Articles for Further Information

In July 1996, Dr. Deborah Mash was interviewed by Pacifica radio reporter Paul DeRienzo. This is a transcript of that interview, which was broadcast on Let 'em Talk over WBAI-99.5-FM in New York.

Interview with Dr.Deborah Mash

by: Paul DeRienzo

Dr. Deborah Mash is a faculty member in the Department of Neurology of the University of Miami, School of Medicine with a secondary appointment in Cellular Molecular Pharmacology. Dr. Mash's area of expertise is called Neuropharmacology and Neuroscience and her doctoral dissertation was on Alzheimer's disease and the study of how the brain degenerates and how to restore function to the brain. Mash completed a fellowship at Harvard University and joined the faculty at the University of Miami in 1986, and currently runs one of the nation's largest post-mortem programs, a human brain bank consisting of tissues from people suffering degenerative and neuropsychiatric disorders. Dr. Mash has studied brain illnesses such as Parkinson's and Alzheimer's disease, but much of her work has centered on drug abuse, how drugs affect the brain and why certain people are more vulnerable to addictions. She is currently studying Ibogaine, a drug originating in the Iboga plant, which grows in Central Africa, primarily in Gabon and Congo. In those countries Iboga is used in religious ceremonies but the active ingredient in Iboga, which is called Ibogaine, has been shown by anecdotal evidence and some animal tests to have anti-addiction properties.

Paul DeRienzo: How did you find out about Ibogaine?

Deborah Mash: Ibogaine came to my attention by a sequence of three somewhat synchronous events that occurred in my life. I had been working with a collaborator on the discovery of coca-ethylene. I don't know if your familiar with this, but if you drink and use cocaine your body makes a third drug, which is the ethyl-homologue of cocaine. We demonstrated, I think in 1990, that coca-ethylene could be formed in the human body by the liver, that is circulated in blood, and gets into the brain, and is more potent and more reinforcing then cocaine itself. We suspected that it might even be more lethal and went on to demonstrate that indeed it is a longer acting and more potent euphoriant then cocaine, so that it has something to do with the cascade of addiction when people co-abuse cocaine and alcohol. We also demonstrated that it's more lethal. We were actually trying to explain an epidemic of cocaine overdose deaths in Dade county.

In the course of doing that research, we were getting credit and a lot of national attention for these findings and I was traveling around giving talks. A gentleman came up to me at a public forum, an African-American man who asked me if I'd heard about something from Africa that could be used to wean people off cocaine and heroin. At the time I was probably quite abrupt with him, rolled my eyes back and said "Uh huh, thank you very much, excuse me but I have to talk to some other people about my recent discovery."

About a month later I heard a presentation by Dr. Stan Glick from the Albany Medical School at the College of the Problems of Drug Dependency who had been feeding Ibogaine to rats that had been trained to self administer opiates and cocaine. Glick had reported that Ibogaine seemed to inhibit drug taking behavior in an animal model of addiction that had some validity, and again, here was this Ibogaine in front of me. The third thing that happened, I received a phone call from someone who actually knew about the Ibogaine project and said this is something I should take a look at.

So with that backdrop, of good things happen in threes, I raised the question, "well what is Ibogaine?" As a scientist I became very intrigued with wanting to know exactly what it was. What's the molecule? What does the structure look like? Who had been using it and was there something to this?

PD: Is Ibogaine like LSD and other hallucinogenic drugs?

DM: No, I don't even think of Ibogaine as LSD or any hallucinogens, but unfortunately Ibogaine is classified with those as a Schedule I drug, which makes it very difficult to study in a laboratory or in an academic medical center. Those type of drugs have no medical use and are basically verboten and very highly regulated.

Ibogaine has a very unique structure, it's almost as if that plant has created a magical structure that has a very rigid backbone, that is somewhat seratonin-like. Seratonin is a neurotransmitter that is associated with drugs like Prozac and with depression and changes in the brain that are normal with aging. Ibogaine also has another alkaloydal piece that hangs off the side of this rigid backbone that seems to resemble cocaine. It's a molecule that seems to have affinity for the opiate side, and has some affinity for the cocaine side and as a pharmacologist that really grabbed my attention. There's something real fundamental about this molecule that maybe explains its efficacy, and if these anecdotal reports that were out there in the addict self-help movement were true and could be validated, then together with our knowledge of the structural chemistry of the molecule, we might get some fundamental insight into the process of addiction itself.

