Conscious Life presents

From Clinical Trial to Public Use

Guest: Andrew Penn

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[00:00:13] Meagen Gibson

Welcome to this interview. I'm Meagen Gibson, your conference co-host. Today, I'm speaking with Andrew Penn, a psychiatric nurse practitioner and clinical professor at the UC San Francisco School of Nursing.

He's been an investigator on studies examining MDMA-assisted therapy for PTSD on psilocybin-assisted therapy for people with Parkinson's disease and depression, with bipolar II depression and chronic pain.

Additionally, he's published widely on psychedelic therapies and their intersections with nursing and is the co-founder of the Organization of Psychedelic and Entheogenic Nurses. Andrew Penn, thank you so much for joining me today.

Andrew Penn

Thanks, Meagen. It's good to be here.

Meagen Gibson

So, a very light question to start things off. Can you discuss where psychedelic-assisted therapies are in the research process and when they might be available for clinical use?

Andrew Penn

Yeah, there are some really interesting things to report. The big one, probably, is that the studies, the phase 3 studies. For those who are not familiar with the FDA approval process, there's this long

process that one goes through where you do what are known as phase 2 studies, which is where you're testing to see if there's an effect and try and understand what the side effect risks are.

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Then you replicate those if they're successful in usually two phase 3 studies. These phase 3 studies are larger than phase 2 studies. That gives you the data that you would then need to go to the FDA with and say, "Hey, we have something that works better than placebo", which is what the FDA requires that you test things against.

And so that process has completed with MDMA-assisted therapy for PTSD, and that operation went into the Food and Drug Administration who regulates drugs in the United States at the end of last year, so at the end of 2023.

And the anticipation was no guarantee that that will be approved. I think there's a good likelihood it will be, but they may come back and ask for additional data. They might want additional subjects run, et cetera.

So that's not a guaranteed date, but at least it's a guaranteed date that there will be some kind of feedback given from the FDA. Then if that is successful, then the process of what is known as commercialization begins. That would be the process of actually creating the infrastructure to get this into patients. That is costly and can take some time.

So probably the soonest we would start to see this being delivered, if it was approved in August, would probably be some time next year. There are a number of different bottlenecks that will need to be resolved, but that's definitely happening.

Meanwhile, in many locations like Oregon and Colorado, and possibly later in California, there are efforts afoot to make psychedelics available to adults in specific settings. Each state has their own program, Oregon, is really more of an adult experience model, supervised adult experience. It's not intended to be advertised as a medical treatment, although many places that offer this seem to be insinuating that it is a medical treatment.

Then Colorado has a different law, which I'm less familiar with, but that will allow clinicians to provide some psychedelics to patients. So there's a lot of things that are happening in tandem with each other and it's interesting to see how it's all going to shake out.

Meagen Gibson

And you bring up a good point. Thank you, by the way, for explaining what the phases of testing are, because that was going to be one of my follow questions. It was like, "Explain this to me like I'm five", which I now understand.

Then one of the other things, too, is the difference between FDA-approved versus legal versus decriminalized. There's different sorts of terminology Which I think... Then when you take the different types of psychedelic-assisted therapy, it all starts to become this really confusing swamp if you're not already in your muck boots and have been in the lay of the land for a while, right?

[00:04:44] Andrew Penn

Oh, yeah. Yeah, for sure. It's worth breaking some of that down, in part because... Well, one of the things that makes us more complicated is that some of these compounds are naturally occurring. You can't grow Prozac in your basement, but you can grow psilocybin. Some of these things are naturally occurring.

There's a difference between decriminalization and legalization. A number of different cities, Denver was one of the first ones, Oakland, California was another one, began the process of decriminalizing certain, usually naturally occurring, psychedelics, such as those that can be found in psilocybin mushrooms or in wachuma cactus, which contains mescaline, things such as that.

So that's decriminalization, which has essentially told the law enforcement in that municipality that this is your lowest level of concerned. So essentially, we're going to not enforce those laws. So that's decriminalization, which is different than legalization.

So legalization, and then there's medical use. And then there's another one that you didn't throw in there just to make things more complicated, which is religious freedom use. The Religious Freedom Restoration Act, which essentially says that... So of course, in the US, under the First Amendment of the Constitution, there is not supposed to be regulation of religious practice.

And so there has been an increasing emergence of these psychedelic churches that offer psychedelics as their sacrament. The requirement under case law, as I understand it, not being an attorney, is that this has to be a sincerely held religious practice.

