Exclusive Interview with Ray Sahelian, M.D.

The Promise of Pregnenolone

It's doubtful that anyone has done more to raise public consciousness about the value of melatonin, DHEA, pregnenolone, and other substances than Ray Sahelian, M.D.

In his well-researched, easy-to-read books, Dr. Sahelian has described the key research and delineated the possible benefits and drawbacks of each of these hormones. Of all of them, though, it appears that pregnenolone, which he calls "the grandmother of all the steroid hormones" and "nature's feel-good hormone," has made the greatest impression on him personally. In this exclusive interview, Dr. Sahelian talks to Life Enhancement's John Morgenthaler and Will Block about the promise of pregnenolone and how it has brought out the artist in his life.


DR. SAHELIAN: Thank you. It's a little more upbeat than my DHEA book, isn't it?

WILL: Yes, indeed. In fact, it's a very exciting read in a lot of ways.

DR. SAHELIAN: Thanks. Actually, it would have been more exciting if Avery, my publisher, had left in one of the chapters entitled, "Pregnenolone and the Intelligent Pursuit of Happiness." [Laughter] Such as going to an art museum or the zoo, or going traveling and seeing beautiful sights, walking in nature and all that; and it borders on the recreational use of a hormone. Actually, it doesn't border. It's quite obvious.

JOHN: There's a thin line between our concepts of enhancement and the concept of recreational use. There's a philosophical bias in medicine that anything not used for treating a pathologic condition or disease is, by definition, recreational. My response to that is, "so, what's wrong with recreational?"
DR. SAHELIAN: My premise in that chapter was that having memorable days makes us happier and generally will lead to improvement in many other aspects of our lives. We crave euphoric experiences. We need them.

JOHN: It's the same set of people who will admit that sex is okay as long as you're only doing it for purposes of reproduction.

DR. SAHELIAN: Exactly. And I was comparing it to the difference between taking pregnenolone one day at a dose of 10 or 20 mg and having an exceptional experience hiking in the woods versus going out at night with a bunch of friends and downing a six-pack. And I didn't see any philosophical difference in that.

Both pregnenolone and DHEA produce similar feelings of well-being and high energy, but I've personally noticed, and many others have too, that pregnenolone has more of a visual and perception enhancement effect.

WILL: Well, one is a lot healthier than the other. There is a difference.

DR. SAHELIAN: There is. And you're not killing your brain cells and you're not numbing out.

JOHN: Could you give us a brief introduction to pregnenolone? What type of substance is it?

DR. SAHELIAN: There are various hormones in our bodies, and many of them are made in the adrenal glands. One of them, specifically, is pregnenolone, and it is the one from which all the other adrenal hormones are made - about 150 of them.

We've known about pregnenolone since the 1930s. A variety of studies were done on humans in the 1940s, specifically testing pregnenolone's effect on rheumatoid arthritis and other autoimmune conditions as well as its effect as an anti-fatigue factor in factory workers. But pregnenolone was put aside in the early 1950s because another hormone, cortisol, was discovered to have dramatic effects on rheumatoid arthritis and other crippling diseases.

Cortisol was changed to cortisone. It was changed to dexamethasone and then to prednisone and to a lot of other steroidal compounds which could be patented. And, since all these synthetic steroids provided more of an immediate effect, pregnenolone was forgotten.
When one looks at the research, hardly any human studies on pregnenolone have been done since the 1950s, and if it weren't for the 1994 dietary supplement law that allows pregnenolone to be sold over the counter, I would suspect that pregnenolone would still be in obscurity today.

A lot of people ask, "why take pregnenolone instead of DHEA? What's the difference between these two?" One effect I've noticed is that pregnenolone has more of a central nervous system (CNS) effect. It's found in the brain in concentrations many times higher than DHEA. Both pregnenolone and DHEA produce similar feelings of well-being and high energy, but I've personally noticed, and many others have too, that pregnenolone has more of a visual and perception enhancement effect. Colors seem to be brighter and clearer, textures seem to be more noticeable, patterns and shapes seem to be in sharper focus. Hearing is even better.

I've personally noticed that I've become much more appreciative of art over the last few months that I've taken pregnenolone. I notice, now that I'm more aware, that I'm actually enjoying going to galleries and antique stores. I'm enjoying going to gardens. When I walk around my neighborhood, I'm paying much more attention to the architecture of the homes, to the windows, to the types of plants they have in the garden, to every minute thing. Everything is becoming sharper and more focused. And this has helped me socially, because I find I can get along better with individuals who are artistic, because I'm appreciating where they're at, in terms of how they look at the world.