PD: How did you begin to study Ibogaine?

DM: I love a puzzle and I'm a woman with a mission. I couldn't believe that this was true and yet there was something that I felt intuitively in my own heart that; if there was something to be gained by this, if by some miracle of miracles that this plant could really be used to help people -- if it where an addiction interrupter, if there was something about the pharmacology, if there was something about the molecular structure? Maybe, it wasn't this molecule, maybe it wasn't ibogaine, but maybe ibogaine was a stepping-stone that would take us in a fundamental direction, then it couldn't be ignored.

I cast aside my good judgment and I was at a point in my academic career when things were going very well and I felt that we've got to have the answer. I began to assemble a team of investigators. This not just me, from the beginning we've had a wonderful collection of over 20 people from various disciplines like pharmacology, cardiology, neuropsychology, neurology,

psychiatry, toxicology and pharmacokineticists, who have come together to study this project. So, it.s not only me.

PD: What's pharmacokineticist?

DM: A pharmacokineticist is someone who models how the body handles a drug. Whether it converts it to a metabolite, how it clears it, the bioavailabiltiy and male-female differences -- We needed a lot of help with this project.

We also needed to get a Schedule I license to work with Ibogaine and that task itself took a considerable amount of time.

We set out on this course to study Ibogaine in a credible laboratory, in a credible medical center with appropriate people looking over everyone's shoulder, so that we could collect appropriate data. Even to possess this drug requires filing with the Drug Enforcement Administration to get permission to go forward, and we did that.

We also had to go to our academic institution to what's called the Human Subjects Review Board to ask permission to put Ibogaine into people. That was no small feat because you have to go up in front of people from all various disciplines, medical ethicists, clinicians and other scholars. I had to convince my university that this was an appropriate path. Luckily I had a good reputation with my medical center and they looked at our proposal for researching Ibogaine and decided it would be appropriate to proceed.

Then we had to convince the Public Health Service to garner some sort of support from the National Institute on Drug Abuse which had been funding my research for a number of years. We had to ask the colleagues 'at the top' for some validation that this was an appropriate path.

Finally we had to get the application submitted up to the Food and Drug Administration and work with the FDA to begin this research. You hear people complain about the FDA, but my experience was absolutely wonderful. I had some of the best interactions with clinicians and scientists at FDA to really help us to craft an appropriate study.

My experience along those paths were very positive and so the Ibogaine project was launched.

PD: I've spoken to a NIDA scientist, whose name I won't use, who feels there's a lot of resistance to Ibogaine research. He say's that there's an entrenched group of people who just don't want to see this.

DM: I think that's probably true. When you think about how science moves and shakes and evolves -- resistance is true in every discipline, it's not just special to Ibogaine. Whether your inventing a new AIDS drug, coming up with something that's left field, any type of novel approach that doesn't come from the established medical community, there is going to be resistance. Unfortunately, Ibogaine is a Schedule I substance and people try to lump it in with some of the things that were abused in the 60's. This is really unfortunate, because we have a stigma attached to something that could be profound in many ways.

PD: I've never heard of people abusing Ibogaine. Is it a widely abused drug?

DM: Ibogaine has no abuse potential, but a lot of mistakes were made in the 60's and we understand that the path of medical research that happened with some of the other psychoactive substances, in the late 50's and early 60's, quite frankly through it all back. People made many mistakes. You cannot have abuse of a substance that threatens the foundation of society, that's just not permitted. Ibogaine got lumped in with some of the others that were out there like LSD.

But let me give you an example:

If you train a rat to discriminate LSD, and you give the rat Ibogaine and you ask the rat to tell you [the scientist] if it looks like LSD? The rat will say no, because Ibogaine is not LSD-like, it is not LSD.

This molecule is unique, this molecule does something to human consciousness, something to the brain, something to craving and withdrawal signs that's very different then anything we know about right now.

PD: What's come of the discoveries of active metabolites of Ibogaine such as noribogaine?

