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What You Need to Know About Estrogen and Serotonin

Analysis by Dr. Joseph Mercola | October 22, 2023

STORY AT-A-GLANCE

- Estrogen is an obesity promoter and well-established human carcinogen
- The Women's Health Initiative studies, which began in 1991, showed estrogen replacement therapy in menopausal women significantly increased the risk of heart attacks, strokes, dementia, Parkinson's disease and cancer, not just in the breast but all female reproductive organs
- The biochemical role of estrogen is to aid in wound healing. In cases of tissue trauma, estrogen reverts the differentiated cells in that specific tissue back to a stem cell-like condition, to repair the damaged tissue. In young, healthy women, progesterone will turn off estrogen's activity. Progesterone declines with ages, but estrogen synthesis typically does not. Hence, if your estrogen is high and progesterone low, your cancer risk will rise
- Estrogen is antimetabolic and radically reduces the ability of your mitochondria to create cellular energy in a form of ATP
- Elevated serotonin destroys empathy, love and wisdom, and contributes to fibrosis, impaired thyroid function, reduced metabolism and reductive stress. High serotonin is also responsible for bizarre, recurring nightmares and may play a role in PTSD as well

In this interview, Bulgarian bioenergetic researcher Georgi Dinkov discusses the downsides of estrogen and serotonin, both of which are generally considered beneficial for physical and mental health.

The drug industry is making a mint on the idea that depression is caused by low serotonin, for example. However, a closer look reveals both estrogen and serotonin can cause severe problems and you do not want high levels of either of them.

Estrogen Is an Obesity Promoter and Known Human Carcinogen

The original name for estrogen was adipin, so called because it was known to make you fat, as in adipose (fat) tissue. In the mid-'50s, when the drug industry started pushing synthetic estrogens, this knowledge faded from memory. One of the most infamous early synthetic estrogens prescribed was diethylstilbestrol (DES), which caused fetal malformations and deaths, and cancers in the mothers who took it.

DES was eventually withdrawn and banned for use in humans. DES is not estrogen. It's an estrogenic chemical, and it does activate estrogen receptors, but potentially more potently than estrogen does, and it has no other mechanisms of action except through its estrogenic effects.

This gives us a strong signal that estrogen excess is of serious concern. That estrogen can cause cancer is well-established. In December 2002, the National Institutes of Health added steroidal estrogens used in estrogen replacement therapy and oral contraceptives to its list of KNOWN human carcinogens.[1]

> *"Even mainstream doctors will admit that there is this thing called estrogen receptor-positive breast cancer,"* Georgi says. *"The role of estrogen there is well known. Nobody's denying it, but the story has always been, it's a localized-only effect. It's a tissue-specific effect.*
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> *If you look at the estrogen levels of menopausal women ... it's undetectable. However, if you take a tissue biopsy from the tumor or the breast tissue around it, you'll see that estrogen levels are sky-high there.*
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> *Begrudgingly, medicine said, 'OK, 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 and all these menopausal women need more estrogen.'"

However, the Women's Health Initiative (WHI) studies, which began in 1991,[2] showed estrogen replacement therapy in menopausal women significantly increased the risk of heart attacks, strokes, dementia, Parkinson's disease and cancer, not just in the breast but all female reproductive organs. In the interview, Georgi also reviews evidence showing that estrogen can play a role in all types of cancer, not just reproductive ones.

Estrogen Therapy Has Seen a Revival, With Dire Consequences

The publication of the WHI results led to a significant decline in estrogen replacement therapy, starting in the late 1990s, early 2000s, until about 2015, when studies refuting those earlier results started coming out. Scientists argued estrogen could be safely used if dosed and timed better. Cancer rates don't bear that out though.

Some people and clinicians believe that bioidentical estrogen solves the problem but it does nothing of the sort. Bioidentical estrogen still has all the negative characteristics described in this article. It increases the risk of all cancers, not just breast and prostate, lowers your metabolic rate, and increases your risk of obesity, diabetes and osteoporosis.

"If you look at cancer rates, not just for breast cancer but for all of the female reproductive organs, you'll see there was a drop in deaths from these cancers 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," Georgi says.

"This coincides perfectly with the gap, which is about 15 years of not using estrogen on a mass scale, and then ... 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, and actually exceeds what it used to be."

Estrogen Myths

According to Georgi, the biochemical role of estrogen is to aid in wound healing. In cases of tissue trauma, estrogen reverts the differentiated cells in that specific tissue back to a stem cell-like condition, to repair the damaged tissue.

In young, healthy women, progesterone will tend to antagonize estrogen's activity. In men, that pro-differentiation factor is androgens. Both pro-differentiation factors (progesterone and androgens) decline with age. However, estrogen synthesis typically does not.