Now, that's a difficult thing to define and of course, there are some fairly large psychedelic churches that exist at this point, and they will provide for a cost their psychedelic sacraments. In many ways, they look like dispensaries.

And so the confusion is understandable. I think one of the concerns that many of us in the psychedelic research community have is that while we know that these compounds can be beneficial, we've tested them only in certain contexts, and we know that they can be relatively safe, again, in certain contexts.

Now, there's plenty of people that have used psychedelics relatively safely and relatively successfully in what we might think of as naturalistic settings. I've worked on papers where we've gathered survey data on that and found in general, people have fairly positive experiences.

But I think as psychedelics become more widespread, even though the incidence of, or the prevalence, rather, of adverse events with psychedelics remains fairly low, as the number of people in the population begin to try them out, we will see an uptick just as a function of those numbers of adverse events.

This is why good public education is really important and what we refer to as harm reduction. Really helping people understand what they're undertaking and how to make that experience maximally beneficial and minimally harmful is really an important focus as these become more part of everyday everyday society.

[00:08:31] Meagen Gibson

Thank you for that breakdown. Again, it's a lot and it can be confusing...

Andrew Penn

Sure is...

Meagen Gibson

I think we've given people good broad brush strokes and by "We", I mean, you. You mentioned harm reduction. What occurs to me as I'm hearing you talk about medical use, religious freedom, legalization, decriminalization is dosage and control of substance, but also intention.

And how much do you know and how much do we know from medical research, what intention and how much intention plays a part in experience and resulting harm reduction, if you will?

Andrew Penn

Yeah. Well, it's an interesting question because usually in these settings - and by these settings, I mean the controlled lab type settings that I work in - but also in a lot of what might be considered underground practice, or the term recreational doesn't really capture it, but more self-directed use, many people will set an intention.

And that intention might be as simple as, "I'm just curious to see what this feels like". I think that's how many people probably stumbled into their first psychedelic experiences was curiosity.

So curiosity can be an intention. In therapeutic settings, often the intention is arrived upon in the preparatory psychotherapy process. So we meet with people in the days prior to the psychedelic dosing session.

And one of the things that we're working on in that, in addition to providing information about the experience and helping them get to know us and we get to know them, is this idea of setting an intention.

The intention, we often encourage people to hold it loosely, hold it lightly, because sometimes you don't always get the experience that you thought you might. But, you know, somebody might come into a session that's intended to treat PTSD with an interest in getting to know their younger self that experienced the trauma better.

So that might be their intention, or maybe they've decided, "How can I be kinder to that younger version of myself that went through this very difficult experience?". And so that might come up during the session. It might not. It might come up, it might be returned to after the session is over.

But the idea is it creates a North Star to keep pointing the experience back towards. So intentions are helpful. They help create what is known as the mindset.

And then the other piece of harm reduction is really thinking about the setting. What is the physical setting that somebody is having this experience in? Is it Coachella with lots of loud music and lots

of people and lots of energy and maybe a certain amount of chaos, which could also be joyful at the same time? Or is it in the woods with your best friends?

[00:11:48]

Those are very different settings. Some obvious physical things. One shouldn't do this in nearby places that you could fall off of or fall into water. I mean, definitely high doses of psychedelics and water are a bad mix, as is being near high places, not being in places where one might have to deal with stressful situations. These are seemingly obvious things, but not necessarily.

Then another area of harm reduction is making sure that there's enough of a buffer before the experience and after the experience, because sometimes difficult things can emerge.

We had a high-profile event with an airline pilot back in the fall who had ingested psilocybin a couple of days before. The media was often quite unsure about how to report on this and often said things like he had just taken psilocybin or that was under the influence of psilocybin.

And he had what we might call a derealization moment where he wasn't flying the plane, he was a passenger in the cockpit and had this experience of becoming very disoriented, felt like things weren't real, and had this delusional belief that if he pulled the levers that would cut the fuel off to the engines, then this all would end.

Of course, thank God, he wasn't successful in doing that. The plane was brought to the ground and he was taken into custody. From all accounts, he was quite ill. He was quite confused and having a real what appeared to be from the news media, a brief psychotic episode. This raised a lot of understandable concern.

It also led to a lot of people in the psychedelic community really doubling down on this message that these things can't happen, which I think was really quite an unfortunate opportunity to talk about the potential risks of these drugs in some people.