DM: When the International Coalition for Addict Self-Help and the Dutch Addict Self-Help movements were in high gear there was information making the rounds that Ibogaine was a magic bullet. Ibogaine is not a magic bullet, but if it does have a long lasting effect, and there was data coming not only from people, but also from Stan Glick's animal experiments where the effect seems to persist. How do you explain that? Ibogaine either sticks around in the body for a very long time or its converted to something else that might stick around in the body for a very long time. Long enough that at least some of the late effects, the "after-effects," to use a word that Stan Glick coined in his papers, might be attributed to an active metabolite.

Working to together with (Hearns) my same colleague that worked with me on the coca ethylene mystery, we discovered that Ibogaine is converted to 12-hydroxyibogamine, or what.s been misnomered as noribogaine, it should actually be decmethylibogaine, but who cares, that's the chemistry and noribogaine is the way it's referred to. The metabolite does seem to persist in the body, at least in humans, it's cleared in some animals much faster then it is in man. We don't know all the parmacokinetics yet in humans, because those studies are still under way, but noribogaine does seem to persist in the body. If noribogaine is formed in the brain, which we don't know yet, it's going to be trapped in the brain because it's a polar metabolite; it has a charge on the molecule that means it's going to be trapped in the brain. We were real excited about that because we thought that this might be a fundamental finding that might point us in new direction.

PD: I recently read an article in the New York Times where it was reported that Ibogaine works on a part of the brain called the cerebellum. What regions of the brain are affected by Ibogaine?

DM: That was a controversial piece of data that came from the Johns Hopkins group where they actually thought that Ibogaine maybe causing a type of activation within the cerebellum. The

cerebellum is a cauliflower looking structure that's in the back of the head. It's associated primarily with the function of balance and fine-motor control. If you learn to ride a bicycle it's your cerebellum, if you learn to play the piano your activating your cerebellum.

The cerebellum has become very interesting right now in neurosciences because we're beginning to think that associated or patterned learning may have something to do with the function of the cerebellum. When you think about self-administering drugs, somebody's whose locked into an intractable self-destructive pattern of drug use, be it cocaine, opiates or alcohol, then maybe the cerebellum is somehow linked in the circuitry.

Nonetheless, I never bought into the idea that this was important because those of us who are interested in the addiction circuit have been focusing on a whole other part of the brain which is up in the forebrain, closer to the frontal lobes, the part of the brain called the nucleus accumbens, and the amygdala and hypothalamus and these other limbic structures of the "old brain," One thing that.s for sure about the brain is that we're just scratching the surface, there could be crosstalk between the cerebellum and these forebrain loops, and how Ibogaine fits into this whole scheme is still quite a mystery.

PD: The article quoted research by researcher Mark Molliver at Johns Hopkins University who reported finding that there was some damage to the brain's "purkinje" cells. Haven't you done a study that found there wasn't any damage?

DM: Neurotoxicity is a flag that can significantly hinder drug development and drug discovery. When the FDA hears neurotoxicity you're slow tracked very quickly. The Johns Hopkins group was feeding very high doses of Ibogaine to rats, who may metabolize the drug very differently then mouse, monkey and man. They did show if you give near lethal doses of Ibogaine in a regimen where you're repeating the administration with only a short reprieve to the animals, a very high dose every 12 hours for about 7 days, what the Johns Hopkins group demonstrated was that there was a drop out in the cerebellar purkinje cells, a certain class of cells, a large cell that lines up along the midline of the cerebellum.

That was interesting data, also very concerning data, but we had the opportunity also to give Ibogaine to primates as part of our safety data that we would submit to the FDA. We were never able to, under relevant dose regimens, to demonstrate any toxicity at all. Researcher Helen Molinari from Albany has done a fundamental study called a dose run-up. She's given so-called efficacious doses in a rodent model, self-administration of opiates and cocaine...

PD: What's an efficacious dose for Ibogaine?

DM: ...pharmacologically effective doses, they block drug self-administration. At that dose a rat is functioning, he's in a cage, he's responding for cocaine, you give him Ibogaine at the efficacious dose and he stops taking the cocaine or he stops taking the opiate. This is the work that's come out of Stan Glick's lab. Helen Molinari demonstrated convincingly that when you look at efficacious doses that there was no toxicity.

If you take too much dilantin, which is a very good drug that's used for seizure control you get neurotoxicity, many drugs that are active in the brain at high doses will damage the brain, but nobody is ever going to take those doses. That's why you do these studies and that's why you work very closely with the FDA so they can make those judgments.