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**When older individuals find they are experiencing declining mental abilities, and doctors prescribe pharmaceutical agents for them, usually antidepressants, they're not addressing the primary problem ... the replacement of the neurosteroids ... When replacement of these neurosteroids is done appropriately, there can be amazing benefits.**

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And my thought is that, as we age, we lose some of our mental abilities; we gradually lose some of our *joie de vivre*, some of our enchantment with life, the excitement, the magicalness, the mysticalness.

Perhaps part of that loss is due to the gradual decline in the amount of neurosteroids within our brain. We were never taught in medical school that the hormones made in the adrenal glands are also made in the brain. I guess the first full reference for that was in 1981. But Dr. Baulieu has an article coming out this year entitled, "Neurosteroids: of the Central Nervous System; by the Nervous System; for the Nervous System." So we're beginning to realize that these steroids have incredibly important functions in the brain. And we're not just talking about pregnenolone, but also DHEA, and probably progesterone, estrogen, testosterone, and the few dozen others that are intermediaries.
When older individuals find they are experiencing declining mental abilities, and doctors prescribe pharmaceutical agents for them, usually antidepressants, they're not addressing the primary problem. The primary problem is the deficiency of the neurosteroids. When replacement of these neurosteroids is done appropriately, I think there can be amazing benefits.

I have one patient - a 56-year-old woman - who's been severely depressed for several years. She's able to manage her job, but when she's not working, she stays home in bed most of the time. She started on pregnenolone at 10 mg a day. A week later we increased it to 20 mg, and she started going outside more. She started walking around. Then we added DHEA at 10 mg. And it's made an enormous - no, an incredible difference. She's a new person now. I talked to her daughter, who said that now she's the life of the party. She urges everyone to go places and do things.

I suspect that she had very low levels of these neurosteroids, and replacing them made a significant difference. I don't know if you've seen the study by Dr. Wolkowitz, who gave DHEA to depressed middle-aged and older individuals and found it to have excellent antidepressant effects. If this is proven to be true and we find over the next few months and years that neurosteroids can act as antidepressants with no significant side effects, this is truly, in my opinion, a revolution in psychiatry, an incredibly huge revolution in psychiatry.

But, I suspect it's going to take a while to convince the public. I just got a fax from my publisher noting that *Men's Health* has a little article on pregnenolone, and this is the way it starts: "While researchers are still busy debunking DHEA, pseudoscience hucksters are pushing another hormone that's supposed to make you smarter, sharper and disease-proof." So here we go; the backlash has already started from *Men's Health.*

So my hope is that we can inform the public about pregnenolone. Although I'll be the first to admit that we don't have the long-term studies, I do feel comfortable with the short-term (4-6 months) use of pregnenolone in those who are young. And in older individuals, I've brought up the concept of PRT, which is pregnenolone replacement therapy, not just by itself, but in combination with DHEA. Women might add estrogen, and men perhaps a little bit of testosterone. I think the concept of using all of these hormones in small doses can, and probably will, be adopted in the future as routine.

I have take pregnenolone for 3 or 4 weeks at a stretch and then stopped, and I didn't notice any fatigue or other symptoms or signs that would indicate that my own production was being inhibited.

**WILL:** What types of dosing regimens do you recommend for these hormones?

**DR. SAHELIAN:** For people in their 40s, to be on the cautious side, I have them take frequent breaks, which I call "hormone holidays." People ask me, how much time should one take off?
And I would say that someone in their 40s, to be on the cautious side, if they're on 5 or 10 mg a day, they should take a week or two off each month. As we get older, we can use them more regularly.

**JOHN:** What's the longest trial that's been conducted on pregnenolone?

**DR. SAHELIAN:** The longest trial conducted has been only about 4 to 5 months. A dose of, generally, 50 to 100 mg has been used, and no toxicity has been reported.

**JOHN:** I understand that back in the 40s, dosages of 400 to 500 mg were used in humans.

**DR. SAHELIAN:** They were used for a month or two without any toxicity. So that's why I feel quite comfortable that 10 mg should not pose any problems. Recently, a study with melatonin found that when you take melatonin nightly at 0.5 mg for a few weeks, when you stop it, the nightly rhythm of melatonin release doesn't change. I suspect that the same would be true with pregnenolone.