> *"That's another big myth that we need to address,"* Georgi says. *"Talk to any doctor and they'll tell you, 'Menopause is a condition of severe progesterone and estrogen deficiency. We've done countless tests of the blood and we've seen that estrogen levels and progesterone levels are undetectable.'*
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> *That's expected because most of the estradiol — which is the main estrogen both for males or females — and progesterone are of ovarian origin in females. In other words, if the ovaries atrophy, yes, you will expect to see declining levels of the steroids in the blood because the ovaries are not working so well. In fact, eventually they fail.*
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> *However, another thing that's probably not well known, 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 circulated precursors are always there, usually cholesterol which, by the way, rises with age.*
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> *So that would imply that if we test tissues, even in menopausal women, we should see 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 I've seen on biopsies done confirms that.*

In 2022, a Chinese group published a very large study with Chinese women where they measured the levels of more than 20 different hormones in hair ... which is kind of like a surrogate for what's going on in the tissues because hair grows out of cells called follicular cells.

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 ...

Progesterone did decline, almost to undetectable levels. Thyroid hormone, the active portion, T3, also declined. Reverse T3 increased, and there was an inverse correlation between body mass index (BMI) and the levels of either T3 and progesterone, and a positive correlation between BMI and the levels of estrogen.

So, to me, that gives you 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 will restore youthfulness in menopausal women."

Estrogen Summary

So, to summarize, low estrogen levels in your blood is not an indictment of estrogen deficiency. This is because most cells can synthesize estrogen from common precursors that are widely available in your body, including cholesterol.

The problem is that the estrogen that these cells produce doesn't equilibrate with the blood, but stays within these cells and gives a false impression of estrogen deficiency. And, while estrogen is an essential component in tissue repair, that growth and repair process needs to be turned off when the job is completed, and if it isn't, the risk of cancer rises dramatically.

The problem is that progesterone and androgens — the off-switches for estrogen in women and men respectively — do decline with age, because cells do not have a

comparable enzyme like aromatase, to synthesize them. Their synthesis is restricted to gonadal tissues. This leads to elevated estrogen levels and decreased progesterone and testosterone, which typically results in unregulated cell growth, the essence of cancer.

Making matters worse, estrogen is antimetabolic and radically reduces the ability of your mitochondria to create cellular energy in a form of ATP by depending on aerobic glycolysis (the Warburg effect) which radically impairs oxidative phosphorylation. This further contributes to its carcinogenic effect. Georgi explains:

> *"When you have to repair tissue, you can forego, for a little bit, the oxidative phosphorylation, but it always needs to come back, because that is the differentiating factor. Stem cells stay in 'cancer metabolism' because ... it's the way cells have to be in order to divide at the maximum rate possible with the minimum consumption of resources possible.*
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> *But if you want this tissue to become an organ instead of 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 [hormone], both of which also prometabolic, are known as the main differentiating factors in humans."*

The Many Health Benefits of Progesterone

As explained by Georgi, progesterone is the main endogenous and most direct and potent glucocorticoid receptor antagonist. This is a profound important point that I was unaware of until Georgi mentioned it. As such, it's also a cortisol blocker, with a similar activity as the anticancer drug and cortisol blocker RU-486, which is now virtually impossible to get.

The primary difference between them is that RU-486 also blocks progesterone, so when you take it you have to be very careful about supplementing. Taking progesterone bypasses this issue, and Georgi believes it has about the same effectiveness as mifepristone (RU-486).

Georgi goes into great detail about RU-486. As I said, it's virtually impossible to get a hold of this compound outside the mifepristone these days, which is why I won't expound on it here, but if you want to learn more about it, listen to the interview.

Progesterone is also a GABA agonist and could be useful to take concomitant with a GABA supplement. You may even be able to use much lower doses of both if you combine them together. This affinity for GABA accounts for some of progesterone's psychological benefits. Georgi explains:

> *"The strongest GABA agonist in the body, slightly stronger than progesterone, is a progesterone derivative, a metabolite, known as allopregnanolone. It was recently approved by the FDA for postpartum depression.*[3]
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> *A company is developing an oral formulation 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, psychosis, sleep disturbances, anxiety — all of these things GABA is known to relieve.*
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> *They're saying, 'Oh, we have the most potent endogenous GABA agonist here, allopregnanolone, for all these conditions.' But we can say, 'Well, you don't have to get allopregnanolone by prescription. You can do it with progesterone, maybe a slightly higher dosage, but still in the same ballpark*."

As mentioned, progesterone also inhibits cortisol, and cortisol has been well-documented to play a major role in depression.

On a side note, GABA and allopregnanolone also appear to have anticancer activity. According to Georgi, GABA is known to improve mitochondrial energy production and inhibit excessive glycolysis. Excessive glycolysis and impaired mitochondrial function just happen to be the classic hallmarks of cancer. In older studies, injecting GABA directly into tumors was found to trigger complete regression in a matter of days.

Progesterone Dosing

In my view, what mature women really need are progesterone and pregnenolone, not estrogen. So, in practical terms, you'll want to make sure your levels of progesterone and pregnenolone are within healthy limits, which are the levels you'd have in your 20s.

According to Georgi, "a physiological dose for a young healthy child before they actually reach puberty is about 30 milligrams of progesterone daily ... so, 30 milligrams seems to be a decent dosage prophylactically."

How to Optimize Progesterone Absorption

To maintain an optimal progesterone level, you can either take preformed progesterone or its precursor, pregnenolone. If you're taking oral progesterone, be sure to take it with a small amount of saturated or monounsaturated fat — something with a carbon chain above 14, to optimize absorption. Butter is an ideal choice.