We've looked at human beings, people who've gone outside the United States to take Ibogaine, addicts who have abused drugs. I hate the word addict, but I'm going to use it because it's simpler.

PD: Why do you hate the word addict?

DM: It does carry a stigma, and it puts a pre-judgment that there's something socially wrong who abuses drugs. I don't look at it that way. Drug dependence is a disease, a neurological disorder in the same way as Alzheimer's and Parkinson's or cancer or diabetes. It's a disorder that needs to be corrected and some people are at risk for becoming drug dependant and many people do self-medicate. We have to humanize the discussion.

We studied people who were desperately seeking some help for their addiction to either cocaine or heroin and we looked at them before and after, with very sophisticated neurological testing. Dr. Juan Sanchez-Ramos developed a very sophisticated way to look for neurological soft signs that wouldn't be deemed clinically relevant by a neurologist doing an exam in their office and we failed to demonstrate any persisting effects of Ibogaine on the part of the brain called the cerebellums. We've always been very confident that this drug could be used in a safe and appropriate way.

PD: We're getting into the more controversial because there have been people who've died after Ibogaine treatments. What do you know about those situations, why did they happen?

DM: There were only two Ibogaine deaths that have been reported, that I'm familiar with and these were deaths that were attributed to Ibogaine. One death happened during a series with a Swiss psychiatrist Peter Baumann, who had used Ibogaine as an adjunct to psychotherapy. A woman reportedly died under the influence of Ibogaine. The woman was very sick, she had a very sick heart and she shouldn't have been given Ibogaine under any circumstances.

It's so important to study Ibogaine in a clinical setting. It comes from the underground that people might be able to get their hands on some Ibogaine. God only knows how they would? Because Ibogaine is a hard drug to make, manufacture and acquire. Nonetheless, people cannot do Ibogaine in a hotel room,.

The second death, the one that occurred in the Netherlands, we don't completely know the mechanism of lethality, but it did appear to be respiratory collapse in this case. The bottom line is that you need to be under medical supervision. Ibogaine cannot be given in any way, shape or form outside an established medical center. If someone turns up and says, "I've heard in the underground that I know where to get Ibogaine" please avoid that. This information needs to get out to the self-help movement; Ibogaine is an important drug but it is not to be used outside the medical establishment, not ever, ever, ever.

PD: That seems like a big difference between Ibogaine and the other so-called hallucinogenic drugs, I've never heard of anyone dying of an LSD or MDMA trip?

DM: LSD has a very wide therapeutic safety margin; you can't easily overdose on LSD, for example. MDMA is another story, there have been MDMA deaths, not due to overdoses but to systems overload. The people who do the dervish dancing under the influence of MDMA and get themselves into a situation where you've been dancing for six or seven hours, not drinking fluids, and then they drop, because their brain doesn't regulate their core body temperature and deaths have occurred.

Ibogaine has been used in Africa, in God only knows what dose range, because nobody has any of that information, but it has been used by millions of people and in addition there have been hundreds of treatments that have been done. While the caution flag has gone up about Ibogaine deaths, and this is something we cannot ignore, if Ibogaine is used in an appropriate clinical setting, with doctors and supporting medical personnel, that there's a low chance of an adverse event.

PD: You have a big clinical trial in the works right now?

DM: Unfortunately that trial is now slow-tracked to the point of stopping because we can't pay for it. We have a grant application to the Public Health Service asking them to pay for the Phase I clinical trial.

PD: What is a Phase I clinical trial?

DM: The stepping-stones for a new drug application are Phase one, two and three. Then the drug is released to the public and you have post-marketing surveillance.

Phase one is safety. We're asking simple questions about how the drug is metabolized, adverse events, who can get ibogaine, who shouldn't get ibogaine. This is the very first attempts to put Ibogaine into people. We have a dose-escalation design, so we're going to walk-up the dose, very slowly in 2 milligram per kilogram increments, until we get to the range where we think it would be active as a blocker of opiate withdrawal or as an active dose range for blocking drug craving.

PD: What is that effective dose range?

DM: We don't know yet. I think that what's been used by the underground is too high. I think that the dose range that's out there, that people are suggesting is an appropriate dose range is way too high. We can probably cut it back by half.

