This page contains comments and links to specific sections, Michael Cheikin MD
General comments:
1) Great ideas, however, neither Mercola or Dinkov have done these things. Mercola has not seen a patient in 14 years by his own statement. Dinkov? I'm sure they are getting some feedback from other practitioners and perhaps by trialing on themselves (Mercola mentions that his prolactin is high and he might try some evening progesterone). Some of the doses, such as pregnenolone, are too high especially as a starting dose. During the discussion of sleep disorder and recommendations for GABA
1) Link to this pdf:
2) Estrogen, de-differentiating, pro-differentiating
3) Hair testing of estrogen, hormones. Estrogen doesn't decline, others do p 5
4) Cancer as a reversion to older modes of life p 6
5)
Abortion pill, RU486 and DHT, p 9

The Deleterious Effects of Excess Estrogen and Serotonin
A Special Interview With Georgi Dinkov
By Dr. Joseph Mercola

Dr. Joseph Mercola:

Welcome, everyone. This is Dr. Mercola helping you take control of your health. And today, we are joined by Georgi Dinkov, who is fresh back from Bulgaria and going to give us some real updates and insights. I want to focus today on some controversial topics, certainly controversial in the traditional medical community. And that is two big ones actually. One is estrogen, and I have a number of friends that are natural medical physicians. They give me a hard time about dissing estrogen, and they claim it's so good.

And there were problems and flaws with the Women's Health Initiative study done about a quarter-century ago. I think the results were published maybe in 2000, 2001, which was responsible for putting the nail in the coffin of most estrogens and radically decreased it. But there's still a big controversy about that. So, we'll start with that. And then I want to progress into serotonin, which is another big myth, and that serotonin is not the happy hormone that's responsible for causing depression. Although, certainly, Big Pharma would have you believe that because they have many, many, many SSRIs (selective serotonin reuptake inhibitors). I think 25%, the last statistics I looked at of the women over 40 are taking SSRIs. That really is something that needs to shift quite dramatically. Fortunately, there's a lot of good alternatives to that. With all that preface, welcome. Thank you for joining us today, Georgi.

Georgi Dinkov:

Thanks for inviting me again. Happy to be here.

Dr. Joseph Mercola:

Okay, well, let's start with your insights on estrogen.

Georgi Dinkov:

Okay. So, estrogen. [The] old name for estrogen used to be adipin.

Dr. Joseph Mercola:

Adipin. A-D-I-P-I-N?

Georgi Dinkov:

That's right, exactly. And the reason they called this is because it was known to be intimately involved in getting people and animals fat.

Dr. Joseph Mercola:

Oh.

Georgi Dinkov:

For some reason, [it] got conveniently forgotten around, I would say, the mid-‘50s. And then after that, because the medical industry and the pharma industry really started prescribing these synthetic estrogens, the most infamous of which is DES, which is Diethylstilbestrol, [it] caused innumerous amounts of fetal deaths, malformations [and] cancers in the mothers that took it, and so on and so on, to the point where I think eventually there were even class-action lawsuits. So, the government withdrew it, banned its use for humans. It's still used in the veterinary industry, but to me, that's one of the first strong evidence that estrogen is probably not as beneficial if you increase it either for too long or beyond a certain level of physiological dose. But the excuse at the time was, “Well, DES is not estrogen.” That's true. It's a nonsteroidal kind of estrogenic chemical, but it does activate the estrogen receptors, alpha, beta, even more potently than estrogen does.

And it has no other mechanism of action except its estrogenic activities. And then of course, even mainstream doctors will admit that there is this thing called estrogen receptor-positive breast cancer. The role of estrogen there is well-known. Nobody's denying it, but the story has always been [that] it's a localized only effect. It's a tissue-specific effect. If you look at the estrogen levels of menopausal women – and by the way, the risk of estrogen receptor-positive breast cancer rises with age. They'll say, “Well, it cannot be estrogen because estrogen in the blood is undetectable when we tested menopausal women.” However, if you take [a] tissue biopsy from the actual tumor or the breast tissue around it, you'll see that estrogen levels are sky-high there.

Begrudgingly, the medicine said, “Okay, yes, estrogen is involved as a causal agent in estrogen receptor-positive breast cancer. However, this effect is specific only to the breast. Elsewhere, estrogen is really beneficial. And that's the reason why we're seeing ovarian uterine atrophy, vulva atrophy in all these menopausal women, and we need to give more estrogen.” I think that's actually what led to the Women’s Health Initiative studies. There were these multi-decade trials in women that basically tested in a double-blind, randomized, placebo-controlled fashion, whether estrogen is really good for women or not. And the results were abysmal for estrogen. The groups that took estrogen, even in doses that will be even lower than what currently healthy young women take as a contraceptive increased drastically the risks of heart attacks, strokes, the ischemic type, also Alzheimer's disease, Parkinson's disease and cancers, actually not just in the breast, but in every other female reproductive organ as well. So, it kind of gave a hint that estrogen is carcinogenic not only for the breasts of postmenopausal women, but also for their uterus, for the ovaries, for the vaginal canal, [and] also for the endometrium, which is the lining of the uterus.

And really, when the results were published, it poured very cold water on all of the people that were advocating Hormone Replacement Therapy, HRT, with estrogen for women. And this continued – Basically, the estrogen winter – because that's the term used in IT, the “AI winter” as they call it. In other words, the disuse or the declining use of estrogen as a therapy continued from about 2000, I would say, 2002 until about 2015, when I started seeing studies come back again and say, “No, these studies really vilified estrogen unjustifiably. It was all about how much

you are given, the dosage, the timing. We could have done better. So, we shouldn't really vilify estrogen." And little by little, I'm noticing that basically estrogen has crept back into the HRT regimens that doctors are prescribing to all kinds of women, menopausal or not.

But if you look at the cancer rates, not just for breast cancer but for all of the reproductive organs, the female ones, you'll see that there was a drop in the deaths from these cancers in the period over the last 20 years. And then that rate started going up, and not just up but exponentially up, over the last five or six years, which coincides perfectly with the gap, which is basically about 15 years of really not using estrogen directly or at least on a mass scale. And then basically the Big Pharma [is] coming back and saying, "No, we want to use estrogen." And started reintroducing it back into the treatment protocols. Both the rates of the cancers and the deaths from these cancers plummeted over this 15-year period, and now it's back to, actually exceeded, what it used to be.

Unbeknownst to most people in 2001, I believe – and I still have the link, which has since been removed, but I took a PDF of it – the National Institutes of Health declared estrogen as a known human carcinogen. Not probable, not possible, not likely, [but] known human carcinogen. So, this thing alone, to me, is sufficient to heavily discount considerations if a doctor wants to use estrogen therapy in men or in women. Now it's an officially known human carcinogen, and when I talk to other doctors, they say, "That's not true. I've never heard of this." But it's there. Check the register. It's published even in the federal register. So really if you look at estrogen from a biochemical point of view, its role is to essentially heal wounds. If there's any trauma in any tissue, estrogen is the differentiating factor, which reverts your differentiated cells in that specific organ tissue that's been injured, sends them back to their stem cell-like condition so they can grow and fill up or replace whatever dead or damaged tissue is there.

de-differentiating

And then, the expectation is that there will be a pro-differentiation factor that will turn the activity of estrogen off. And that pro-differentiating factor in young healthy people is usually progesterone for women and/or androgens for males. And it just so happens that these pro-differentiation factors decline with age. Well, the synthesis of estrogen never does. And that's probably another big myth that we need to address. Talk to any doctor on the street, they'll tell you, "No, menopause is a condition of both progesterone and estrogen severe deficiency." We've done countless tests in the blood and we've seen that estrogen levels and progesterone levels are undetectable. And that's expected because most of the estradiol, which is in the blood, which is the main estrogen both for males or females, and progesterone, they're of so-called ovarian origin in females. So, in other words, if the ovaries atrophied, yes, you will expect to see declining levels of the steroids in the blood because the ovaries are not working so well. And in fact, eventually they fail.

However, another thing that's probably not very well known out there, even among doctors, [is] that every cell in the body expresses the enzyme aromatase and contains the machinery to synthesize its own estrogen from circulating precursors. And those circulating precursors are always there, usually cholesterol, which by the way, rises with age, right? So that would imply that if we test tissues, even in menopausal women, we should see [an] increase in estrogen, especially in women that are having problems with their health, versus decrease, which is what's seen in the blood. And every test that I've seen biopsy done confirms that. Recently in 2022, a Chinese group published a very large study with Chinese women where they measure over 20

different hormones, their levels in hair. And they came up with some really interesting results. In hair, which is kind of like a surrogate for what's going on in the tissues because hair, it used to grow out of cells called follicular cells.

And basically, the levels of steroids in these cells are probably representative of what gets deposited into a hair. If you look at the estrogen levels of these women, which span all age groups, estrogen levels not only did not decline with age, they actually slightly increased. So, there was no estrogen deficiency as far as hair testing is concerned in these 250 or even more Chinese women. Progesterone did decline, in fact, almost to undetectable levels. Thyroid hormone, the active portion T3, also declined. Reversed T3 increase, and there was an inverse correlation between body mass index and the levels of either T3 and progesterone, and positive correlation between body mass index and the levels of estrogen. So, to me, that gives you a very strong evidence that estrogen is really not what we're being told it is, in the sense that you can freely administer it and, basically, it will restore youthfulness in all of these menopausal women. And another study that corroborates-

Dr. Joseph Mercola:

Let me-

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

Let me hold here. I just want – You are the hydrant. Fire hydrant worth of information. So, let's give people a pause here and we can digest this because you presented so many concepts. You'd said that the estrogen is undetectable in blood, but if you take tissue biopsies, you'll find it [in] really elevated levels. And then you went on further to talk about the hair levels, which you'll also find it low. And I think you said that progesterone levels decline with age, and they're not in tissues and they're not in the hair.

Georgi Dinkov:

Exactly.

Dr. Joseph Mercola:

Okay, thanks for confirming that. And then you would know because you have a lab, you constructed a lab to actually measure these items, not minerals. Well, I guess you do, but you measure steroid hormones in the hair, right?