Now, that's not going to happen with the vast majority of people who have these experiences. But if that pilot had to go back to work two days later, I wonder how this might have played out without this high-profile incident. Thank God the plane didn't come down because this would be a very different conversation had that been the outcome.

And so I think it's important to understand that we're working with power tools here. When my dad taught me how to work in a woodshop he said, "You gotta be careful with these...These saws are really helpful. They can also cut your hand off".

Anything that's that powerful for benefit can also have the potential for harm. The outcome of this is not what Prohibitionist policy has tried to attempt, which is like, "Let's just make it go away", because that obviously has been an abject failure. But it's like, "Let's talk honestly about risks and learn how to mitigate them, learn how to minimize them".

And that's part of what I think we're going to have to work towards if psychedelics are going to become more a part of mainstream society. There may be some people for whom they're really just not a good idea for at all. And there may be times in people's lives when it's just not a good idea to

have this experience. And we have to figure that out just as much as we need to figure out who can benefit from this.

[00:15:28] Meagen Gibson

Absolutely. I talked to the author, Jennifer Chesak just a few weeks ago, who did *The Psilocybin Handbook for Women*. Even something as much as estrogen fluctuations throughout the month for women or people who are menstruating can deeply impact the effects of psilocybin in your system.

And so, just those kinds of things that we're discovering every day and finding out and that can deeply affect and impact a person's experience, and then thereafter, their beliefs about the experience is just important and we're learning more every single day, aren't we?

Andrew Penn

Yeah, absolutely. There's just so much... It may seem like this is the finish line here. I think this is actually just the beginning or it's just the first lap around the track. Certainly, as these compounds become more readily available to work with in clinical work and in research settings, I think we'll begin to develop more knowledge about how to best use them from that practice.

That iterative process of learning from our mistakes, making corrections, and seeing what goes better is going to be really important for fine-tuning this process.

Meagen Gibson

I want to pivot into something else that I'm curious about, too, when it comes to medical research, because when I started doing research for this conference, I was looking up all the clinical studies. I would not encourage people to do this, because if you don't know what you're looking for or you don't pause, it looks like all of these psychedelic medications and medicines are being used to cure and treat literally everything, when that's not actually the case.

It's not psilocybin will cure cancer. It's being studied on people with cancer to treat specific side effects or other things that are going on. But it's like, ketamine is not going to fix Parkinson's, but it's going to impact the experience of the person having Parkinson's, perhaps in a beneficial way. I'd love if you could also talk about that. Not only that, but the conclusions that we would draw from studying people either with illness or mental illness or PTSD.

We have all the illnesses we're trying to treat with psychedelic medicine. But there's also a lot of studies on, I'm going to put "healthy" in quotes, but people who aren't coming in with some pre-existing giant condition so that we also know what people without pre-existing giant conditions do on psychedelics as well, right?

Andrew Penn

Yeah. Let's break that down a little bit. Part of what's happening in the psychedelic research space is a broadening of what you might call exclusion criteria. Any clinical study will have a set of what is called inclusion criteria and exclusion criteria.

[00:18:20]
Inclusion criteria are the things that we're generally trying to treat. If you're coming into a study in my lab that we're trying to treat depression and you don't have depression, we can't include you, because that's part of the inclusion criteria.

Then there's a whole set of exclusion criteria. Usually in early research, exclusion criteria is quite broad. You exclude people with any history of, say, a family history of bipolar disorder or something like that, or any history of neurological disease because we don't know how this is going to interact with that.

So your early results tend to be not very applicable to general populations because many people will have these complexities. Also with scientific research, you're also trying to isolate a variable to see if it changes.

So there's always a tension with that because in clinical practice, most people come with multiple variables. Somebody might come to see me in my practice who has depression, but also has alcohol use disorder and also has a history of trauma.

There's really three different problems going on, but I really need to treat that patient. So I'm going to make decisions as a clinician about how I go about treating that or how I'm going to prioritize that. In a research study, you're really trying to isolate one variable.

So if somebody comes in and they have, say, depression and alcohol use disorder and a history of trauma, we might have to exclude them because they're just too complicated. For example, in our lab, we did a study, what's called a feasibility study. What this is, is basically just trying to see, can you do this thing? Is it practical to actually do a study? They're usually small. They don't usually have a control group, so there's no placebo arm.

