given a treatment plan, and then

almost forced or coerced to follow that treatment program by virtue of the fact that they're in a public health and safety occupation, that they had five year outcomes that were 80 percent or more, 80 percent or more ... And I mean by outcomes, full return to work, family and spouse ratings, drug free in urine testing and global health. So it was quite remarkable, and maybe many times greater than what you'd see for somebody who's not in a physician's health program with the same disease.

An anesthesiologist with intravenous opioid use disorder, who's even had an overdose, treated in a physicians health program, has an 80 percent success rate. So the people have looked at them and said, "Well, you don't use MATs very often. And you have an 80 percent success rate." But we do use MATs in anesthesiologists who are opioid users because of the high relapse to overdose rate and also their continued ... If they were to return to work, they would have so much access to opioid drugs and medications that they would be in a perilous situation. But I do think the physician's health model could be applied to many more people in our population. That doesn't exclude the use of medications at all. It just means you have a case manager. Somebody who is responsible for organizing a multi-disciplinary evaluation of the person up front, and then, making sure that the treatment plan is followed.

Mark Gold: I'll give you another example. When you look at treatment, and Mrs. Ford picked this out right away ... At Betty Ford, they separated the genders. It is very common for female substance use disorder patients to have sexual, physical and emotional trauma. So she separated the genders, so gender specific programs have had greater success in female patients than others. So I think we're to the point where we have to realize that we have a huge opioid use disorder problem. We have the overdoses and then we have the chronic relapsing disease issues, and that one treatment won't fit everybody.

Bill Glovin: You mentioned the physician assistance program. And those people are highly motivated, highly educated. Does the socioeconomic status of somebody come into play when it comes to recovery?

Mark Gold: It's one of the things that people have said about the program, that the applicability of the physician's health model to other people. They say, "Well, doctors are really well educated. Doctors have so much to gain." I think it illustrates that treatment is complicated, that once you've developed an affinity, a fatal attraction toward drugs, it's helpful to have a carrot and a stick, not one or the other. And I do think that the success of the physician's health treatment model has been applied in other settings. I'll give you ... Some very strong employee assistance programs use a similar model. The airlines use a similar model for pilots and flight attendants, and have similar outcomes. The secret service, other kind of public health and safety, nuclear power plant operators ...

So, I don't think it's socioeconomics per se, but I do think that the carrot side, for people who have a job that's meaningful for them and that helps support their family, just that's a bigger issue than we give it credit for often times.

Bill Glovin: Some new research suggests that marijuana is helpful in fighting opioid addiction. Any thoughts about that?

Mark Gold: If you look on the DEA's website, or search the DEA's website for Bruce Goldberger and Mark Gold for opioid epidemic, we did a recent teleconference from the DEA headquarters. And in that, one of the questions to Doctor Goldberger, I believe ... And he's responsible for reporting the CDC pathology findings for the opioid overdose deaths. When he analyzed them, about 50 percent of the decedents had cannabis in their system at the time of their death. It's hard to imagine that cannabis is helpful for someone who is an intravenous heroin addict.

Bill Glovin: So that won't help get them off of it?

Mark Gold: No.

Bill Glovin: Okay. How about neuro steroids which you mentioned in the article?

Mark Gold: I think there are a number of experimental treatments that could be considered. But I would like ... I'd look back and say ... When we think about the tobacco use epidemic, and it was a huge problem, we had over 50 percent of the population smoking. We had nearly 500,000 deaths per year. It was 400 to 450,000 direct and then second-hand smoke deaths per year. We had huge public health problems. And then, the pharmaceutical companies and basic researchers, and I wrote a book on tobacco and did some of the second-hand smoke research, and new treatment for smoking cessation, we had nicotine replacement which is analogous to Methadone or buprenorphine. We had varenicline, which is a dopamine like medication you used for smoking cessation. We had a variety of patch, gum, pills. We had a variety of medications available that you could call MATs. But if you look backward and say, "Well, what really made the difference?" One thing that made a difference was we didn't have intravenous nicotine use or intravenous tobacco use. We didn't have overdoses.