Georgi Dinkov:

Yes, 25 plus different steroids, including not only estradiol but also estrone and estriol, which the three combined are basically all of your active estrogens. There are other ones, but they have

much weaker activity. But if you take the estradiol, being the strongest, estrone and estriol together, this gives you your estrogenic profile. And we are seeing the exact same thing as the Chinese group did. There's no decline of any of these estrogens with aging. In fact, if anything, there is an increase. So, it's very difficult to speak of estrogen deficiency except in the blood, because at least in the follicular cells, there seems to be estrogenic synthesis going on without any problem. But progesterone, which in most people – in females, it's mostly synthesized in the ovaries and the brain, but the rest of the tissues cannot really synthesize it. While in males, it's mostly synthesized in the gonads, which is the male version of the ovaries and the brain.

So progesterone levels decline both in the blood and in the tissues, or in this case, in the hair. Estrogen does not. Estrogen is always there, always ready to come in and help. Actually, it's a helpful steroid if you are damaged and there's some repair that needs to be done by triggering cellular division and growth. But that process needs to be turned off because that is the very essence of cancer. And I remember there was a – a study came out, I think, in 2015, one of the – I'm blanking on his name. One of the foremost experts in oncology in the world said, "We've been thinking of cancer wrong. It's not trying to kill you. Cancer is simply a reversion to the cellular life that was on earth 2 billion years ago when the conditions simply did not allow for higher rates of metabolism to occur." So, cancer is just the cell doing the bare minimum possible to survive, which means producing energy through very inefficient means. In other words, aerobic glycolysis, which is the Warburg effect.

Dr. Joseph Mercola:

Right.

Georgi Dinkov:

And estrogen strongly, strongly, I emphasize, supports that primitive metabolism while turning off the oxidative phosphorylation. And it makes perfect sense for estrogen to do that because when you have to repair tissue, you can forgo for a little bit the oxidative phosphorylation, but it always needs to come back because that is the differentiating factor. Stem cells continue and stay in their "cancer metabolism" because it's really not cancer. It's just the way cells have to be in order to divide the maximum rate possible with the minimum consumption of resources possible. But if you want this tissue to become human and you'll be an organ instead of just a blob of cells that consumes all your energy, you need to turn off that estrogen signal and either high metabolism and/or progesterone and/or thyroid, both of which [are] also pro-metabolic, are known as one of the main differentiating factors in humans.

Dr. Joseph Mercola:

Yes. All right. Clearly, estrogen is anti-metabolic. It shuts down or radically reduces the ability of your mitochondria to create cellular energy in a form of ATP (adenosine triphosphate). So, it's not good. And in many ways, in so many ways – You had mentioned earlier that it's clearly associated with an increase in female reproductive cancers, but I think it's even broader than that. It appears to be associated with all cancers. And in so many ways, and I want you to go into this, it's similar to linoleic acid because both of these work in similar ways in that they're both anti-metabolic and they turn down the mitochondrial function.

And interestingly, I was reading this in a Peat article recently. They tend to increase the amount of extracellular calcium into the cell, to intracellular. And when the intracellular calcium goes up, that's responsible for increasing superoxide and nitric oxide. And those guys, instantly, in the tiniest fraction of a second, combine and form peroxynitrite, which is a really, really bad reactive nitrogen species that causes incredible damage in the cell. And both of them seem to do that, which is interestingly – And I read that because that's exactly the proposed mechanism of how EMF (electromagnetic field) causes damage in your cells.

Georgi Dinkov:

Yep.

Dr. Joseph Mercola:

Increasing intracellular calcium concentrations.

Georgi Dinkov:

Did you see the discussion on Reddit that happened maybe six or seven years ago?

Dr. Joseph Mercola:

No, I'm not a Reddit follower.

Georgi Dinkov:

Well, they had an AMA, like an ask me anything, and they invited this professor from University of Toronto or University of Waterloo.

Dr. Joseph Mercola:

Yes.

Georgi Dinkov:

And basically, they butcher him, but he kept saying, “Listen, all I'm trying to say, and I'm not saying this causes disease, but what is indisputable in our experiments, exposure to EMF, even at what you expect to get from your phone or even your router, it basically increases intracellular calcium. And the main effect that we're seeing is decline in oxidative phosphorylation.” And the response of the Reddit group was like, “Well, okay, so it's just metabolism. That doesn't mean it's going to cause any structural damage, which is cancer and Alzheimer's, and so on.” But now we have evidence. Actually, the evidence has always been there, but our discussions are about the fact that if you interfere with the usage of oxygen, the cellular usage of oxygen, specifically in regards to oxidative phosphorylation, eventually this will cause structural problems.

And perhaps the most direct example – remember I sent you a study the last time we exchanged emails about the reduced versus the oxidized ubiquinone, ubiquinone versus ubiquinol? In the

cell, all that is required for complex I of the electron transfer chain to be dismantled physically is a drop, basically a shift, of the redox state towards reduction. And that means increasing ubiquinol and reduction of ubiquinol. So, declining metabolism or shifting the redox state towards reduction causes structural changes directly into the cell. And I think that's the part, that once doctors accept that the functional issues can cause structural ones, and of course we know the opposite is also true, then I think the picture of cancer in many of these degenerative diseases starts to become much clearer. You don't need genes for that. They may be for some diseases, but you don't need genes because simply interfering with metabolism is enough to prevent your body from maintaining its proper structure.

Dr. Joseph Mercola:

Yeah, and the Complex I, you have NAD (nicotinamide adenine dinucleotide) primarily, and then Complex II is FAD (flavin adenine dinucleotide), and then I think [Complex] III is ubiquinone, is that correct?

Georgi Dinkov:

Yes. Then [Complex] IV is cytochrome c oxidase. And since you mentioned nitric oxide, its primary anti-metabolic effect is the fact that it forms a covalent bond with cytochrome c oxidase. So, it turns it off in a very bad way. Unless you knock that bond, break that bond, which methylene blue and magnesium are known to do, but we don't know how efficiently, the only way to restore the function of that cell is if that cell synthesizes, creates a new Complex IV but it cannot do that since it needs energy. So, it's a catch-22, a really bad situation. So, nitric oxide is a very, very potent metabolic inhibitor. In my book, it ranks right up there with something called rotenone, which is the classic one used to inhibit Complex I.

In the studies that have compared them both, they seem to be equally bad for the organs for which the rotenone is known to be bad. The liver, the spleen, the reproductive function [and] the brain especially. Rotenone is a known causal agent of Parkinson's disease, and it's used as a reliable causative agent to create a Parkinson's model in animals. It's known to do it in humans too, because there've been so-called ambient exposure to rotenone because it's an herbicide. So, it's known that it can cause it in humans, too. It's just not used directly because it's unethical.

Dr. Joseph Mercola:

Let's get back to estrogen again. Do you agree with the fact that it increases cancer overall, all types of cancer, not just female reproductive cancers?

Georgi Dinkov:

All types of cancer.

Dr. Joseph Mercola:

[inaudible 00:18:56].

Georgi Dinkov:

There is a very famous cancer called estrogen receptor-negative breast cancer. In fact, triple-negative breast cancer, that medicine says it expresses no steroid or receptors. Steroid therapy should not work on that cancer. Well, guess what? Recent studies came out showed that if you administer an androgen, which by the way is a known estrogen antagonist. And the androgen administered was dihydrotestosterone, the very evil steroid, yes, actually caused immediate regression and reversal of the cancer cells to normal. Then they use another chemical, which is known as a glucocorticoid antagonist known as RU486, [which] caused the exact same regression in the cancers.

Clearly, these cancer cells are receptive to steroidal modifications and they may not have the steroidal receptors, but it doesn't mean that – steroids are known to have so-called non-genomic effects. And it just so happens that estrogen, when you administer it to even non-estrogen receptor-positive cells, it stimulates their growth. While if you administer anti-estrogenic, or in this case, anti-cortisol substance as well, then the cancer cells revert back to their normal metabolic phenotype. This, to me, heavily implicates estrogen. Estrogen is also a reductant. And like I said before-

Dr. Joseph Mercola:

That's for sure.

Georgi Dinkov:

Basically, just a simple shift of the redox state towards reduction is enough to start causing negative structural changes in the electron transfer chain complex.

Dr. Joseph Mercola:

So, it would seem that for treatment of almost all cancers and probably most resistant obesity, that using a strong potent androgen that is resistant to aromatization like DHT (dihydrotestosterone) and a cortisol blocker like RU486 or mifepristone would be a useful strategy. The problem is, though, those are difficult to get. I was looking at – Because I was considering using mifepristone, but it's hard, really hard to find even [from] almost all regular conventional pharmacies. Do you have any strategies for finding that?

Georgi Dinkov:

I [inaudible 00:20:57] strategies, but I've noticed that it disappeared over the last five years. Before that, it was widely available because at least both of these steroids are widely used by a body building community. But over the last five years, I noticed that all of the western chemical companies simply either stop offering the RU486. DHT is considered a DA-controlled chemical. That's a separate story. It's available, but it's still harder to get. But it used to be [that] mifepristone was easier to get than DHT. Now it's the other way around. Now mifepristone is completely gone. I don't know [if] it's because of all the studies that have been coming out with RU486. A couple of really remarkable case studies. An end-stage terminal pancreatic cancer

patient went to the hospital and said – Found one of the studies that I did, and really told the doctors, “Listen, I'm not interested in any of your therapies. I'm about to die. Give me this drug.” So, the doctors applied to the FDA (Food and Drug Administration) for compassionate – I think it's compassionate case approval or whatever it's called-

Dr. Joseph Mercola:

Compassionate use.

Georgi Dinkov:

Yes. [The] FDA said, “Sure, go ahead.” So, they had a limited supply in the hospital, gave him 100 milligrams of mifepristone daily, the cancer regressed, and the guy was alive for three years, even though he was expected to die within two months. And then basically the supply ran out. FDA said, “No more, we just can't continue with this. You proved your case, now go ahead and die, please.” They didn't say that, but basically, that's what happened. They stop his RU486 supplies and ask him, “Do you want to go on chemotherapy and radiation because now the tumor has regressed and it's actually treatable?” He said, “No, leave me alone.” And then he died.

But then there's also another case, basically, of RU486 stopping triple-negative breast cancer in a human female. So, a number of different case studies, and I'm starting to think that pharmaceutical companies are starting to really hoard up on their supplies of that chemical. Probably in expectation of getting some kind of Emergency Use Authorization, because the legal landscape, as you well know, changed dramatically since the pandemic. Now, a lot of pharma companies are saying, “Oh, we don't have to go through these 10-year trials. Who has $2 billion to spare on something that may or may not work? Let's just try it out on people and see if it works.”