But this is in people who had Parkinson's disease but also had depression. That's an important population to study because, well, about half of people who get Parkinson's disease will also get depression at some point.

People with progressive neurological diseases like Parkinson's had been excluded from previous psilocybin depression trials. So this is a good example of just starting to widen out that circle a little bit of people that can be included in a trial.

Similarly, we've been doing studies with people with bipolar II disorder, which is this chronic cyclical depression condition that doesn't have full-on mania like bipolar I does. Nobody's tried this on bipolar I because that seems like there may be some real risk, but there may come a time when that seems like an appropriate thing to try, maybe with mood stabilizers on board or something that would mitigate the potential risks of triggering a manic episode with psilocybin.

But the point is that in research, you start with this very narrow focus, and then you slowly work it out and make it bigger. Now, what this could appear to, to the layperson, as you point out, is that it looks like we're using psilocybin for hangnails. That certainly adds to the confusion.

[00:21:33]
But really, generally, usually what we're looking at are the psychiatric symptoms that are associated with a medical condition. But we are broadening the areas of interest of different psychiatric conditions.

So for example, one area that's really starting to grow is looking at eating disorders, which are notoriously difficult to treat and have huge impact on people's lives and that we don't have fantastic treatments for. Looking at eating disorders as another behaviorally rigid phenotype (getting all science-y here), but an expression of a mental illness, that's a phenotype that is very difficult to change.

There's other conditions that we've been looking at with psychedelics that are also similarly rigid, difficult to change conditions, like depression or like substance use. PTSD. Chronic pain is another one we're starting to look at as well, where the brain gets stuck in one mode, and it's very difficult for that to shift.

And anybody who has one of these conditions knows that, and anybody who's treated somebody with one of these conditions knows how difficult it can be to get the needle to move. This is why psilocybin in particular is being looked at for a lot of these different conditions which are difficult to change.

Meagen Gibson

Again, I appreciate that breakdown. It's so much clearer, it's the psychiatric conditions or mental health conditions associated with things. The anxiety and existential dread is not the word that I'm looking for, but end-of-life anxiety, say, a stage 4 cancer patient that's having...that needs to go into palliative care.

It's all the things that you would expect to come up when you know that you're at your last stage of treatment. This is going to alleviate or move or change how that feels so that you can not just spend that part of your life gripped with anxiety and worry, right?

Andrew Penn

Yeah, absolutely. That's an area that we haven't really talked about until now about how do we change people's experience with the end of life, right? Oftentimes, the outcome that we're looking at is something called demoralization, which is a concept in palliative care of like...

It has some similarities with depression, but it's not necessarily depression. It tends more to have to do with this feeling of like, what's the point and difficulty maintaining hope.

There have been some early studies that were really quite important all the way back in 2016. And earlier, there was an important study that Charlie Grob did at UCLA back in 2013, looking at psilocybin. And then that pair of studies came out in 2016 from Hopkins and NYU, really looking to see, we're not trying to cure anybody's end-stage illness with psilocybin, but we're hoping that perhaps we can change that relationship that they have with the illness.

[00:24:43]
And it was interesting because the Parkinson's study, having worked on it as a therapist, one of the themes that I saw was that, to be clear, we were not trying to treat anybody's Parkinson's. We did monitor people's Parkinson's symptoms because we wanted to...We wanted to see if psilocybin was going to make that worse or if there were going to be...

Meagen Gibson

And there are stages - I'm sorry to interrupt you - but there are stages of Parkinson's as well.

Andrew Penn

Totally.

Meagen Gibson

Just like in cancer, there are stages of development where Parkinson's progression, and so that monitoring their symptoms, I assume, also helps you delineate at what stage of the disease its having this particular kind of impact.

Andrew Penn

It goes back to what we were saying earlier about inclusion and exclusion. We only included people that had mild to moderate Parkinson's. If people had very severe Parkinson's, we couldn't include them. There are some things that are unique to Parkinson's disease. People have difficulty maintaining their blood pressure, for example, it goes up and down, and psilocybin can have effects on blood pressure as well.

Also there were questions that we had around, could we do this safely with people with Parkinson's? But by no means were we trying to treat the Parkinson's. We were trying to treat the depression that accompanied the Parkinson's, and that's an important distinction to make.

But what I found working on that as a therapist was that there was this palliative theme that came through that. While people weren't necessarily at the very end of their lives, they were experiencing an illness that had a great impact on their quality of life.