The second thing that made a difference was we had clear public health policy because of the smoke. It was so clear that second hand smoke was first hand smoke for the non user, that flight attendants and just the general public successfully sued for clean air laws. We then had public health initiatives to raise the price of the pack of cigarettes. When I was first in training in medical school, cigarettes were 17 cents a pack. And they were free. And now, it would be 8 dollars or more in some locations. We used to have people who smoked three packs of cigarettes a day, every puff being an injection because inhalation equals injection. So we had to have public health initiatives, raise the price. We had cigarette vending machines. So we took them out. We had underaged

smoking enforcement. So I think we've been much more successful from the public health side and the public health initiatives for smoking, than we are for other drug use. It's confusing to me as to why that's occurred.

But without public health initiatives, we're unlikely to solve any addiction problem by MAT alone. And that's an improvement, at least in a Stanford University model that was published quite recently where they said if we just continue doing what we're doing over the next decade, at least 510,000 people will die of opioid use disorder. That's a paper by Allison Pitt from the Stanford Group in September or so. And they clearly said that no one intervention would make a big difference here. I'll give you an example. They said all interventions together would help, but if you took 11 policy responses ... And I can't off the top of my head remember all 11. But it would be things like needle exchange, MAT, drug free rehabs, pain medication limitations, education ... If you took all them together, the one intervention that would have the greatest effect is just naloxone or narcan, and making antidotes available for overdoses.

And that was only going to change the epidemic by about four percent. Others had really a much, much smaller effect. And they found no effect or negative effect from limiting pain prescriptions from legitimate pain patients. That's in the American Journal of Public Health if somebody's interested in Allison Pitt's work. But that resonated with me. And if you do look at the surgeon general's page on the web, he too has said that we have cardio aversion we have available in public facilities and all over the place. People have learned CPR. But very few people can respond if they've seen an opioid overdose because they don't have narcan. And there's a recent article that highlights this on addiction hope, which said ... the headline was, "Is There an Opioid Overdose Onboard an Airplane?" And if you do encounter that, you'll find out that there's no Narcan on airplanes.

Bill Glovin: Hmm. That's interesting. Yeah.

Mark Gold: It's very important that ... I'll say one other thing. I can go on this for a long time, but naloxone or narcan is a wonder drug. A person could be totally unresponsive, unable to talk, limp, their face is pale and clammy, they have blue fingernails and lips, and they could turn even purple, and I've seen this. They have slow breathing or no breathing. And they have slow pulse or no pulse. And I've seen that too. And you give them a dose of Narcan, and now it's available as an intra nasal spray, so you don't even need to be a doctor to give it. You don't even need a prescription. You give 'em a narcan. Literally, they just wake up. They just wake right up. It is just so remarkable. Now, you still have to call 911, because the opioid tends to last longer than the Narcan. And you'll run out of doses.

But you can save a lot of lives. And as the Pitt article points out, if we lose 50,000 to opioid overdose deaths, those are 50,000 people that we just can't save. And everybody knows the Heimlich maneuver and most everybody knows

how to do CPR. And if you can do those kind of basic life saving maneuvers, given the number of people who are dying of opioid overdoses, it would be worthwhile to have Narcan widely available.

Bill Glovin: One other thing. Your article points out that naltrexone is sold under the brand name Vivitrol.

Mark Gold: Yes.

Bill Glovin: Is it affordable for people? How does that work in terms of getting it to those who need it?

Mark Gold: So it would depend by state by state. So in Florida, a community resource that we use, Gateway Recovery, which has suboxone, buprenorphine, naltrexone, and through River Region has methadone, all of the treatments are supported either by state or federal reimbursement. So that has not been an issue. In other states, it's really a state by state question. But in the private administration of either suboxone or buprenorphine or Vivitrol injection, the patient would be paying the local provider. The director of Gateway, I asked her this question, Candace Hodgins, directly one time, and she said, "All of the treatments are essentially reimbursed for our clients. And that is not a determinant of which treatment is chosen, or which treatment they adhere to."

Bill Glovin: So, if you are on a drug prescription plan at a company and your insurance carrier is going to pick it up, that's one thing. But if you wanted to just go get it at a pharmacy with a prescription, you're just saying it varies by state.