But you need the actual chemical. Long story short, the only sources that I know is either my lab that can synthesize it or there's another company in Europe that still seems to sell it but wants an actual proof that it's going to be used for medical purposes. And then of course, the infamous Chinese sources, which by the way, have also dried up. I used to work for at least four or five different suppliers over there, they all had RU-486. Now, only one of them has it and only will synthesize it if we actually ask for it. They claim to not have it in stock. Something's going on regulatory or financially, and my guess is that the potential of RU-486 is being recognized and whoever's going to come approach the FDA and say, “Hey, give me approval for X, Y and Z conditions,” is probably hoarding up on that drug.

Dr. Joseph Mercola:

Now, just to give a little backstory on RU-486, it was primarily developed as a cortisol blocker. That was its primary function. But the people who developed it, they determined they couldn't really sell a lot of it because that's a very limited indication. They also found out that it blocks progesterone. I think it's progesterone?

Georgi Dinkov:

Progesterone, yeah.

Dr. Joseph Mercola:

Yeah, you have to – You don't have to, but if you're going to give it to block cortisol, you really, really need to supplement with progesterone, because it will block both and having adequate levels of progesterone is truly – it's really the hormone that most women need. It is not estrogen; it's progesterone and pregnenolone. I'm wondering if we can dive into the practical aspects of this, because you made it very clear RU-486, and what was the other? Oh, DHT-

Georgi Dinkov:

DHT.

Dr. Joseph Mercola:

-[inaudible 00:24:41] really, really difficult to find. But if you're in the weeds with a severe problem, it's certainly worth exploring. But for most people, it is not going to be easy, even for someone like me. The practical thing that almost everyone needs to adopt is to make sure, make sure that your levels of progesterone and pregnenolone are okay. Now, are those hormones – The test in the blood, are they sufficient or do you need to go do a tissue analysis like hair?

Georgi Dinkov:

I would say it depends on the age. I mean, after a person is over 50, so to speak, the levels of progesterone DHEA (dehydroepiandrosterone) decline in both sexes. It's a well-known decline. In fact, they have different ranges based on how old you are when you go and do the test. But I think the ranges should not be adjusted according to the age. They should actually stay to the levels that-

Dr. Joseph Mercola:

For optimal health. Right.

Georgi Dinkov:

Exactly, which is whatever you had in your 20s. In fact, the cortisol-to-DHEA ratio is now known, whether in blood or tissue or hair or nail, has now been established as the single most reliable predictor of all-cause mortality and morbidity throughout the entire lifespan.

Dr. Joseph Mercola:

What should that ratio be? Less than 0.5?

Georgi Dinkov:

Less than 0.3. In other words, heavily in favor of DHEA. Anything over 0.5 is known to start causing at least mood disturbances. In other words, cortisol, [there's] corroboration that it can cause depression. Anything over 1, you're probably at risk of diabetes or cardiovascular disease, or worse.

Dr. Joseph Mercola:

Okay, perfect.

Georgi Dinkov:

And then progesterone, that's something that's not even discussed in the medical books anymore, but the older studies would've demonstrated that it's actually perhaps the main endogenous and [the] most direct and potent glucocorticoid receptor antagonist. Progesterone is really like RU-486, but without blocking your progesterone receptors. You really need to maintain the levels optimum, as you said, either can be taken preform or you can take pregnenolone. However, the conversion-

Dr. Joseph Mercola:

Wait, wait, wait. Stop there because I'm confused. Did you say progesterone was a cortisol blocker?

Georgi Dinkov:

Yes, it is a cortisol blocker. Yes.

Dr. Joseph Mercola:

Because you said glucocorticoid receptor, so it's blocking cortisol.

Georgi Dinkov:

Yes, it is.

Dr. Joseph Mercola:

Wow. But it's not as effective as RU-486, is it?

Georgi Dinkov:

I would say pound for pound or milligram for milligram, it's about as effective as RU-486.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

It has the same [inaudible 00:27:09].

Dr. Joseph Mercola:

That is really, really good news because progesterone is really easy to get. But however, I used to use it in the ‘90s after I read a book by John Lee, who was a physician in California. He's since passed. He was widely responsible for the widespread adoption of that, but he was using a cream and there are definitely complications with using a cream, at least a traditional cream. And so, the key is to get that molecule into the blood and not develop resistance transdermally. Why don't you walk us through the ideal way to get progesterone and pregnenolone?

Georgi Dinkov:

Progesterone, I mean, if you're going to take progesterone orally, it better be taken with ideally a combination of something very lipophilic that can avoid going through first-pass metabolism. And the long-chain fatty acids, of course, preferably saturated or at least monounsaturated, with chain length of 14-carbon atoms or more, are ideal for that because they've been shown to be mostly absorbed through the lymphatic system, which then basically circulates and eventually gets drained into the systemic circulation through something called the thoracic duct. This way, you are avoiding first-pass metabolism through the liver and if you actually – if you don't avoid the first-pass metabolism, you're going to waste about 85% of the progesterone taken.

Dr. Joseph Mercola:

85%.

Georgi Dinkov:

Yeah.

Dr. Joseph Mercola:

And let's just get specific, you said a long-chain fatty acid, longer than 14 carbons. That would be something like butter.

Georgi Dinkov:

Butter, olive oil, yeah.

Dr. Joseph Mercola:

Olive oil. Or we're not a big fan of olive oil, but in small doses it's okay. But this means you do not want to do it with coconut oil because the vast majority of the carbon chains in coconut oil is below 14. I mean, [inaudible 00:28:50].

Georgi Dinkov:

Yeah, C-12 is the max, I think. And then there is a tiny amount of palmitic acid, which is C-16, but it's a very small amount. Mostly medium chain triglycerides, which are going to go through the portal vein. Now, coconut oil is very good for enhancing transdermal absorption. If you want to try that, maybe mix – just make an emulsion of a little bit of progesterone and coconut oil and rub it on your skin. I think it will work quite well. But the transdermal absorption from most people is limited, and it is very slow, so even if-

Dr. Joseph Mercola:

It's less than optimal. Less than optimal.

Georgi Dinkov:

Yeah, exactly. Yeah.

Dr. Joseph Mercola:

Yeah, and I think it's Ray Peat's company, he put a Progest LA compilation or product that is a combination of progesterone and vitamin E.

Georgi Dinkov:

Yeah, Progest E. And basically, the progesterone is dissolved into vitamin E, which if you look at its structure, it's similar to and it absorbs very similar to very long-chain saturated fatty acids. In other words, it goes mostly through the lymphatic system. And if I understand correctly, because I've asked him, of course he doesn't disclose the exact composition, but it's about 90% mixed tocopherols, which is the vitamin E part, and about 10% long-chain fatty acid triglycerides, saturated ones. That's really the product. And you can vary the ratio of tocopherol to the fatty acids because some people find that higher concentrations of tocopherol when taken orally can irritate their gut. It's a well-known side effect of vitamin E, but this can be avoided if you dilute the tocopherol-progesterone combination with a little bit of more oil. However, there is some evidence that the less tocopherol remains, the bigger the risk that higher portions will go towards the portal vein. The tocopherol is important there. I find that a 1-to-1 ratio works perfectly fine and it doesn't cause irritation in the GI (gastrointestinal) tract.

Dr. Joseph Mercola:

Yeah, I think you just had some posts on your blog. I think they're the most recent posts about how that product is particularly useful, maybe not that specific product but the combination of vitamin E and progesterone, at transporting that into the brain.

Georgi Dinkov:

And also, yes, and confirming what Dr. Peat had said, I would say 40 years ago when he actually first filed the patent for progesterone and vitamin E, in that pattern, he describes vitamin E as a

very strong brain-protective nutrient. And this study demonstrated – discovered by accident, basically – that if you combine, if you dissolve some brain-protective substances in tocopherol, or at least mix them with tocopherol and administer them-

Dr. Joseph Mercola:

That would be progesterone. Progesterone.

Georgi Dinkov:

Yes, progesterone. Yeah, that one, but they use something else. But I'm saying in my blog, I said progesterone is the natural thing to try. Then, [it] not only targets preferentially the brain, but it seems to go directly to the area that has been damaged by, in that case, stroke. This means you can actually increase in selectivity and specificity while reducing the concentration needed simply because you're directly targeting the actual damaged area. That's incredible and very unique because it means that if progesterone and pregnenolone are dissolved in vitamin E, you can actually increase their effects on the brain and you will be focusing on the area that's been damaged. And both pregnenolone and progesterone have been used for things like traumatic brain injury, Alzheimer's disease, Parkinson's, mostly in animal trials, but now some human trials as well, specifically for progesterone.

But from what I see, the formulations there, none of them use vitamin E, they just use peanut oil, which means peanut oil and progesterone – There's a product on the market called Prometrium, and it's been shown to have no more than 12% to 14% systemic bioavailability. You are using more than 85% of the progesterone. Worse than that, even when you have the systemic viability of the optimal level 12% to 14%, the half-life is only about 40 minutes so that progesterone disappears. You want something – And tocopherol is great in that respect because tocopherol's half-life is about 48 hours, which means that if you take the tocopherol, the progesterone dissolves in tocopherols, you'll actually circulate in the bloodstream, [and] you will have the same half-life or similar to tocopherol, which means two days. [It] means you don't even have to take it every day. If you discover a dosage that works for you, you can take it every other day or every two days, whatever works best. It's really a very good invention [crosstalk 00:33:04].

Dr. Joseph Mercola:

Well, let's get into the specifics because that's where it counts. So, the Progest E can be taken – ideally, you say don't dilute it. You could, but there's a chance that you're going to decrease the absorption. And how many drops? I mean, it comes in a 1-ounce dropper bottle. How many drops would you say, and where do you apply it? Do you apply it under the tongue, on the buccal mucosa on your cheeks? And then what's the frequency? And do you suggest or encourage any monitoring just to make sure you're in the target window, or do you just look at your clinical symptoms and judge the dosing by how you feel?

Georgi Dinkov:

Well, it really depends on what it's being used for, but as far as the dosage, how it's taken, it depends on the part of the – Progest E, I think, has about 4 milligrams of progesterone per drop,

and a physiological dose for a young healthy child before they actually reach puberty is about 30 milligrams of progesterone daily. Another thing that most people don't know is that both males and females produce equal amounts of progesterone before they hit puberty. That's probably one of the reasons why the sexual dimorphism is not as highly expressed in children, simply because before they hit puberty, they have a very similar hormonal profile. Anyways, 30 milligrams seem to be a decent dosage prophylactically. In fact, I think for some people, [that] may even be too high. I've seen people with very bad cases of rheumatoid arthritis, where basically all of their joints are swollen and they can barely move, improve in a matter of hours from either 20 to 30 milligrams taken orally, and you can rub it on the mucosa or on your gums.