We had some subjects who had been very physical in their younger years, and now we're struggling to do some fairly basic physical things because of the Parkinson's.

And so some of those same themes I think come up in palliative care of reflecting on one's life and grieving losses, incremental losses, grief is often a staged process, especially as people lose capacity as an illness progresses. And sort of grieving a younger, healthier self was one of the themes that came up in that study, which we're hoping to publish soon.

[00:26:56] Meagen Gibson

I bet also grieving the future you thought you had, like how you envisioned whatever stage in your life you're at, whatever age you are, you often imagine when I'm 70, what it's going to look and feel like, or when I'm 50, what it's going to look and feel like, and grieving the loss of that image.

Andrew Penn

Yeah, absolutely. One of the things that's interesting about psychedelics is that they sometimes give people this what they call in space travel, the overview effect. When they first started sending astronauts out into orbit, they would see the Earth from up in space and have this experience of awe because you just realize this amazing place that we live on that we forget about.

I think we had that experience recently with the eclipse, just this feeling of being part of a really big universe. But it is human to get caught up in our little neurotic day-to-day worries. I do it, we all do it. There's something about that opportunity to maybe pull back and take a look at a big picture.

This is actually something that's been studied in psychedelics, of this phenomenon of awe. Is awe a...one of the pathways that people have this experience of change, because when we have an experience of awe, we often experience something called the small self, which is like, "Okay, this is great. My worries that I spend all day worrying about aren't really all that important. And what's really amazing is that I'm part of this huge interconnected world and that I don't need to get the answers to everything".

When people have mystical experiences, often they're more comfortable with uncertainty. There's this feeling of like, "I don't know what happens next, but I think it's going to be okay", versus like, "I know exactly what happens next". That, for many people, is a source of relief. And maybe that's partly what's happening here.

There's a lot of interest in trying to understand from a neurological level Why do these compounds engender these enduring effects? There's lots of different things we could talk about there. But it's a fascinating phenomenon that people can have one or two, three experiences maybe, and have these profound effects that last for at least some period of time.

I think one of the other areas that we're walking back a little bit is the one and done model. I think there was a lot of...There was a lot of hope that this might be curative, that people would have...And for some people, maybe it will be.

But I think most people will say who've had treatment-resistant depression are probably going to need treatment again at some point down the road. Now, is that going to be three months from now? Is that going to be three years from now? Also to be determined.

But this idea of 10 years of therapy in a day, and "I don't ever need to do that again", that was probably a little overstated for most people. But I don't want to downplay that these are still very powerful experiences for many people.

[00:30:22] Meagen Gibson

Yeah, and you bring up a good point, which is in talking about the after effects, it's not just in the room, you get this feeling of the big blue marble as you were talking about the space effect of this feeling of awe and this relief of depression in some cases, but that there's a lasting effect that can vary for a lot of people that not necessarily you walk around feeling quite like you did when you were under the influence, but that there's this lifting...

People are theorizing about the neuroplasticity of it, that there's different connections being made in your brain and that you're more able to make different kinds of connections after you've had one of these experiences. So what do you know about what we know about that? And how important is the integration phase of one of these experiences in that?

Andrew Penn

The integration piece is really important. Neuroplasticity is getting a lot of...That word is getting thrown around a lot and it does appear that some psychedelics probably trigger these sort of plastic pathways. I mean, the brain is always growing and remodeling itself. Every time we learn something, it's growing and remodeling.

So this old idea that your brain stops growing at a certain age is really not true. I mean, there are some processes like myelination that happen through childhood and into adolescence and then tend to slow down in adulthood. But the idea that your brain stops growing at a certain age is really just not true.

Neuroplasticity is great, but there are other conditions which can be considered neuroplastic as well and one is addiction. So addiction is a neuroplastic process in which one's brain becomes rewired to find a certain stimulus, like a drug, to be very salient, very interesting, and very desirable.

Neuroplasticity by itself is not necessarily the goal...

Meagen Gibson

Good..

Andrew Penn

Yeah. But lots of things are induced neuroplasticity; exercise, meditation, social connections, sleep are all generators of neuroplasticity. Now, do psychedelics engender a more rapid neuroplasticity? Possibly. You can think of as all psychotherapy as learning. You're learning different ways to be with feelings, with other people, with situations.