Ibogaine is a strange drug, the preliminary data suggests Ibogaine's bioavailabiltiy is poor. There maybe some tricks that we can develop in the laboratory to improve bioavailabiltiy. The more we learn about the drug the better we are at designing how the drug should be administered and what's the safe range for the drug. We need to get up to probably 14 to 15 milligrams per kilogram and we'll be in striking distance of asking the next fundamental question; is this drug efficacious? Does it work?

This is a Phase two design now where the FDA would give us permission to design a small study and ask very specific questions, either in a cocaine dependant, patient volunteer group, or an opiate detoxification program.

The gold standard comes when you move into what's called the double-blind study that would be done at multiple medical centers. There would be many more people joining in that to test Ibogaine in a way to say is it efficacious or not. If it stands the test of the double-blind then you've got a winner. How are we going to blind it? is the problem.

PD: What's going to be the placebo?

DM: We do have some ideas about how we might blind this and I'm sure the FDA would have their own set of suggestions and if National Institute on Drug Abuse was supporting it, they would have some ideas too.

How do we pay for this study? You can't do this kind of research without money and as an American population hooked on her pharmaceuticals, we all know what it costs. My mother spends nearly $400 a month on her medication to stay alive. She's 73 years old and a lot of the elderly cannot afford to get their medications. It costs a lot of money to bring a drug to market. Unfortunately Ibogaine doesn't meet the orphan drug standard and there's nobody to pay for it.

PD: Orphan drugs being drugs that don't have enough potential users to justify its development?

DM: Exactly! So there's other mechanisms to pay for development of an orphaned drug, but ibogaine doesn't fit. There's the dilemma, we have someone who holds use patents who hasn't been lucky enough or smart enough, and hasn't been able to get out of the box. And in terms of getting an investment strategy together, you don't have venture capital backing Ibogaine, you don't have the public health service backing it and you don't have an angel whose stepped out of the shadows say I'll pay for this.

PD:Why not? Something that has this potential that so many people seem to recognize, why hasn't an angel stepped out of the shadows?

DM:The National Institutes on Health struggles every year in the congress to get money to take care of a lot of different diseases. We spoke about the AIDS activists and the great work that they have done to make sure medications are in he pipeline. They fought very hard to make sure that dollars were there. Anytime that you have a disease with that kind of national and worldwide impact together with cancer, schizophrenia, Parkinson.s, Alzheimer.s. One in five the nations elderly by the turn of the century will be afflicted with Alzheimer's disease. Who is going to pay for all big-ticket items that are going to cost our society a lot of money? It all comes back to you and me, because it comes out of our tax dollars and the wisdom of the congress and the president to put those tax dollars behind an institute.

National Institute on Drug Abuse, under the direction and leadership of Dr. Alan Leshner, has fought very hard to secure dollars for substance abuse, but our institute compared to some of the others, like cancer, is a small institute. When you look at the research pie and you see how Dr.

Leshner and the peer review system are going to spend those dollars and allocate that money for a lot of great ideas that are coming right up the pipeline, Ibogaine looks like its kind of left out.

PD: What about other addiction treatments and their supporters? Is the methadone establishment, which is unpopular in segments of the African-American community, effecting what's being studied?

DM: Addiction is multi-factorial and I've been trained to look for the left and the right sides of an argument and of your data. Addiction is something that involves the brain, we're learning more about that, but it's also a disease of the spirit, it's also a disease of personality. A disease of the way a person looks at him or herself, his world, his society and his family and school. It's clear to me that if you want to get at the addiction process you've got to hit it on multiple levels, you can't just hit it on a neurochemical level.

Methadone is important, and many people tell me "thank God for methadone," and there is an industry that's grown up around methadone. I'd like to see people come off the drugs all together, but for some people methadone seems to work and helps addicts to function in life and it gives them a quality of life that's meaningful. It's also very hard to get off methadone and people who use methadone substitution for an illegal opiate find out that after they've been on it for a while that it's very scary to detox off of methadone.

There are certainly a lot of good protocols for detoxing off of opiates, Ibogaine is one way but there's a lot of other ways too. Again, we've got to study it. That's all I've ever wanted to do, I just want to be able to study it. If Ibogaine has an ability to detox off of opiates, which I have seen with my own eyes, because I had an opportunity to go to the Netherlands and sit with someone who was coming off quite a bit of methadone, heroin and cocaine that he'd been using for a long time.