But the good thing about tocopherol is that even if you just directly ingest it, you'll still be getting mostly the systemic effects. In other words, you'll be avoiding the first-pass effect, but if you rub it on your gums, or on the inside of – the buccal so-called approach, on the inside of your cheeks, because the mucosal there is so thin, I think the effects are much more rapid. If you want a very rapid effect within a minute or two, then rubbing on the gums or putting under the tongue or rubbing on the inside of the cheeks, I think it's the way to go. If you don't care that much about the fastness of the effect, then I think taking [it] orally is fine and probably most people prefer it that way.

Dr. Joseph Mercola:

Okay, good. Are there any specific symptoms that one should look for to recognize that you're getting close to the optimal dose and frequency?

Georgi Dinkov:

I would say, because progesterone is a strong sedative – in fact, several derivatives of progesterone are still used in veterinary medicine as general anesthetics. And there were a few of them that were developed for human use as well, but they caused – And I still haven't found those studies that claim that. I mean, the studies claim they caused some kind of side effects, but I haven't found what kind of side effects they cause. It's just a rumor. Anyway, progesterone is a strong sedative. Once you start getting to a point where you're basically getting disorientation, slowing of the thought or speech and getting sleepy, you've probably overdone it a little bit.

Now, by overdone, I mean if you want to be functional and it's in the middle of the day, you probably don't want to be sedated, or you're operating machinery and whatnot. In fact, a hefty dose of progesterone causes symptoms indistinguishable from being drunk. And an interesting side story, because it's a GABA (gamma-aminobutyric acid) agonist, a company in England – actually [an] American company, but now working in England – has already released on the market an alcohol substitute, which consists of nothing but GABA, the actual gamma-aminobutyric acid. Taking progesterone mimics that very closely. In other words, if you take a hefty enough dose, you will be legally drunk. Actually, you will legally be drunk, so don't operate machinery when you're taking a lot of progesterone.

Dr. Joseph Mercola:

No, then clearly the dosing is taken before you go to bed or maybe an hour before you go to bed, because GABA itself an amino acid, which is an inhibitory neurotransmitter, is magnificent for sleep and we need [for] people from SSRIs, and we're going to talk about that in a bit when we transition to serotonin. But it never occurred to me that – I didn't realize that progesterone was a potent GABA agonist. It would seem that would be useful to use with a GABA supplement.

Georgi Dinkov:

Yeah, and actually you can probably get away by using much lower doses of either one when you combine them together. The strongest GABA agonist in the body, slightly stronger than progesterone, they're actually pretty close in terms of affinity for GABA, is a progesterone derivative, in other words a metabolite, known as allopregnanolone, and it was recently approved by the FDA for postpartum depression.

Dr. Joseph Mercola:

That's right. That was earlier this year.

Georgi Dinkov:

Yep. And now, a company is developing an oral formulation exactly through the methods that you and I discussed with the long-chain fatty acids called LYT-300, and now they're applying to the FDA for clinical trials for post-traumatic stress disorder (PTSD), for psychosis, for sleep disturbances, for anxiety and all of these things GABA is known to relieve. They're saying, “Oh, we have the very potent, the most potent endogenous GABA agonist here, allopregnanolone, let us strive for all these conditions.” But we can say, “Well, you don't have to go and get allopregnanolone because of the prescriptions – you can do it [with] progesterone, maybe [a] slightly higher dosage, but still in the same ballpark.”

Dr. Joseph Mercola:

So, taking the 30 milligrams of progesterone will convert to a significant amount of allopregnanolone?

Georgi Dinkov:

Allopregnanolone. Yes. Yeah.

Dr. Joseph Mercola:

Yeah, that's a good one. I think that has some anticancer benefits too, doesn't it?

Georgi Dinkov:

Yes, which also confirms the fact – and GABA is actually a known strong pro-differentiating factor, and it's also known to enhance oxidative phosphorylation and inhibit excessive glycolysis. All of these things are basically the hallmarks of cancer. In other words, excessive glycolysis and

low oxidative phosphorylation. I think Dr. Peat mentioned very old studies about injecting GABA directly into tumors and causing complete regression in a matter of days.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

Yeah, cancer cells are very excited, and one of the reasons is that extra calcium that they're actually increasing the uptake of under the influence of estrogen and a lot of other factors. GABA acts in a way opposite to calcium, and in a way very similar to magnesium. In fact, magnesium was known as the old GABA agonist before they discovered GABA directly.

Dr. Joseph Mercola:

Wow. Wow. Yeah, and magnesium is also – something that became obvious when I was studying the EMFs, it's a supplement to take to mitigate EMF complications because it limits calcium influx into the cell.

Georgi Dinkov:

Yep.

Dr. Joseph Mercola:

Would it be safe to assume that progesterone, or Progest E, since it's such a potent cortisol blocker, would also be useful for the treatment of obesity and restoring metabolic dysfunction, mitochondrial metabolic dysfunction related to a low-carb diet? Obviously, the solution is to get back on some carbs, but would it be helpful in the short term?

Georgi Dinkov:

Unfortunately, all the studies that I have with high doses of progesterone for obesity are in animals simply because medicine currently doesn't believe progesterone should help with obesity. In fact, they're saying it's causing it. However, if you look at the evidence for RU-486, and assuming progesterone is just as effective [as a] cortisol blocker, there is a study with women with Cushing syndrome, they're overproducing cortisol, and they're invariably very, very obese. They have the typical Cushing phenotype, central obesity, very thin limbs, loss of muscle mass, which is well-known the cortisol can cause, and about 60% of them [have] severe clinical depression, which cortisol is now also known to cause. RU-486 not only led to a weight loss and normalization of all of their mental symptoms, the weight loss was [also] sustained.

In other words, after their cortisol went back to normal – or at least their cortisol activity, since the RU-486 doesn't lower synthesis of cortisol, it blocks its effects – after they got restored to a normal glucocorticoid sensitivity of receptor state, their weight loss remained. And in order for them to lose the weight while taking the drug, they didn't do any dietary or exercise

modifications. They just kept eating and living normally. I mean, they continued their current regimen. They didn't go on a diet, they didn't start exercising more. All they did was take a cortisol blocker, and that led to a repeat sustained weight loss. It's not that difficult to lose weight. It's difficult to maintain it as everybody who's ever been on a diet or an exercise regimen knows, especially those people in the Biggest Loser show.

Dr. Joseph Mercola:

Biggest Loser. Yes, absolutely. Let's finish up on progesterone and pregnenolone and transition over to serotonin. The Progest E dynamite, it works, no question. We'll seek to put a link to that in this article. But are there other forms of progesterone? I don't know that it's available as a powder. I mean, many of these supplements are. I mean, you could buy DHEA and pregnenolone easily online, but I don't ever remember seeing progesterone as a powder. I mean, it comes as creams and stuff.

Georgi Dinkov:

Yeah, I haven't seen powder.

Dr. Joseph Mercola:

You've never seen the powder? I haven't. Are there any other formulations that you would recommend, or is it just Progest E?

Georgi Dinkov:

You can make your own. There are some other people now selling progesterone in vitamin E, trying to mimic Dr. Peat's formulation. But I wanted to add a little bit in regards to weight loss, another steroid, which is also a known potent anti-glucocorticoid, is DHEA. With DHEA, we do have human trials, and in fact, there are two or three of them that are really remarkable. But they used absolutely massive doses, which I, under no circumstance, recommend. I think they used 1,600 milligrams of DHEA daily. That's ridiculous.

Dr. Joseph Mercola:

Oh my gosh. That's a hundred times higher [crosstalk 00:42:39].

Georgi Dinkov:

Yeah, but it led to a 30%, 36% reduction of central fat in humans. Of course, with such a massive dosage, because DHEA is a very reliable precursor to estrogens, you are expected to massively increase the synthesis of estrogens. However, if you combine it with progesterone, not only both will synergize the blocking of the cortisol receptor, [but] progesterone is also an aromatase inhibitor, [so] depending on the dosage, it will greatly prevent the conversion of DHEA into estrogen. And as far as dosages, of course, like I said, that's really an insane dose. I like physiological doses. And for most people, that is between 10 to 12 milligrams of DHEA

daily. That's how much you produce when you're young, when you're in mid-20s, and then after, it declines.

If you're still producing DHEA, which you can verify on blood tests, you can calculate the delta between what the optimal interval was when you were – the optimal levels were 500 [milligrams], and now you are in your 60s, and now the range says, “Oh, you're fine, but your levels are 200 [milligrams].” The delta is about, what, 60%? You need to take 60% of that daily dose that you used to be producing when you were in your 20s. 60% of 2 milligrams is what you really need to be taking in order to restore the levels to the youthful levels without running into that risk of really raising estrogen too much. And if you combine it with progesterone, you should be getting an even stronger anti-cortisol effect while further preventing its conversion of the DHEA into estrogen.

Dr. Joseph Mercola:

Yeah. Along those lines, is it true that if you aromatized DHEA, which means you increase your estrogen, wouldn't that increase prolactin?

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

Yeah, [inaudible 00:44:21].

Georgi Dinkov:

Yes. You should be very careful. And in fact, there are studies showing, [in] both animals and humans, that if you administer too high of a DHEA dose, prolactin level rises, which is [an] unmistakable sign of estrogenicity.

Dr. Joseph Mercola:

Yeah, because I'm personally struggling with that, and my prolactin level is a lot higher than I would like, but it didn't occur to me that progesterone – it's a really good strategy to halt aromatization because is it really the aromatized androgenic steroids that are responsible for increasing prolactin, or is it another route?

Georgi Dinkov:

There are some myths in the bodybuilding community. All the steroids that are raising prolactin are either convertible into estrogen such as, let’s say, nandrolone. Nandrolone is actually an estranged steroid. Its core is 18-carbon atoms, and so is estrogen's. It is an anabolic androgenic steroid, but it gets converted into estrogen much more easily than even testosterone. If you're taking nandrolone, it's perfectly natural to expect that your prolactin levels will rise. Non-aromatizable androgens usually do not raise prolactin. In fact, they lower it.