And maybe this is an accelerated learning process, hard to know. But yeah, the integration piece is probably, I would say, as important, if not more important, than the drug experience itself. I mean, obviously, you have to have the drug experience to have something to integrate.

But if you just walk away from a psychedelic experience and say, "Well, that was weird, huh!" and then just go back to regular life, it's probably just going to be a novelty. It'll probably just, "Oh, this

one time in college, I did this thing", you know. It might be a good story, but maybe no change comes out of it.

[00:33:35]

One of the things I'm interested in looking at in the integration period, which is what happens after the drug wears off, is how do you weave these learnings into your daily life? It's one thing to have big epiphanies. It's another thing to actually put them into practice.

One of the goals of integration is to look for really actionable things that we can do that allow us to continue that change and continue to change the way we see the world or we interact with other people or we interact with our own thoughts and feelings.

I'm working with one of my mentees who's done a brilliant job of looking at mindful self-compassion as a modality for integrating MDMA-assisted therapy, which makes a lot of sense because there's been an interesting recent paper that Bessel van der Kolk and his team put out looking at some of the data from the MDMA, assisted therapy study, finding that people have increased ability for self-compassion and a decrease in what's known as a alexithymia.

That's just a fancy word for saying that you don't know how you feel. When you ask somebody how they're doing, and they say, "I don't know, fine". That's alexithymia. That's the inability to name your feelings.

And so it appears that people in that study who are in the MDMA arm compared to the placebo arm, were more able to name feelings and were more able to have compassion for themselves, which makes a lot of sense. Phenomenologically, MDMA tends to make people feel pretty gentle with the people around them.

And in a therapeutic setting where the focus is on themselves, often with themselves or with people that have done them harm, or with the way that they feel like they wish they'd been differently when they were being harmed. There's that capacity for really gently looking at oneself and making some changes.

But you got to practice it. It's like any other change. I'm looking across the room at a guitar that stares back at me every day for years. I have a lot of good intentions to really learn how to play guitar, but I'm at the same level playing the guitar as I was 25 years ago, which is advanced noodling.

It's one thing to have an intention. It's another thing to actually take steps to... If I were to actually sign up for guitar lessons, for example, that would be a real movement of progress for me in my guitar journey.

Meagen Gibson

Well, and as you were talking about mindful self-compassion as well, I was considering, because I know you also are working with people - we've talked about Parkinson's and pain and anorexia - but I know you also have worked with people with PTSD.

[00:36:33]
Something that I've seen and have felt is that self-compassion has a really hard time coming online when you don't feel safety, when you fundamentally don't have safety.

I guess if you can tell me what you know about the sense of safety you can reconnect to that allows the pathway for self-compassion or compassion for other people through these experiences.

Andrew Penn

Yeah, absolutely. Well, one of the things that's interesting about MDMA in particular is that there is often this felt somatic sense of something different. I'll never forget one of my old patients who decided to pursue being a subject in one of the early studies of MDMA said, as we were talking about it, she was asking me, because I was saying MDMA, and she said, "Is there another name for that drug?" And I said, "Yeah, you might remember it as ecstasy".

And she says, "Oh, yeah". I said, "Have you tried it before?". And she said, "Only once", when all this recollection of childhood abuse was coming forth for her when she was a young adult.

I said, "Well, what was that like for you?" And she said, "I remember it was the first time I ever felt safe in my life". She really felt that on a somatic cellular level.

And so this ability to drop in and feel safe is something that many people with trauma have never really had the experience of feeling. I think there's a lot of potential for integrating this with other kinds of practices.

I know there's some interest in looking at somatic experiencing and some of the polyvagal theory work, but really just trying to cultivate places where people can have a felt sense of safety and to return to that. Trauma sensitive yoga is another area that I think is particularly interesting, where people can, on a regular basis, practice that sense of safety.

Meagen Gibson

As you're talking about the ways that these medicines can give people a sense of safety, I'm reminded of, I think it's Dan Siegel has the seven Cs, and then Richard Schwartz has eight Cs, but they all have connection and curiosity and safety and play, all these themes.

All of those things that give a life a lot of meaning are really inaccessible to people who are dealing with depression or trauma or things like this, even eating disorders and things like that. It's either outside or inside when we're talking about safety in our felt sense, and this is not necessarily what's real, but what we're experiencing.

I guess what I'm trying to say is that I think other people, people who haven't experienced those things and people who aren't entertaining doing these trials and taking these medications, don't know that there are other people that don't remember how to feel those things.