Mark Gold: You couldn't do that.

Bill Glovin: You can't do that.

Mark Gold: Right. So, for Vivitrol, as you mentioned, it's an injectable. There is an oral naltrexone. Both of those are by prescription. A doctor could prescribe for you any of these medications and administer them within the confines of either a drug program or a private office. The only one that has special federal requirements that are independent of these other MATs is methadone, which has much stricter rules and regulations around who can prescribe and where it can be prescribed.

Bill Glovin: And lastly, as I said in my introduction, you can't open a newspaper or turn on the news without hearing about opioids. And a lot of politicians have gotten behind it. Where I live in New Jersey, the former governor, Chris Christie, became sort of the opioid national spokesman. So a lot of money is being thrown at the problem. Is it helping or is it not being channeled properly? What is your view on the funding?

Mark Gold: I don't think there is ... the funding has made it to the street. I mean, the bill was just passed. I think it's very important to note that, from a research point of view, the budget for the National Institute of Drug Abuse and the National Institute on Alcoholism is minuscule compare to other institutes. From a disease point of view, the coverage and parity for mental health disorders, behavioral health disorders, and addictive disorders is significantly less than for comparable chronic medical disorders. Those are major factors in how we can help people who already have problems.

From a prevention point of view, as I mentioned, the public health and prevention initiatives that were so successful in our efforts with tobacco and second-hand smoke are largely ignored for drugs of abuse and opioids. We don't see educational events like we used to in the 70s and 80s. I think some of the funding to family and parent groups will be much needed because, keep in mind that prevention is the only 100 percent safe and effective treatment that we know about.

I mean, it's true that prevention is not as successful as we hope. But if you could prevent one case, you would be making a major contribution. And I think most experts see the lack of prevention as highly relevant to the current problem. Education is not, by itself, prevention or treatment. And that's been a misunderstanding that the public has had. Think about it. Among physicians, the group with the highest amount of drug problems and the highest number of overdoses turns out to be the physicians that understand drugs of abuse the best, the experts in morphine like drugs, the experts in intravenous drug effects are anesthesiologists, and they are, far and away, number one in drug misuse, overdose and addiction, so that it's naïve to say that teaching or education is prevention. That's not prevention at all. And that's been shown again and again in medicine.

And by the way, the same thing applies to nursing. The number one group in nurses that have substance use disorders are nurse anesthetists. And it also applies in veterinary medicine, where the large animal vets are number one, and in dentistry. So no, it's not simply teaching about drug effects that's prevention. It's literally preventing. You need to prevent drug use throughout brain maturation and development. And most neuroscientists would say that's at least to 21 for females and 25 or more for males.

Bill Glovin: Wow, well I think that's a great place to end, and very well said. This was a wonderful look at this whole world of opioid addiction and drug treatment. And I can't thank you enough for the article and for being patient and spending a lot of time explaining things. So, thank you very much Mark.

Mark Gold: Well, thank you. I'm really grateful that you had an interest in this, in naltrexone and narcan or naloxone or drugs for decades that I've worked with them. And I'm grateful that people can learn about them and think about them, and about those limitations and the strengths of medication assisted therapies.

Bill Glovin: And that's our *Cerebrum* podcast for this month. You can find all our *Cerebrum* podcasts at Dana.org, or by going to any number of platforms: Spotify, iTunes, Sound Cloud, and others.

In the coming weeks, we have two huge guests. Jazz guitarist Pat Metheny, who is one of the keynote speakers at the Society for Neuroscience conference, will be my guest in mid- November. And Tom Insel, co-author of our next *Cerebrum* article on digital phenotyping, will also join us sometime in November. For 13 years, Tom directed the National Institute for Mental Health, the component of NIH committed to research on mental health disorders. Tom is co-founder and president of Mind Strong. Last year, Tom was profiled in *The Atlantic* in an article titled, "The Smart Phone Psychiatrist."

So, we hope you can join us for those two very special podcasts. Good-bye for now and thanks for listening. These podcasts are brought to you by the Dana Foundation in New York city.