DHT is approved in several countries for treating gynecomastia, which is well-known to be caused by high prolactin because the approved treatment in most countries, including the United States, is bromocriptine, which is an anti-prolactin medication. DHT does not increase prolactin. In fact, it lowers it. However, there are other non-aromatizable steroids, such as trenbolone, which is known to increase prolactin and it has always been a mystery as to why. Well, if you look at the structure of trenbolone, it is also an estranged steroid. The core is estrogenic, and it also has three double bonds. It actually, structurally, is not very different from estrogen, and just based on its geometric structure, it is expected to activate the estrogen receptors, which probably explains why trenbolone and other non-aromatizable steroids can increase prolactin. But things like the dihydrotestosterone and its derivatives do not, and in fact, [they] lower it.

Dr. Joseph Mercola:

Yeah, it has more double bonds than linoleic acid.

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

No, DHT has no double bonds, right?

Georgi Dinkov:

No double bonds, fully saturated, so does allopregnanolone. And in general, the fully saturated steroids being lipids as well, they tend to have a calming, pro-metabolic relaxing effect, while the unsaturated ones tend to make you feel the same way linoleic acid does, hyper and agitated, and you feel like you have a lot of energy, but you're really running on cortisol.

Dr. Joseph Mercola:

Okay, so, Progest E is the way to go. Let's just finish this up with pregnenolone and then we'll shift into serotonin and GABA, which is the solution I believe. So pregnenolone is, I'm assuming the dose is oral? I actually do a suppository and I do it in cacao butter, which is a very long-chain fat. So, it facilitates the absorption, bypassing the liver, as a rectal suppository. But I think that about a hundred milligrams is the way to go with the pregnenolone mostly. And then you could do it rectally, but it's a hassle to create the suppository. And most people are absolutely not fond of doing a rectal suppository. So, you could take it, just swallow a 100-milligram pill, as long as you take it [with] a half a teaspoon, a teaspoon of butter? What's the dose?

Georgi Dinkov:

Half a teaspoon of butter is fine. Just mix them together so they make an emulsion. You don't have to dissolve it.

Dr. Joseph Mercola:

Oh, so you can't swallow it. You have to actually open the pill and mix it around in the butter?

Georgi Dinkov:

Now, you can swallow the pill, but of course it's going to have less effectiveness than if the powder is well-emulsified with the butter.

Dr. Joseph Mercola:

See the devil's in the details for sure. I've been incorrectly recommending that. I didn't realize it needs to be mixed in with butter. So, do that and you have a really good strategy. So, is the dose about 100 milligrams or do you recommend-

Georgi Dinkov:

Yeah, I think for most people, this seems to be a pretty good dosage. Some human trials just came out this year with two different doses, 300 milligrams and 500 milligrams, and both doses were shown to block cocaine cravings in addiction, and also block alcohol addiction and cravings. Really remarkable studies, with a 300-milligram dosage being more effective for some reason. So, 300 [mg] dose. So, if you don't want to take a hundred milligrams, you can try the 300 [mg] one. But 100 milligrams seems to be okay to restore your steroidogenic balance back to normal.

And pregnenolone is really unique in the sense that if you have an excess of a specific steroid, it will likely lower it. And if you have a deficiency of a specific steroid, it will probably raise it. Some of the earliest studies with pregnenolone were done by Dr. – What's his name? Hans Selye in Canada, who coined the term “general adaptation syndrome.” In other words, the non-specific disease of being sick, you're looking sick, you're acting sick.

Anyway, so he removed the adrenal glands of animals and did experiments with different steroids and found out that both pregnenolone and progesterone can partially fill in for cortisol. Well, of course, they're precursors. But also, in the opposite direction, if the rats are keeping their adrenal glands but they're being stressed – in other words, their cortisol is high – pregnenolone and progesterone lower the excess cortisol back to normal. So, they're really great modulators, is what I like to call them.

And then pregnenolone, about a hundred milligrams is probably enough because it's going to convert downstream – being the top-level hormone – it’s going to convert downstream into whatever you need. I don't know of many studies with 100 milligrams. I know some that showed 30 milligrams blocked the sedating effects of benzodiazepines and alcohol. And then I know of a study with schizophrenia where 50 milligrams decreased significantly both the symptoms of schizophrenia and bipolar disorder. And then the dosages further beyond that that I've seen are 300 and 500 milligrams. But I don't see – I think 100 milligrams sound about right, if you look at how many steroids you're synthesizing downstream of each type, and you add all these up, and it gets to about 100 milligrams of a precursor such as pregnenolone.

Dr. Joseph Mercola:

Okay. So, we know that progesterone converts to allopregnanolone.

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

Does pregnenolone convert to allopregnanolone?

Georgi Dinkov:

Yes, by first converting to progesterone.

Dr. Joseph Mercola:

Okay. All right, well that's clever. So, let's transition to serotonin. And we can use what we've already talked about to do that transition, which is GABA. So, serotonin is not the happy hormone. It's actually making huge problems. It used to be called enteramine. It was produced in the gut. Adapine was [inaudible 00:50:45]. I never knew that. So, it was called enteramine before serotonin. And it has lots of problems, and I'm going to let you elaborate on that.

But clearly, one of the ways, the most powerful ways to treat depression and insomnia – because so many people are not just taking antidepressants, they're on hypnotics, which are sleeping pills, and they may be on benzos like Xanax, or Restoril, [or] Ambien. So, these are toxic, toxic drugs over the long term. And actually, they help you go to sleep, but your sleep is radically impaired. So, the solution for these, the antidepressants and the sleeping pills and the antianxiety agents, would be GABA, simple GABA, and as you wonderfully elucidated earlier, is progesterone, because progesterone is a GABA agonist. So, you can take progesterone with GABA and get a great result.

So, I believe you told me directly, or it was on one of your posts that it was previously thought that GABA, which is an amino acid, was not thought to cross the blood-brain barrier. But I think you uncovered studies that show that it does. So, if you can confirm that and what dosing do you recommend? I mean usually it comes as 500 milligrams. And especially elaborate on the dosing with respect to those who are in the process of weaning off of their dangerous medications.

Georgi Dinkov:

The proof – I mean, probably the officially proven – though there've been isolated studies that oral GABA is bioavailable, medicine claims it's not. And I think you could immediately realize why. If oral GABA is bioavailable, then overnight the entire industry of, at the very least, antianxiety medication goes away. They're all GABA agonists. So clearly this is a big threat. Anyways, the study that actually – Not the study, but the final confirmation that oral GABA is bioavailable is the company that I mentioned just half an hour ago that's now selling the alcohol replacement. So, the main effects of alcohol that most people like [is] because alcohol is a GABA agonist.

Dr. Joseph Mercola:

GABA agonist, right.

Georgi Dinkov:

So, the disinhibition, the calming, the chattiness, the improved mood — all of these stem mostly from its effect as a GABA agonist. And there's another one, NMDA antagonist, which is N-methyl-D-aspartate, another receptor, which is that receptor [that] is excitotoxic. So, anything that inhibits it calms you down. Magnesium is perhaps the strongest natural NMDA antagonist followed by ethanol.

So, this company looked and said, "Okay, we don't have to take alcohol because it has a lot of other bad effects. Can we do the exact same effects with something else?" And they said, "GABA. Let's just –" They don't disclose what the dosage is, but now that I know there are human studies with it, even 100 milligrams of oral GABA were enough to lower the assessments of patients with anxiety and depression disorders, to lower their score on whatever assessment worksheet is being used – I think it's called the Beck's depression scale. It's for depression, and there's another one for anxiety. Just 100 milligrams of GABA were sufficient to lower significantly in the score on both scales. And combining with another GABA agonist amino acid known as L-theanine, which is found in tea, actually drastically increased the effects. So, they synergize.

Dr. Joseph Mercola:

Is theanine a GABA agonist? Is that what you've said?

Georgi Dinkov:

It is an agonist, yes. And theanine lowers the levels of serotonin in the brain.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

Perhaps the most direct evidence that serotonin in the brain is not good in elevated levels.

Dr. Joseph Mercola:

Geez. So, what is the range on the doses? I mean, you said [it] worked at a hundred milligrams. And I'm specifically concerned about people who are taking massive amounts of antidepressants, SSRIs specifically, antianxiety agents and sleeping pills, which is a tough – My girlfriend's sister was on this, and I basically weaned her off of everything except still some of the sleeping pills. So, what's your strategy or recommendation in this?

Georgi Dinkov:

So, for people that are on antidepressants, one of the first things that I would do is go to a doctor and ask about two drugs that are approved for treating depression but are non-serotonergic. In fact, here's the proof that serotonin is probably not good for you. Both of these drugs are anti-serotonergic. One of the drugs is called mianserin, also known as mirtazapine. And if you look at the structure, it's very structurally similar to a drug called cyproheptadine, which is a known selective serotonin antagonist. Mianserin or mirtazapine is approved for treating patients in the United States. [If] you want to get your psychiatrist angry, please ask him or her to explain how come an anti-serotonin drug is approved for depression, considering that all the other pro-serotonin drugs are also approved for depression. Something doesn't add up there. Another drug is called tianeptine. And it works-

Dr. Joseph Mercola:

Well, before we go there, let's just finish off on cyproheptadine because it's wonderful as a serotonin antagonist, but it does have some side effects. It's basically a sleeping pill too. It'll put you to sleep. And maybe you don't even – I think it comes as low as 2.5 milligrams, but if you don't have problems sleeping, you don't want to take a 2.5 [mg], you cut it in half or even a quarter. And I think it's somewhat like – I tried it once. I think everyone should have some cyproheptadine because it's such a potent histamine blocker so that if you get a bee sting or something where you have a severe allergic reaction, it's probably a pretty good drug to take for a short term. But it does definitely impair your sleep and you wake up kind of feeling drugged when you're taking cyproheptadine.

Georgi Dinkov:

Yep. So, I was just comparing, because cyproheptadine, it’s agreed that it's a serotonin antagonist. Mianserin is a very close structural analog. And even though medicine tries to dance around the mechanism of action of mianserin, it's very hard to deny. And in fact, even the Wikipedia page says that mianserin is also a known specific serotonin antagonist, but they claim its antidepressant effect comes from something called SNRE, selective norepinephrine reuptake inhibitor. So, it decreases the uptake [of] norepinephrine, and that's its antidepressant effect. I think it's the fact that it's actually a very good serotonin blocker that is the effect.

And there's another drug called tianeptine, which actually works in a manner 180 degrees to the SSRIs. Tianeptine is a drug known as SSRE. It's a selective serotonin reuptake enhancer, [a] potent antidepressant. So, just the existence of tianeptine and its mechanism of action, and then the existence of the SSRI drugs and the claims that are associated with them, something here does not add up in regards to serotonin. You can't have two drugs that work in exactly [the] opposite way, both working for depression, unless there are other mechanisms of action at play. And for tianeptine there is no other mechanism of action. So, it's basically an anti-serotonergic drug.