**JOHN:** To clarify, let me just interject that what that means is that taking melatonin, and probably pregnenolone or DHEA, doesn't cause your body to stop making it. Right?

**DR. SAHELIAN:** Right. I personally can notice, when I take melatonin for a while and stop, that I continue sleeping well the subsequent nights. This is unlike some other sleeping pills I've taken where, after taking it for a week and stopping, there is what's called rebound insomnia: the sleep is actually worse for a few nights until the body gets adjusted to it again.

And with pregnenolone, I have taken it for periods of 3 or 4 weeks at a stretch and then stopped, and I didn't notice any fatigue or other symptoms or signs that would indicate that my own production was being inhibited. So I'm not concerned that older people taking pregnenolone in a low dosage as a replacement would suffer any problems. In fact, I guess all of us agree that there are obvious risks of not taking any hormones as we age.

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We do know that there are risks to not taking anything as we age. These risks include the continual decline in our mental function, our memory, our mood, our ability to think clearly, and our visual and auditory sensitivity.

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**JOHN:** Let's clarify that, because some people might not understand that concept thoroughly.

**DR. SAHELIAN:** We do know that there are risks to not taking anything as we age. These risks include the continual decline in our mental function, our memory, our mood, our ability to think clearly, and our visual and auditory sensitivity.
JOHN: I understand the consequences can even lead to death?

DR. SAHELIAN: Exactly. Not taking anything can be fatal. There is a decrease in muscle mass and an increase in body fat, a decline in immune function, a decline in cardiac function, and an increased risk of cancer as we age. My suspicion is that by selectively and intelligently taking small doses of certain hormones, we can significantly slow down all those aspects of aging.

If I were 60, I definitely would not even think twice before taking 5 or 10 mg of pregnenolone or DHEA or both.

WILL: The Wolkowitz study showing the benefits of DHEA on depression [see Biomedical Tidbits – Jul. 1997] suggests that DHEA may help preserve dendrites and, thereby, enhance signaling in the brain. Isn't this another way of saying that DHEA affects the engaging of the brain?

DR. SAHELIAN: Oh definitely. We know estrogen works in that way, too. So perhaps, there's a variety of different steroid-like hormones that play a role in the health of our brain cells. Estrogen may help some areas and DHEA may help other areas. Perhaps pregnenolone would help additional parts of the dendrites or parts of the human nervous system that we don't know of yet. Unfortunately, we can't give any 100% accurate statements at this time. But what I find truly amazing with pregnenolone is its impact on perception, as I already described, and that has to involve effects on certain areas of the brain.

JOHN: So it clearly has a psychoactive effect.

DR. SAHELIAN: ... and I'm really wondering how the public, and the media, and the government, and the medical establishment will react when they find out about pregnenolone's ability to enhance perception. I'm really curious about that.

I believe we're going to find that pregnenolone has amazingly more CNS benefits than estrogen.

JOHN: One thing that you haven't mentioned yet is the natural decline of pregnenolone with age. That is one thing that makes me feel a lot more comfortable about taking it. Because, if what you are doing is merely replacing physiological levels that have dropped off in your body, it's hard to imagine it having any serious safety consequences.

DR. SAHELIAN: Yes. When you think about it, estrogen itself is also a neuroactive steroid, and doctors have little reluctance in using it as replacement therapy. We've found that it can slow down the onset of Alzheimer's disease and has some mood-enhancing and some neuropreserving abilities. So the medical establishment has already accepted that one hormone can do that.
Medicine is still in a dynamic phase of learning and growing. Often, though, it is learning and growing in areas not necessarily in the best interests of the patient or our store of medical knowledge. Instead, it is focused on those areas where large pharmaceutical companies stand to reap the greatest economic rewards. And that's the primary reason pregnenolone and DHEA have been ignored for so long.

I believe we're going to find that pregnenolone has amazingly more CNS benefits than estrogen. I asked Dr. James Flood, who is a researcher involved in testing the effects of pregnenolone on memory in mice, "What do you think about hormone replacement with pregnenolone in older age? Do you think it is appropriate?" And he said, "Of course." His feeling was that replacement would lead to more energy, and more positive outlook, and certainly an improvement in memory, but he is concerned about young people in their 20s who have relatively normal pregnenolone levels taking excessive amounts for many, many years, because he thinks that may down-regulate certain receptors in the brain. But I don't think any of us are recommending that young people take it continuously.