I have just so much compassion for people who have literally lost all sense of safety or connection to themselves or other people. I don't think we totally understand why these medicines can give

people a sense of meaning and connectedness. But my view is if it can give people a taste of that and bring them back into the world of meaning, then I'm all for it. Yeah.

[00:40:13] Andrew Penn

Yeah. I mean we do have data that supports that, particularly with MDMA, that that drug does decrease activity in the right amygdala, which is this structure on top of your brainstem, which I think of it as airport security or like a smoke detector; its job is to screen every bit of input that comes into the brain.

And so that's what goes off when you're crossing a street and you realize that car isn't going to stop and you jump out of the way. And in that way, it's life-saving. But the problem with people with PTSD is often their amygdala just never shuts off.

And so it becomes like the smoke detector that goes off every time that you make dinner. It's no longer serving its function, which is to warn you that the house is on fire. It's now just become an impediment to you being able to live your regular life.

And so what's interesting about MDMA is it seems to turn those structures down for a few hours. And so you have access to this feeling of that you can bring up memories of a difficult experience and not have it totally overwhelm you or shut you down.

Meagen Gibson

The way I understand it - I don't do this, you do, so please correct me - but the way I understand it is not only does it tamp down that reaction so that you can work through and process difficult experiences.

But then also you've got the memory of like, "Oh, I am capable of accessing this or enduring a difficult thing", and it takes some of the sting away from it, reminds you of like, "Oh, I do have this capability", and "Oh, I do remember somewhere what it feels like to feel calm or to feel connected or to feel safe".

Andrew Penn

Yeah. I think that's an excellent point. It's probably worth also just circling back on this as we get towards the end of our conversation here, that there's a lot of hype in the space around these compounds being magic bullets, right? That one undone or "My depression is gone" or "My PTSD is gone after one session" or something like that, which is very enticing.

And I think will draw a lot of people who have these conditions who are curious and understandably are not wholly satisfied by what psychiatry has had to offer, which has often fallen short. I'll be totally candid about that. But it's important to understand something about these things, and that involves a psychological concept called experiential avoidance.

And so experiential avoidance are all the things, we all do it. It's all the things that we do to not feel our feelings. And that might be scrolling on your smartphone, that might be drinking, that might be shopping. It doesn't matter. They're all things that allow us to distract ourselves from our feelings.

[00:42:59]
And one of the appropriate critiques of, say, antidepressant medication is that while they decrease depression symptoms, they often actually contribute to a decrease in overall feelings.

So people...my patients will tell me, "Well, I don't feel as depressed, but I also just don't feel much of anything. I don't feel a lot of pleasure. I don't have a lot of sexual desire. I just feel meh".

For some people, that's better than being depressed, right? But it's not optimum. Now, psychedelics, for the most part, have the opposite effect. So if conventional antidepressants contribute to experiential avoidance, and you don't have to think about your feelings if you don't want to.

Well, psychedelics tend to take whatever it is that you've been avoiding, looking at, and spin you around and say, "No, we're going to spend the next several hours taking a look at this", right? And particularly if you've gone into a setting where that's your intention, but also sometimes, you know, when people are doing this in what they think are going to be recreational settings.

I've done harm reduction at Burning Man for many, many years and seen many people in the Zendo project there who thought they were going to go out and go dancing to a DJ and ended up remembering when their dad died, when they were a child, and it really upended them.

And so you can't always steer where these things go. And they tend to take people with regards to emotional experiences and sometimes trauma experiences, to a place where that experience is actually bigger and louder.

And that's why you need this container for that to be not an additional trauma. You want that experience to feel safe and contained and you feel cared for. And that's a key component of setting an intention and having that setting in place.

But it's just important to understand that people understand that these are not panaceas. It's not one and done. It's not you take this, you feel good for a few hours, and then you never have to feel your difficult feelings again.

Probably what may happen is things are going to get worse before they get better. And that's something we need to understand better is how do they sometimes get worse? How do we help people with that process of getting worse?

Because one of the places where maybe we've made some missteps in this research process is assuming that anybody that has a negative experience is just about... It's like we've flared up their psychological immune system, if you were, after you had your Covid vaccine or something, you felt cruddy for a few days.

For some people, that may be true. For other people, it may portend a more difficult experience that they're having with that psychedelic and may need additional care in those days afterwards in order to really help make sense and process whatever has come up for them in that. And so these are powerful tools, but they're not toys. And I think that's really important to understand.