So anyways, if somebody is on antidepressants and if they are SSRI antidepressants, my advice is to go to your doctor. First one is [to] get on something that's non-serotonergic. There are pharmacological options available if you prefer to go that route. However, you don't really have

to go that route. And taking [a] higher dose of GABA on the range of 500 milligram to 2 grams daily has been shown to relieve the anxiety and the insomnia of people who are already taking SSRI drugs.

Ironically, elevated serotonin is actually probably the cause of insomnia, even though doctors try to blame it on depression. Every single anti-serotonin drug ever tested – and most of them are not approved for human use, but I can send you at least 20 of them – every single one of them, no matter how selective serotonin antagonist [inaudible 00:58:17] serotonin antagonist is, has demonstrated both antidepressant and prosomnic, basically anti-insomnic effects in animal studies and some human studies as well. So, serotonin is known to actually cause insomnia. And people will be thinking, "Well, how? If serotonin is a precursor to melatonin, how can it actually cause problems with the sleep?" Serotonin is the most potent activator in the body of the release of cortisol.

Dr. Joseph Mercola:

Wow, I didn't realize that.

Georgi Dinkov:

Through ACTH (adrenocorticotropic hormone). And in fact, the first antidepressant drug, Prozac, which is a classic SSRI drug, there are publications about it, that the way Prozac works is because Prozac is a partial serotonin antagonist and it blocks specifically the serotonin receptor responsible for the release of cortisol. And that is the serotonin receptor 2C, C as in Charlie, 5-HT2C. Prozac is a potent inhibitor of that receptor while maintaining the rest of its serotonergic effects. So, really, it's the perfect coverup, right? You can claim that serotonin is great for your depression, while in reality you're giving a drug, actually, it's blocking the effects of serotonin and lowering cortisol, but it's unknown to most people, even doctors that I've discussed it with.

So, if you take higher doses of GABA, another side effect of GABA is that GABA increases the degradation rate of serotonin even when it's taken orally. So, you cannot have high of both. So, people that are high in GABA, they're usually low in serotonin. They're very calm, they're very gregarious. And people who are high on serotonin, it's not a happiness hormone. Multiple studies, in fact, even a court case recently agreed that serotonin actually destroys empathy, love and wisdom. Those are specific quotes from the court study. And another animal study found that crabs exposed to very low levels of SSRIs because of the sewage that's being dumped into the ocean – So they're getting exposed to amounts a thousand times lower than we are when taking these drugs. The crabs turn extremely violent, homicidal and cannibalistic. They turn on each other. There's nothing else that can explain this behavior except for the SSRI drugs.

So really that's what serotonin does. It's a metabolic inhibitor. And [in] the recent study that came out of Oxford that said, "The serotonin hypothesis of depression is dead, we need to move away from it," one of the lines there was that we've been looking at serotonin the wrong way. The primary role of serotonin is metabolic. It's a metabolic inhibitor. And the reason – the evolutionary role of serotonin is probably for numbing pain when you're under stress. So, it turns off your pain reaction, even your grief reaction, but at the expense of also turning off all the other emotions as well. Multiple studies demonstrated that serotonin is basically a lobotomizing

chemical when it comes to emotions. Sure, it'll numb your depression, but it will also numb everything else too. You'll be walking around like a zombie.

Dr. Joseph Mercola:

So serotonin, as I mentioned earlier, is primarily produced in the gut. I think 95% of it. And it was initially called enteramine because that's where they found it. So, I believe there's some similarity between serotonin and endotoxin, and that it increases inflammation. And obviously, I didn't realize that it was a cortisol agonist, which is really not a good thing. So why don't you talk about some of the other downsides with serotonin and why you don't ever, ever, ever want to consider a drug that's designed to increase your serotonin levels.

Georgi Dinkov:

So, one of the earlier studies with serotonin was done on people with so-called carcinoid syndrome. It's a very specific type of tumor that's developed in the enteric nervous system. And then these people are known to have – very often, they have face flushing, they have chronic, very severe diarrhea, and both of these things are known to be caused by serotonin.

But then they started looking at other conditions associated with things like – And by the way, these people with the carcinoid syndrome, they don't die from the tumor, they die from disseminated and massive fibrosis. So, for a long time, people didn't know what exactly is causing this fibrosis, but then they narrowed it down to serotonin, specifically serotonin acting through something called the serotonin receptor, 5-HT2B, 2B, B as in boy. And once they realized that this receptor, which serotonin activates of course, is causing the fibrosis, some antifibrotic drugs started to be developed. And one of the more potent ones currently in clinical trials is an ergo derivative known as terguride. And terguride is a very potent 5-HT2B blocker. Conversely, some of the older drugs that were used for-

Dr. Joseph Mercola:

And that drug is still in clinical trials. It's not available yet?

Georgi Dinkov:

By Pfizer. Yeah, Pfizer bought the rights and removed it from the market, and is running clinical trials for cardiac fibrosis and for pulmonary fibrosis, both of which are invariably lethal and considered incurable. So, it's an admission that serotonin causes both of these conditions at the very least.

Dr. Joseph Mercola:

That is just beyond extraordinary because cardiac fibrosis is a real common contributor to heart failure, which is pervasive in the United States population. So, any strategy that's going to reduce the primary precipitant of fibrosis like serotonin would be good to do. So even putting on an antidepressant, it's going to accelerate your – The antidepressant that increases serotonin will

accelerate that process. And pulmonary fibrosis is just as bad, if not worse, and typically terminal.

Georgi Dinkov:

Yeah, cystic fibrosis, too. Recently, they discovered it's also driven by serotonin. Anytime you hear the word fibrosis-

Dr. Joseph Mercola:

Could you put – Obviously cystic fibrosis is a genetic disease. It's a bad luck of the draw. Could you put someone on a strong anti-serotonin, GABA agonist and progesterone? And that would – It seems like it would be a good strategy to keep them healthier longer.

Georgi Dinkov:

In fact, the combination of GABA and progesterone would probably be enough because progesterone is also a TPH (tryptophan 5-hydroxylase) inhibitor. It inhibits the enzyme that synthesizes serotonin, which probably explains, together with progesterone's GABA effects, why progesterone has antidepressant effects when it was being tried in both animals and humans. So just progesterone at a higher dose is both anti-serotonergic and pro-GABA, and both mechanisms – by the way, the being pro-GABA is not only calming you down, but also increases the degradation of serotonin. So, progesterone both inhibits the synthesis of serotonin and increases its degradation. And similar effects are seen in some of the androgenic steroids such as testosterone and especially dihydrotestosterone, which cannot aromatize, so it's probably safer.

Dr. Joseph Mercola:

Wow, this is huge. It's interesting. We're talking about two radically different subjects, serotonin and estrogen, but there's so many similarities between the two.

Georgi Dinkov:

Serotonin activates aromatase and estrogen activates tryptophan hydroxylase. So, they’re really like each other. One cannot go without the other.

Dr. Joseph Mercola:

Yeah, they're bad news bearers, both of them. And you really want to minimize both, keep your serotonin levels as low as possible, along [with] your estrogen levels. And the solution is, interestingly, there are many commonalities in that progesterone, pregnenolone and GABA itself would be good strategies for both of those.

Georgi Dinkov:

So probably the easiest thing will be to find oral GABA and make sure it's a clean supplement. And I don't see any downsides to taking even very high doses. Just make sure you're taking it with food.

Dr. Joseph Mercola:

What do you qualify as a high dose? 2 grams?

Georgi Dinkov:

Or more. It's an amino acid. And by the way, if you take too much of it, some of it will get deaminated and get converted to something called succinic acid, which is the-

Dr. Joseph Mercola:

That's a supplement actually, is it?

Georgi Dinkov:

Yeah. Yeah. It's the intermediate of the Krebs cycle.

Dr. Joseph Mercola:

So, it's a health supplement for [the] mitochondria?

Georgi Dinkov:

That's probably one way to reach GABA, boost mitochondrial function.

Dr. Joseph Mercola:

Oh geez, I didn't know that was a succinic acid precursor. Wow. That's great. So, what do you think is the highest dose you can go on? 3 grams, 4 grams, 5 grams?

Georgi Dinkov:

Until we release symptoms, but I've seen people in very severe cases of anxiety and depression plateau at about 3 to 4 grams. After that, basically it starts getting deaminated. And you may have some pro-metabolic effects, but the mental effects usually plateau at about 3 to 4 [grams].

Dr. Joseph Mercola:

Okay. And many people are only going to need a half a gram or 1 gram, right?

Georgi Dinkov:

Or even 100 milligrams, which was that study with people with people with chronic anxiety and depression. They were diagnosed with official conditions.

Dr. Joseph Mercola:

And the beautiful thing about this – and I would just not take a GABA supplement by itself, I would definitely take it with theanine, and many of them also have magnesium, which is really good, unless you go too high, then of course, you're going to get loose stools. But the good thing about these is they're relatively inexpensive. This is not going to seriously impair your budget at all in any way, shape or form. And they're really easy to find. They're all over the place.

Georgi Dinkov:

Yep. Yep. I can count at least 20 vendors selling theanine on Amazon, probably more than 50 selling GABA. All of these things – magnesium, countless, right? There's probably not a single vitamin vendor that doesn't sell magnesium somehow.

Dr. Joseph Mercola:

Yeah, but it'd be [inaudible 01:07:12] just to take one supplement. It combines all of them.

Georgi Dinkov:

I would do one after the other. Take one on the first day by itself, see how it affects you.

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Yeah. Maybe play with the dosage a little bit. Find out which one of the supplements works best and what dose, and then when you start combining them, try to lower the dose of each one and then arrive – Because they should synergize. So, let's say just as an example, if 500 milligrams of GABA by itself is enough to lower your anxiety, 500 milligrams of magnesium by itself is enough to lower your anxiety and improve sleep, and let's say 200 milligrams of theanine is enough to cause both of these, then maybe 100 milligrams of each combined should be enough. My personal experiment is like that. I actually tried all three, and 100 milligrams of each in combination is a very good pressure relief valve for me, and also improves sleep.