For certain medical conditions, let's say PMS or maybe some arthritic condition, I think it would be appropriate for young people to take it for perhaps 3 or 4 months. But when we're talking about hormone replacement, we're talking about the 40+ age group. I'm very conservative about dosage. When people look at my dosages they say, "Are you sure that's going to do anything?" because I'm recommending that people between the ages of 40 and 50 take only 2 to 10 mg each morning. Some people think that's way, way too low, but it does have an effect at that level.

JOHN: Has anybody done any studies to look at how much you have to take to bring your blood levels up to the high-normal range?

DR. SAHELIAN: The problem is that there's been so little studied on actual pregnenolone levels in the body. I called quite a few laboratories, including some of the major ones like Corning, and spoke with the director of the laboratories, and they had no idea. I looked in medical textbooks, but only could find rare, rare areas where it was listed. Recently, I did come across one study done way back that reported some levels. But the truth is, we really know very little about levels of pregnenolone in the blood. Levels in the blood may or may not tell us what the levels are within the central nervous system.

JOHN: Then, what leads you to recommend the dosages that you do?

DR. SAHELIAN: I'm opting, with pregnenolone replacement, not to rely necessarily on blood studies, although they could give us some information. I'm relying more on a clinical evaluation of how a person feels on pregnenolone, their mood, their alertness, their motivation, their memory. Is it interfering with sleep? If you take it in the morning and you experience insomnia that night, then it's too much, even if your blood level says it's low.
I've heard several anecdotal reports from women saying that pregnenolone does help with PMS. That made me curious, because we know that progesterone is involved in PMS, and pregnenolone, of course, converts into progesterone.

JOHN: That makes a lot of sense. It reminds me of Dr. Ward Dean's philosophy regarding replacement of thyroid hormone. I take Armour thyroid, and I was really into the blood tests. I wanted to know my blood levels, and I wanted to test them every few weeks and get it just right, and he said, "Don't worry about it so much. Just tell me how you feel. Stop worrying about the blood tests so much." His point was, "Treat the patient not the blood test."

DR. SAHELIAN: Yes. In fact, certain laboratories are not going to be happy with my pregnenolone book, especially the chapter on the pros and cons of testing, because I'm not pushing testing this time. I'm more interested in evaluating the whole person. If we're going to be using pregnenolone in combination with DHEA and maybe estrogen in women and testosterone in men, we need to measure weight, blood pressure, muscle mass, body fat. In men, we need to check the prostate gland, look at the flexibility of joints, and aerobic capacity. In women, we need to do breast exams and possibly mammograms, and pap tests for cervical and vaginal tissue.

This is very different from saying, "Okay your blood level of pregnenolone is low, so here's some pregnenolone supplements to take. Let's check it again in a month and base the decision on that." Maybe we can do that with DHEA, but with pregnenolone, it's much, much harder. Plus, we don't know: Do we check pregnenolone levels? Do we check pregnenolone sulfate levels? Do we check 17-hydroxy pregnenolone levels? Nobody knows. So, not knowing all this, I go back to evaluating the experience of the person.

WILL: Ray, you talk about starting at a high loading-level dose and then dropping back to a lower level, without any fall-off in the benefits. Are you backing off?

DR. SAHELIAN: I'm not sure if it's the same benefit, but one is more in tune with what one is feeling, what one is noticing. So once you know what the feeling is like, then you become more in tune with noticing the visual enhancement on a lower level. And I'm not sure what is going on there, whether the pregnenolone accumulates in the central nervous system or whether some memory areas get enhanced. I don't know precisely what's going on.

JOHN: The same thing is recommended with a lot of other smart drugs. But way back in 1990, in Smart Drugs & Nutrients, we recommended the use of a loading dose for some substances, including piracetam. We found anecdotally that a lot of people did not register what piracetam was doing. They didn't notice the changes unless they used that method of taking a loading dose at first. There is some kind of feedback mechanism or interaction between the conscious
perception of a big change, learning about what that change is, and then attuning to the subtler differences later.

It's an oddball metaphor, but you probably know that users of marijuana often find the same thing. Very often, when someone tries it for the first time, they don't notice anything, unless they smoke a whole lot and get really stoned, but thereafter they do notice the subtle differences.

**DR. SAHELIAN:** Exactly. And the few people that have tried pregnenolone who have used other substances in the past seem to notice the effect of pregnenolone much more quickly, very likely because they are familiar with experiencing slight alterations in mental alertness.