[00:46:12] Meagen Gibson

Absolutely. Yeah. And that a difficult or challenging experience doesn't mean that the experience was a failure. It just means that there's a different assessment of support afterwards, if I'm hearing right.

Yeah, that's right. And also not to be too Calvinistic about this, pleasure can be therapeutic, too. And so people can sometimes have an experience under a psychedelic of joy and realize, "Jeez, I've been keeping myself from this feeling". For whatever reason that maybe you can unpack an integration, "I've not allowed myself to feel these feelings of pleasure and joy".

So I don't want to be Debbie Downer here and say that a psychedelic experience has to be painful and unpleasant for it to be valuable. I mean, Joyful experiences, awe experiences, beautiful experiences can be really important and therapeutic, too.

But you don't always know what you're going to get. And there's this old adage in psychedelics that you don't always get the trip you want, but you'll probably get the trip you need. You don't always know exactly what that is when you go into it, which is why having a good support structure around somebody is really important before they enter into these states.

Meagen Gibson

Absolutely. I can't believe I'm going to make a Disney metaphor analogy here, but I just went to Epcot a few weeks ago with my kids for the first time, and there's a ride there that they warn you about. They're like, "This ride has 5G forces. It might make you sick. Please don't go on it, blah, blah, blah, blah". You read all of it. The signs are everywhere. You go in. It was miserable. It was a terrible experience.

Andrew Penn

They can't say they didn't warn you.

Meagen Gibson

That's what I'm saying. But my kids - we were in separate cars - one car full of people absolutely loved it, thought it was the best thing ever. The other car that had me in it, we were all just like, "Oh, my God, never again".

There's no guarantees. Experience is subjective and everybody's chemistry is different and background is different. Having the container and the intention and the facilitators and the integration afterwards is absolutely key, right?

Andrew Penn

Yeah, absolutely.

[00:48:24] Meagen Gibson

Speaking of that, I wanted to talk about OPENurses for sure. Please tell me about OPENurses, your organization, and what the purpose of it is.

Andrew Penn

Yeah. I'm a nurse practitioner by training, and I co-founded an organization called the Organization of Psychedelic and Entheogenic Nurses, which, fortunately, our website is much simpler to remember. It's O-P-E-N-U-R-S-E-S.Org, opennurses.org.

The reason for this is realizing that nurses are really well suited to doing this work, that there's probably a nurse around when you were born, and there'll probably be a nurse around when you die. And nurses are really exquisitely well-skilled at holding space, providing care and presence for people while they go through experiences. And in this case, while they go through an experience of psychedelic healing.

And so we started this organization, me and some colleagues that went through psychedelic therapist training together to really advance this idea that nurses not only are well suited to doing this, but we're necessary because we're going to have a huge workforce problem when this rolls out, because I don't know how it is where you are, Meagen, but in a lot of places in the country, therapists are really hard to come by.

And if suddenly everyone is going and doing psychedelic therapy, which is very labor-intensive, we're going to have some real challenges in getting this rolled out and accessible to people. And I think one of the key solutions to that is going to be nurses, because there's five and a half million nurses in the United States.

So if we trained even just 1% of them to do psychedelic therapy, we'd have a ready-made workforce of 50,000 people. I think people like nurses. They trust nurses. We're the most trusted profession every year in the Gallup Poll, I believe. And it just seems like a natural match to psychedelic therapy. And so that's what we're trying to advance.

Meagen Gibson

Absolutely. I'm so glad that you told us about it because you're absolutely right. Even if the FDA approval and commercialization happens in 2025, we'll still have the problem of who's facilitating all of these sessions and training and all of the safety measures that are so important to it. Thank you for your work and your research.

Andrew Penn

Well, thank you for your interest, and I'm glad we had a chance to chat again.

Meagen Gibson

How can people... Give me the actual URL again for OpenNurses.

Andrew Penn

OPENurses, it's O-P-E-N-U-R-S-E-S.Org. OPENurses, just one N, that's the one that trips people up. If people want to get in touch with me, my lab at UCSF is psychedelics.ucsf.edu, and my website is andrewpennnp.com, as in nurse practitioner, .com.

Meagen Gibson

Fantastic. Andrew Penn, thank you so much for being with me today.

Andrew Penn

Thanks, Meagen. Always nice chatting with you.