Dr. Joseph Mercola:

Yeah. So, there are two subsets of people that will be trying this, healthy people like you, or really sick people who will have submitted to the pharmacological paradigm and are taking these drugs. So, in my view, there's really limited time to have them play with it, especially when your goal is to increase compliance. So, you'd want to hit them with the kitchen sink initially so they get relief, and then work down. So, I think what you're doing is perfect if you're a biohacker and you're healthy. Do it singly and increase. But if you're already taking medications for these conditions, then I think you might just want to shotgun it and then go down from there.

Georgi Dinkov:

I agree. Yeah. Take as high [a] dose as it relieves your symptoms. And the main thing to remember is if you're on an SSRI drug, your GABA is, by definition, low. Serotonin inhibits the synthesis of GABA.

Dr. Joseph Mercola:

A GABA antagonist?

Georgi Dinkov:

Yes. And also inhibits its synthesis. You'll be very low on GABA in general, not to mention the serotonin can block the GABA receptor. Really nefarious substance when it comes to GABA.

Dr. Joseph Mercola:

Man, it's worse than I thought. Maybe review the impacts of serotonin and estrogen on being antimetabolic, and the connection between those two items and the thyroid gland.

Georgi Dinkov:

Well, serotonin is derived from tryptophan, and tryptophan is the only amino acid that is known to be directly carcinogenic. Probably why it's found in the lowest amounts of any amino acid, no matter where you look in nature in terms of food or any kind of protein composition. Tryptophan-

Dr. Joseph Mercola:

It's an essential amino acid, but it's one that you should not take as a supplement.

Georgi Dinkov:

Yes. It caused actual deaths, if you remember, in the early ‘90s.

Dr. Joseph Mercola:

Oh, yeah, yeah.

Georgi Dinkov:

There was this thing called the-

Dr. Joseph Mercola:

I think it was [the] late ‘80s.

Georgi Dinkov:

Late ‘80s. Eosinophilic myalgia syndrome, and they blamed it on impurities. But if you look at the symptoms of those people, they all died from serotonin syndrome, classic signs of serotonin syndrome. Yeah, needless to say, if you have high serotonin, it can kill you directly. In fact, medicine has a special term for it. It's called serotonin syndrome. Recently they discovered that the so-called post-surgery delirium, which many patients experienced, or post-anesthesia delirium, it's a mild form of serotonin syndrome, and cyproheptadine completely stops it.

So, serotonin and tryptophan are actually thyroid inhibitors. Multiple studies have demonstrated injecting tryptophan or serotonin into the blood raises the levels of TSH (thyroid-stimulating hormone), which is a sign that thyroid gland function has been inhibited or something is going on – maybe increased degradation of thyroid hormone? Because the body perceives the presence of these two amines as an antithyroid signal, so it amps up its own production of thyroid. [Other] things that serotonin also does, it blocks the activity of the enzyme pyruvate dehydrogenase. So, you're going to get into basically excessive glycolysis and high levels of lactic acid situation. Another situation where you're shifting towards the redox state, towards reduction – serotonin itself is a reductant.

Dr. Joseph Mercola:

Oh, I didn't know that.

Georgi Dinkov:

Yeah, just like estrogen. So is cortisol.

Dr. Joseph Mercola:

They're both reductives. And cortisol, geez.

Georgi Dinkov:

Yeah, so all of these steroids and amines and neurotransmitters are basically antimetabolic, simply by interfering with the proper flow of electrons from food to oxygen. So, estrogen also is known to inhibit the work of pyruvate dehydrogenase, [and] also [an] inhibitor directly of cytochrome c oxidase. And I think it's an inhibitor of also complex II of the electron transport chain, which is now also known as succinic acid dehydrogenase, which also participates in the Krebs cycle. So, estrogen can inhibit all of these.

And again, it makes it sound like these are very toxic and bad things, but they're there for a reason. And the revolutionary reason is probably that in times of stress and trouble and injury and whatnot, these things rise in order to help you repair. But it should be acute only. And unfortunately, these days we have them chronically elevated, and that's a signal to the body that things are chronically bad, and it will dispose of any known essential function that it thinks it can do in order to conserve energy, which means your high metabolism, which means you're gaining weight. Means your good mood, which means you're going to be depressed. Then eventually, if things go down that route, the body will start turning off non-essential organs, if it thinks that there are some, by turning them into fibrotic clumps of meat, and so that they don't have to waste

energy on repairing them, and that's how you get fibrosis. And ultimately the end stage of fibrosis is invariably cancer, unless you die from organ failure before that.

Dr. Joseph Mercola:

Yeah. So again, further proof that serotonin and estrogen are precursors of cancer. So, you had mentioned earlier that serotonin is the precursor for melatonin, so we need some of that. So how do you reconcile that? My guess is it's just because it's a relatively small level of serotonin you need to make adequate melatonin and you don't need anything excess, that there's always a basal level that will produce an optimal amount of melatonin, and anything extra is going to be detrimental. What's your take on it?

Georgi Dinkov:

Healthy people have been demonstrated to have high levels of melatonin, and medicine has used that as an excuse to start advocating for supplementation with melatonin. But what we need to keep in mind is that if you take melatonin, it has basically a reverse feedback, [a] negative feedback effect.

Dr. Joseph Mercola:

Oh, I didn't-

Georgi Dinkov:

It's going to raise your serotonin, and it's [a] very well-known side effect.

Dr. Joseph Mercola:

Oh, it will?

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

I talked to [Dr.] Russel Reiter, who's probably the world's foremost researcher on melatonin. He never mentioned that at all. I did not realize that, but it makes perfect sense.

Georgi Dinkov:

[A] very easy way to prove it [is to] take a hefty dosage of melatonin, which means 3 milligrams or more, and just watch what kind of bizarre nightmares you're going to have at night. And the nightmare driver is serotonin, and that's being recognized by psychiatry because now it's doing clinical trials with cyproheptadine to cure a very, very pernicious sign of PTSD, which is chronic recurring nightmares, and another sign that probably PTSD is driven by serotonin as well.

Dr. Joseph Mercola:

Wow, that's pretty crazy. So, any other insights to share with serotonin and estrogen that you'd like to conclude with?

Georgi Dinkov:

So basically, since you mentioned endotoxin, and most of serotonin is produced in the gut, keeping the bowel clean, keeping bowel transit rapid and frequent without getting to [a] diarrhea case, obviously, because then you're interfering with absorption of the nutrients. Why? Because anytime you overproduce endotoxin, it acts on something called the enterochromaffin cells, which are lining the intestine, and those cells are the main factories for producing serotonin. So, endotoxin, by activating a receptor and just mechanically irritating those cells, it's a signal for these cells to start producing serotonin. Things that mechanically injure the intestine, or stresses, such as stretching, bouncing around, are also probably not beneficial. And in fact, there's this thing called runner's diarrhea, and it's a mystery of why it occurs. But now that we know that serotonin causes diarrhea, and running for extended periods of time, all this bouncing and stretching and twisting of the intestine causes mechanical irritation, and these cells start to overproduce serotonin. So, [it's] clearly not a good situation. Long-distance runners are also known to have higher levels of peritoneal and pulmonary fibrosis, both of which are known to be caused by serotonin.

Dr. Joseph Mercola:

I did not know that. So glad I stopped running about 20 years ago.

Georgi Dinkov:

You can run, but don't get it to the point where people are killing themselves. So, I think the good thing is to keep it – I call it, glycogen bound. Once you deplete the glycogen and you start getting to fatty acid synthesis, then the problems start.

Dr. Joseph Mercola:

Yeah. And actually, that's the strategy for many seriously competitive long-distance endurance athletes, is that they focus on that. Their specific training is to increase their ability to utilize fat and increase beta-oxidation as their primary fuel source. And I just interviewed Tim Noakes from South Africa who actually wrote books on this thing. He's a big low-carb proponent. And I shared with him some of the stuff and he just reverted back to Richard Veith, who interestingly – I'm sure you're familiar with Veith, who passed away a few years ago, but he was not a fan of high-fat diets. I did not realize that. He was okay with ketones. And interestingly, I was watching a podcast discussing this, but it seems like ketones by themselves are actually pretty good fuel, unless your body is making them. And if your body is making ketones, then you have activated the stress pathways.

Georgi Dinkov:

Exactly.

Dr. Joseph Mercola:

You don't want to do that, but you can take exogenous ketones to help. And do you think there would be any benefit to taking them at night?

Georgi Dinkov:

First of all, ketones, which is – we talked about GABA, as you well know, there's this infamous ketogenic diet for intractable epilepsy, which is how I think initially ketogenic diet started becoming popular in the mainstream. They started using this as an excuse to do the ketogenic diet. Ketones, especially when produced from saturated fatty acids, are GABA agonists. And some of the most effective drugs for epilepsy, such as valproic acid, are also GABA agonists. So yes, that's how – The ketones are good for you, especially for the brain, but the brain cannot go for an extended period of time on ketones only. It prefers sugar. And that's why even the ketogenic diet for epilepsy, it's done in a metabolic ward, they constantly monitor them. Usually children are being put on this diet. And after about three months, basically until the child starts responding to the medications, then they stop the ketogenic diet.

I've talked to several doctors who are administering these diets in the metabolic wards. None of them is recommending going on this indefinitely. It's all until you restore your metabolic state, in other words, or your sensitivity to medication, and then they wean you off of the diet. So, taking ketones actually is very beneficial because they also shift the redox balance – I know we've been repeating all this so many times – back to oxidation. One of the most beneficial of them you can take is something called acetoacetate. And basically-

Dr. Joseph Mercola:

Isn't that a ketone?

Georgi Dinkov:

That's a ketone. Exactly. And another one, which is not so good for you is known as beta-hydroxybutyrate. In fact, it's not a ketone. It's the reduced form of acetoacetate.

Dr. Joseph Mercola:

I did not know that. Are you serious?

Georgi Dinkov:

I'm very serious. And the ratio of acetoacetate to beta-hydroxybutyrate is the same ratio as pyruvate to lactate as GSSG (glutathione disulfide) to GSH (reduced glutathione), cortisone to cortisol-

Dr. Joseph Mercola:

NAD (nicotinamide adenine dinucleotide), NADH (reduced nicotinamide adenine dinucleotide).

Georgi Dinkov:

NAD to NADH, yes. So, if you take acetoacetate, it's as if you take an NAD+ or niacinamide to shift the redox ratio towards oxidation.