**JOHN:** Is pregnenolone a reliable way of increasing your DHEA levels?

**DR. SAHELIAN:** I think so. Especially people who are young or middle-aged have all the enzymes to quickly convert pregnenolone into DHEA and progesterone. As we age, some of those enzymes may not function as well. So it would take a little higher dose to make those conversions. When I take DHEA at a very low dose, I get pimples, probably because my body is converting it to testosterone and DHT very quickly. With pregnenolone, it takes me about three or four times the dose to get this effect. If it takes 10 mg of DHEA for pimples, it takes about 30 to 40 of pregnenolone to do that. Older individuals probably would not get acne unless they took massive doses.

**JOHN:** It didn't work that way for me. My DHEA levels were low before and after taking pregnenolone.

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PREG is an anti-fatigue agent, which could be beneficial in those who need to work long hours, especially if they have physical work. I've taken it on hikes in the mountains and hiked 12 miles, came back in late afternoon and could keep going and going and going.

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**DR. SAHELIAN:** I have a case study in the book of an 80-year-old person whose DHEA levels were checked before and after pregnenolone. The pregnenolone did elevate his DHEA levels. So I guess we'll need more studies with that.

**JOHN:** Is there any way to encourage your body to make pregnenolone out of cholesterol?

**DR. SAHELIAN:** I haven't been able to find any information even hinting about how to do that. I don't know whether people who ingest more cholesterol will have more pregnenolone or not. It would be interesting to correlate an individual's cholesterol and pregnenolone levels to find out whether people with high cholesterol have high pregnenolone and vice versa.
JOHN: What about PMS, and sex, and intelligence enhancement? What are pregnenolone's benefits here, if any?

DR. SAHELIAN: I've heard several anecdotal reports from women saying that pregnenolone does help with PMS. That made me curious, because we know that progesterone is involved in PMS, and pregnenolone, of course, converts into progesterone. It stimulated my interest enough to fund a study with the Southwest College of Naturopathic Medicine in Tempe, Arizona. We're doing a 3-month trial in which women with PMS take pregnenolone for about a week to 10 days before their period to see if there's any effect. They're going to start with 10 mg and if, after a day or two, they don't feel anything, increase the dose to 20 mg and maybe even 30. There's also another group that will get a placebo.

JOHN: What about other effects?

DR. SAHELIAN: With arthritis there's a slight effect, and I believe it should be combined with glucosamine, although I'm still not sure whether I would want people to take more than 10 or 20 on a very, very long-term basis. But for short term, perhaps 10 mg in combination with glucosamine 500 mg three times a day might do well for them.

JOHN: Even in light of the work from the 40s, taking 400 to 500 mg a day?

DR. SAHELIAN: They only took it for 2 to 4 months.

WILL: But often the loading itself is enough to arrest the continued inflammation.

DR. SAHELIAN: Right. So one option could be giving 50 or 100 mg for a month or two and then backing off to 10 mg. Or maybe starting with 10 mg and gradually increasing to the level where it really starts working, and then gradually backing off and taking the least amount that works. I think it's very important that people start at 10 mg and not at the 50 or 100 mg level because a good number of those who start high may get such side effects as irritability, insomnia, overstimulation, or headache.

JOHN: By the way, I'll put another plug in for Meridian Valley Labs' 24-hour urine test that Dr. Jonathan Wright is so fond of. For about $129 you can get a picture of a 24-hour average of DHEA and the downstream metabolites. They don't have pregnenolone yet but may soon.

DR. SAHELIAN: Any information that we have can be helpful, but I do want to emphasize looking at the whole picture and not over-relying on one particular piece of information.

One very interesting article appeared recently in Family Practice News: "Hormone Pills Help Some Epilepsy Patients." The authors were referring to progesterone affecting seizures that occur in some women in the premenstrual period. That was fascinating for me because, while I was writing the book, I had a call from a lady who had intractable seizures, mostly premenstrual. She had been given all the anti-seizure medicines without any help. After her naturopathic doctor started her on pregnenolone, she noticed an incredible reduction in the number of her seizures. Her experience suggested to me that there might be something to the idea of neurosteroids.
influencing seizures, especially in women in the premenstrual time. So we may find another benefit for pregnenolone as an anti-seizure medication since it does influence GABA receptors.