I saw it block signs of opiate withdrawal, I sat there at is bedside and with him while he was under the influence of the Ibogaine and watched him step out of his opiate dependence. That was a profound observation, he's a very special young man, and I've watched him progress. He was someone who had all the strikes against him, his mythology, who he was, who he believed he was since he was 14 years old made him a very afflicted young man. I've talked about Ibogaine being a chemical bar mitzvah by allowing you to make that transition from arrested development -- to borrow a rock and roll term -- to be locked into an adolescent pattern to being able to delay gratification and to look at yourself in a way where you become an adult and merge with the tribe.

How do you feel normal? How do you visualize yourself? What is the road to recovery? And does Ibogaine have something to do with this? Is there a piece of Ibogaine that makes sense in changing and developing coping skills so that you're not going to be vulnerable to relapse? I think there is, but I want to study it.

PD: You mentioned about how Ibogaine was used in Africa as a bar mitzvah or coming of age in Gabon. One of the reasons given by the non-scientists who are experimenting with Ibogaine for

using such large doses is that there's something to be learned from the actual visions born of the passage within the Ibogaine experience as practiced in Africa.

DM: I'm ok with that idea too and I think as a scientist, whether or not you have to have the visions, or those visions are healing is something that could be studied empirically. We could test that and I've designed a protocol that would allow us to get at that. Again, we've got to have the money to study the drug. Unless someone steps out and says this is an appropriate way to go and should be studied I'm not very optimistic about Ibogaine. It need something now, we've taken, together with my collaborative team at the University of Miami School of Medicine, we've taken this thing just about as far as we could launch it. Without the finances, without the research dollars, without a foundation to support us, without venture capital money this thing ain't going to go much farther.

PD: How much does it cost?

DM: It's going to cost millions. The Phase one protocol itself is a million dollar protocol. Are you going to take a million dollars out of the precious research budget and give it to something that's a little far left.

PD: Where do people go if they want more information about Ibogaine?

DM: You can also call me at 1-800-UMBRAIN begin_of_the_skype_highlighting 1-800-UMBRAIN end_of_the_skype_highlighting. People who want information about Ibogaine should go to the scientists and clinicians and we can provide you with information. Please, if you think you can get your hands on some Ibogaine, God only knows if it is Ibogaine, someone could be telling you it is Ibogaine and it could be something else, it's very dangerous. If adverse things occur and they're linked to Ibogaine for any reason, it will close the door on research permanently. For those who need it, for those who are desperate for a treatment, we want to be able to provide that opportunity in an appropriate medical establishment. Please don't support individuals who are using Ibogaine in an illegal and illicit way, in unauthorized medical settings, or no medical settings.

It's so important that this message get out to the community, to the self-help movement that unauthorized use of Ibogaine is inappropriate and it will close the door forever on Ibogaine research.

PD: What about Ibogaine and cigarettes?

DM: There was the suggestion Ibogaine would be useful for nicotine addiction. I've seen it actually block nicotine use, at least in the first few days after Ibogaine was administered. I'm not certain if it has long-term efficacy. Nicotine is really an addictive substance, we've had this whole debate in the congress, in the media about nicotine. That is a damn addictive substance for sure, and nicotine fits right in the addiction circuit we were talking about in the brain, this is why Ibogaine is very intriguing, because it maybe affecting the circuit by hitting or tweaking a few different pieces of the chemical circuit in a way that makes it multifunctional, so it is efficacious against alcohol, nicotine, cocaine, heroin and other opiates. That's neat, if Ibogaine is

multifunctional, it's a real fundamental finding. I don't know if Ibogaine is going to be useful for long-term treatment of nicotine addiction. I don't think that administering it in the same way as for heroin and cocaine detox would be appropriate for nicotine, but there might be some indications.

PD: It could be that studying Ibogaine will give insight into how the brain operates that could lead to a whole new class of drugs that haven't been discovered yet?

DM: I do believe that Ibogaine will open the door for some fundamental information about how the brain works, what goes wrong when the brain becomes addicted, how we can heal the addicted brain and how we can heal inner wounds.