Dr. Joseph Mercola:

Wow. I'm glad I pivoted to that. But most people who have been studying Peat's work and knew it would be the classic illustration of that, understand and would not dispute that pretty much every healthy human being, once they've able to resolve metabolic inflexibility, needs about 150 grams of carbohydrate a day, at a minimum. If you get a lot of activity like I do, I frequently go up to 500 grams a day. So, anyone who's taking that, an appropriate amount of carbohydrates, is getting enough carbs. So that's not an issue. I'm wondering if you believe there is an additional benefit of taking a ketone like acetoacetate, and if so, would the best time be before bed?

Georgi Dinkov:

Well, because they're GABA agonists. And I have taken acetoacetate, it does make you sleepy. Probably depending on the dosage, it's probably reasonable to take them before bed or at least try them before bed and then see how they affect you. And if you're not groggy the next morning, maybe you can try taking some during the day. But like anything, that shifts the redox balance towards oxidation, it helps you metabolize the carbs. So, by taking the ketones, you're going to be able to get by on less carbs, so you don't have to eat as many carbs. And in fact, you're going to be metabolizing them better so you'll produce more carbon dioxide. In other words, your caloric intake requirements, at least for carbs, actually decrease. Maybe a reason why some people have noticed that if they're taking ketones, they can actually lose some weight without changing their dietary regimens or exercise regimens much. So yes, I think there is a benefit to taking ketones. But to me, it's not very different than taking methylene blue or GABA agonists or niacinamide, anything that makes you utilize oxygen more properly.

Dr. Joseph Mercola:

Okay. Or the new alcohol-free drinks that they have [inaudible 01:20:51].

Georgi Dinkov:

That's fun. It sounds fun. You know what? I'll buy a bottle and maybe if we meet each other in person, we'll share it.

Dr. Joseph Mercola:

There we go. Right before bed. So, you had mentioned carbon dioxide, and for those who don't know, I'm just going to review it, one of the benefits of oxidizing glucose in the mitochondria is it gives you two huge byproducts. Well, three things are going – you're contributing to forward electron flow, which is minimizing reductive stress, but also minimizing reductive stress means

that you have 30 to 40 times less production of ROS (reactive oxygen species). But the cool thing is that you're making two metabolic byproducts. One is metabolic water or deuterium-depleted water, and the other is carbon dioxide. So, there's a lot of confusion. I don't think we went over [this] in the past, maybe we did, but nitric oxide and carbon dioxide. Now, nitric oxide is considered a vasodilator, and there are many, many products and therapies designed around increasing nitric oxide, but that seems to be a fool's errand and maybe highly, highly counterproductive when the ideal strategy you want to do is increase carbon dioxide because it's a far more effective and safer vasodilator.

Georgi Dinkov:

It's the main endogenous beneficial [inaudible 01:22:12] – it's the default vasodilator, which prevents – First of all, it allows the blood vessels to dilate, but also what carbon dioxide does is in the process of getting released from the cell through simple diffusion, because it's a Lewis acid, it draws excess calcium with itself outside of the cell. So, it decalcifies your soft tissues. And the Soviets had an extensive research done with it in the '60s and '70s, they had these resorts where you can go and you can bathe in these bathtubs filled with carbon dioxide as a way to reverse or at least retard the development of cardiovascular disease, or the very least hypertension.

So, carbon dioxide is your main and preferred vascular dilator. If you don't have it for whatever reason, which means your metabolism is not working well, the emergency one that immediately activates – the deficiency of carbon dioxide is a signal for the activation of something called inducible nitric oxide synthase, iNOS, and it starts producing nitric oxide as the emergency vasodilator. This is what happens actually if you do long distance running to the point where you stop producing sufficient amounts of carbon dioxide because of anaerobic glycolysis. In other words, you're running so much, just the energy production process cannot catch up, then carbon dioxide levels decline, and then basically you get vasodilation because of nitric oxide, and that contributes to the flushing and the redness of your skin and your face when you're running for too long.

Histamine is also a factor, but carbon dioxide basically increases the synthesis of histamine for histidine, so they really go together. So, nitric oxide is what's really driving a lot of that flushing and redness that you're getting when you are overexerting yourself. So nitric oxide, even though it is a vasodilator, as I mentioned earlier, a very nefarious effect of it is that it can form a covalent bond with cytochrome c oxidase.

So, you can get permanently metabolically inhibited in specific cells. Well, [it] doesn't mean you die, even though it can kill you. In fact, it's now being proposed to replace basically the euthanasia drugs and the death penalty drugs in the United States and several European countries, because you breathe it in and you basically drop dead without even realizing it, and it's considered more humane. So, in high amounts, nitric oxide is not that different from carbon monoxide in the fact that it can bind irreversibly with the respiratory enzymes. And that's the process to which it kills in the high doses.

Dr. Joseph Mercola:

Well, is it truly irreversible? And you're talking about complex IV, right?

Georgi Dinkov:

Yeah.

Dr. Joseph Mercola:

But I thought it could be dissociated, even though it's a covalent bond-

Georgi Dinkov:

Okay, I shouldn't say irreversible-

Dr. Joseph Mercola:

[crosstalk 01:24:52] red light and methylene blue.

Georgi Dinkov:

And so does carbon monoxide. For a long time, it was thought it's irreversibly binding, but methylene blue can do it. In fact, methylene blue is used as antidote to carbon monoxide poisoning.

Dr. Joseph Mercola:

Yeah, so that's why I think everyone should have some methylene blue at home just in case you get an accidental exposure to carbon monoxide. Or cyanide poisoning, in case your spouse decides to take you out prematurely.

Georgi Dinkov:

So, nitric oxide, in addition to being a metabolic inhibitor, it's also toxic to living tissue and living organisms. Its second main function, other than an emergency vasodilator, is killing foreign pathogens. One of the first things that happens when you get a viral or bacterial or even fungal infection is that your white blood cells, a subset of them, start producing and releasing massive amounts of nitric oxide as a way to kill off these pathogens, which is the reason why, when you get endotoxin into the bloodstream, you are also getting a hefty dosage of nitric oxide released because this portion, the endotoxin fragment in your bloodstream, is interpreted by the immune system the same way as if you had a bacterial infection, because it is a portion of the bacteria wall.

So, nitric oxide is actually toxic, and the best example is that it's being used to kill invading cells that are not your cells. A recent study, I don't know if you saw on my blog just a few days ago, demonstrated nitric oxide is so toxic to the brain that just giving precursors to nitric oxide can reproduce all of the signs of autism and giving things that-

Dr. Joseph Mercola:

Oh, yes, that was great. I'm speaking at an autism event next month, I sent it to the organizer.

Georgi Dinkov:

Yeah. And inhibiting the symptoms of nitric oxide or blocking its effects can actually reverse all of the signs that they were able to notice for autism. Methylene blue can directly scavenge nitric oxide, which is great, and can also inhibit its synthesis through inhibition of iNOS. Niacinamide, [a] very good iNOS inhibitor. Magnesium, [a] very good iNOS inhibitor. Progesterone and GABA, both of them very good iNOS inhibitors.

Dr. Joseph Mercola:

Now, there are three enzymes that make nitric oxide. iNOS is the one you've been referring to, but there's also two others, nNOS, which is neuronal nitric oxide.

Georgi Dinkov:

And the endothelial, yeah.

Dr. Joseph Mercola:

And then eNOS. So, there's got to be a role, an appropriate physiological role, where some low level of nitric oxide performs a beneficial physiological function.

Georgi Dinkov:

Yeah, the eNOS and the nNOS, they do synthesize it, but it's usually, basically, like I said, in response to perceived deficiency of carbon dioxide. Now, even those can actually get – But they're very tightly controlled. The majority of the pathological levels of nitric oxide can only come from iNOS. That's why I think there are drugs even that have been tried to inhibit specifically eNOS and nNOS, and they didn't notice the same benefit as the things that specifically inhibited iNOS.

Dr. Joseph Mercola:

Okay, iNOS is the bad one. You do not want to activate that puppy at all. Oh my gosh. Now I just have to digest this and resynthesize my health program. But this is fantastic. It is really extraordinary. You provided such important fundamental, foundational strategies to treat some very, very common pervasive challenges that most people watching this are going through, or their friends or family are. So, I can't thank you enough for guiding us through this and confirming some really solid information that I think will help a lot of people. You are incredible.

Georgi Dinkov:

Thank you. One last piece of evidence against nitric oxide. There is a molecule that's used clinically to inhibit the synthesis of nitric oxide. It's known as L-NAME.

Dr. Joseph Mercola:

Like L?

Georgi Dinkov:

L-NAME. L dash NAME, because it's the L-isomer. So, N as in Nancy, A, M as in Mary, E. L-Nitroarginine Methyl Ester. And basically, because it's structurally similar to arginine, it fills into that enzyme that synthesizes nitric oxide and results in lower levels of nitric oxide. It's currently in clinical trials, I think in several European countries, for treating cancer, even very advanced cases of cancer. Yet another direct example that nitric oxide contributes to that and probably through its role as a metabolic inhibitor.

Dr. Joseph Mercola:

Well, I deeply, deeply appreciate you carving time on your schedule to help us review these really important topics, and people want to find more. You were in Bulgaria for a month, I think, at least. And when you're traveling, you tend not to post on your blog, although you're still reading the articles, but your posting goes down. So, there wasn't a bunch of posts for a month, but I think you got to be out of your mind if you really enjoy health and you want the latest to not subscribe to your blog. It's really easy. It's haidut.me, H-A-I-D-U-T.M-E, and you'll get the latest in there. And then you say, I think your Twitter account is the same combo, right?

Georgi Dinkov:

Yeah. Just the blog feeds directly into Twitter, and I use Twitter for discussions occasionally with people. I had a few classes with doctors recently about nitric oxide. I don't know if you saw that.

Dr. Joseph Mercola:

No, I didn't. I don't go on Twitter at all, for the most part.

Georgi Dinkov:

And you're right to do that. It can be a very toxic environment.

Dr. Joseph Mercola:

Yeah, yeah, yeah. I choose consciously not to do that. I love RSS feeds. I think that's one of the best IT innovations, and it's really surprising and was shocking that it was never widely adopted. It's such a powerful IT tool, and people who are in IT, they understand it. But Google had really one of the best RSS feeders, but they got rid of it. Probably [for] some other nefarious reasons.

Georgi Dinkov:

Well, all the good things disappear. It's called the crapification of the economy. There's an article in The Economist about that.

Dr. Joseph Mercola:

Yeah. So anyway, it's been great. All right. Well, thank you, Georgi.

Georgi Dinkov:

Well, thanks very much for inviting me. Looking forward to more discussions.