I've been experimenting with different forms of Pregnenolone. Today, I'm on 20 mg of sublingual. I've tried the regular pills, the micronized, the sublingual, the cream. Some company up in Toronto called me to send me the spray form. I like them all. They seem to have different effects in subtle ways.

JOHN: Pregnenolone influences GABA receptors?

DR. SAHELIAN: Yes, it does.

JOHN: Does it then have a sedative effect similar to GABA?

DR. SAHELIAN: It has more of a stabilizing effect. This is a very fascinating area. If we were to find that pregnenolone would allow the dosage of anti-seizure medicine to be reduced, that would be another revolution in neurology.

JOHN: Have you come across the libido enhancement effects of pregnenolone?

DR. SAHELIAN: I didn't come across anything in the published literature. The many people I have given pregnenolone to have said that they didn't notice much, libido-wise. And those very people I had previously recommended DHEA to had definitely noticed sex-drive improvement from DHEA. So my suspicion is that its effects are going to be subtle. However, some notice an enhanced urge for intimacy.

JOHN: I know a number of people, most of them are women, who claim to get libido-enhancement. Maybe it's a placebo effect. How about other benefits that you've come across or that you've written about? If you could just go down the list.

DR. SAHELIAN: PREG is an anti-fatigue agent, which could be beneficial in those who need to work long hours, especially if they have physical work. I've taken it on hikes in the mountains and hiked 12 miles, came back in late afternoon and could keep going and going and going. So perhaps we could explore its use in those who go mountain climbing or people who are carrying backpacks or maybe it could be tried in athletes who are doing long-distance events.

It can be beneficial in terms of physical stress. But in certain cases of mental stress, such as when having an argument with someone, I have found a high dose can make some people irritable.
And it can lead them to become aggressive or to give a snappy response, or it might just make someone angry. So it's got kind of a mixed effect there.

We talked about arthritic conditions, especially rheumatoid arthritis and autoimmune conditions. Again, glucosamine works better for osteoarthritis, but pregnenolone could be an additional help. With these conditions, I don't think pregnenolone is going to be curative on its own, but it could be combined with other medicines and maybe reduce the dosage of drugs and their side effects.

Pregnenolone has a lot of potential in neurological conditions: Maybe low dosages for Alzheimer's in combination with other nutrients like acetyl L-carnitine, ginkgo, ginseng, and many other cognitive enhancers, piracetam and so on. In multiple sclerosis or Parkinson's disease, low dosages in combination with other things may help. One study showed some potential with nerve injuries.

And then there's skin wrinkling. There was a study back in the 1950s in which a cream form of pregnenolone was found to rehydrate the skin, making wrinkling less apparent.

WILL: There's one other question I have, Ray. It has to do with the bioavailability of pregnenolone. I know you told me you prefer the micronized form.

DR. SAHELIAN: I've been experimenting with different forms. Today, I'm on 20 mg of sublingual. I've tried the regular pills, the micronized, the sublingual, the cream. In fact, today some company up in Toronto called me to send me the spray form of pregnenolone. I like them all. They seem to have different effects in subtle ways.

And my thought is that with each form, we're getting a different set of steroid hormones circulating in our system. Let's say you ingest the oral. It goes to the liver, where much of it is changed from pregnenolone into 17-hydroxy pregnenolone and to DHEA and to progesterone, and the whole mix and whatever is poured into the blood stream goes into the central nervous system giving a different effect. With the micronized form, most of it goes into lymphatic system, and it gets to the bloodstream, mostly as pregnenolone or 17-hydroxy pregnenolone. And in the brain, well, it would have a little different effect. Sublingually, you get most of it as pregnenolone, quicker to the brain.

As to the cream? Who knows how much of it is getting in and how it's changing before it gets into the blood.

So basically, practically speaking, I'm telling people I don't know in the long term which one of these forms is going to be healthiest for us. If you're taking it for 5 or 10 years, it may be better to let the liver work with it a little bit. But for practical purposes I tell people, try at least two or three different forms and stick with the one that you prefer, the one that's giving you the best
CNS effect or the best effect for your particular mental or medical condition. Or sometimes you can even combine two forms.

**JOHN:** This is really interesting because the people who told me they were getting libido-enhancement from pregnenolone said that it only worked when they took a capsule and opened it up and put about half the contents under their tongue. So, in other words, they were taking it sublingually. I ignored that because I thought there wouldn't be any difference other than rapidity of onset.