> *"If you don't avoid the first-pass metabolism, you're going to waste about 85% of the progesterone taken,"* Georgi says.

But the key, and what I had misunderstood from my previous conversations with Georgi, is that the pregnenolone or DHEA, can't be merely taken at the same meal with butter. It needs to be taken out of the pill and mixed well into the butter.

You don't need much butter (or ghee), just about one-fourth of a teaspoon. You can mix it with a toothpick or similar small tool and put on your food and you are off to the races avoiding the 85% destruction that typically occurs when you swallow the capsule without this trick.

Progesterone has potent sedative effects, so if you're getting to a point where you're getting disoriented, or your thinking or speech slows or you're getting sleepy, you'll probably know that your dose was too high and have taken too much. You can take advantage of its GABA agonist effect by taking it 30 to 60 minutes before bedtime.

"A hefty dose of progesterone causes symptoms indistinguishable from being drunk," Georgi says, "so don't operate machinery when you're taking a lot of progesterone." Of

course, if you have trouble sleeping, then taking the progesterone in the evening can be helpful.

One commercial product that Georgi and I discussed was Progest-E which the late biologist and thyroid expert Ray Peat developed, and contains progesterone mixed with vitamin E. Since our interview, however, I did some research and now would strongly recommend avoiding Progest-E.

Why? For two reasons. One, it is put into a cheap plastic squeeze bottle. I'm not sure why Peat did not realize that flexible plastic is loaded with plasticizers like BPA and phthalates and are strong estrogen mimics.

But, the more important reason is that it is virtually impossible to squeeze out a precise dose of "one drop" from the bottle. My experience suggests that one drop could be a small fraction of a drop or five or even more drops. So, this product needs to be avoided.

Fortunately, there is a far better one available called **Simply Progesterone** that you can get at Health Natura.[4] It has the same progesterone concentration of 3 mg/drop as the Progest-E. **Simply Progesterone** comes in a glass bottle with a real glass dropper that you can easily and accurately measure. This product is a winner and the one that I personally use and believe most people would benefit from taking.

DHEA Dosing and Considerations

For optimal health, you also want to keep an eye on your cortisol-to-DHEA ratio.

> *"The cortisol-to-DHEA ratio — whether in blood, tissue, hair or nails — has now been established as the single most reliable predictor of all-cause mortality and morbidity throughout the entire lifespan,"* Georgi says.
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> *"That ratio should be less than 0.3. In other words, heavily in favor of DHEA. Anything over 0.5 is known to start causing mood disturbances [like] depression. Anything over 1, you're probably at risk of diabetes or cardiovascular disease, or worse."*

That said, DHEA is a precursor to estrogens, so you don't want excessive amounts of DHEA. For most people, 10 mg to 12 mg of DHEA is more than adequate. That's how much you produce in your mid-20s.

It would be highly unwise to simply swallow DHEA, as 85% will be broken down by your liver and we have no idea how harmful the liver metabolites are. You can use the same butter trick described above for pregnenolone, to avoid this. But it would also be wise to not take doses over 10 mg without professional supervision. You do not want to increase your estrogen and prolactin levels.

You must be careful, though, as taking DHEA can easily be converted to estrogen by aromatase and subsequently increase prolactin levels. It you are going to take DHEA it would be best to take it with progesterone as that will inhibit DHEA's conversion into estrogen since progesterone is a potent aromatase inhibitor.

> *"As far as dosages [are concerned] … 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 young [and what it is now].*
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> *Let's say the optimal level was 500, and now you are in your 60s. The [lab] range says you're fine, but your level is 200. The delta is about 60%, so you need to take 60% of that daily [amount] that you used to produce when you were in your 20s.*
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> *Sixty percent of 12 mg is what you really need to be taking in order to restore the level to the youthful level without running into the risk of raising estrogen too much. And if you combine it with progesterone, you should be getting an even stronger anti-cortisol effect while further preventing the conversion of DHEA into estrogen."*

Pregnenolone Benefits and Dosing Suggestions

Pregnenolone, which your body makes from cholesterol, converts first to progesterone and then to allopregnanolone. Pregnenolone is also converted to DHEA, which is a

precursor for estrogens and androgens.

> *"Pregnenolone is really unique in the sense that if you have an excess of a specific steroid, it will likely lower it,"* Georgi says, *"and if you have a deficiency of a specific steroid, it will probably raise it.*
>
> *About 100 mg is probably enough because, being the top level hormone, it's going to convert downstream into whatever you need ... I know of a study with schizophrenia where 50 mg decreased significantly both the symptoms of schizophrenia and bipolar disorder."*

While most people opt for oral pregnenolone, I prefer rectal suppositories. I make my own by mixing the pregnenolone with cacao butter, a very long chain fat that facilitates absorption. For most people, 100 mg is sufficient. If you opt for oral pregnenolone, mix it into half a teaspoon of butter to make an emulsion.

Low Serotonin Is Not the Cause of Depression

Next, we discuss serotonin, which used to be called enteramine because it's produced in the gut. Enteric refers to things related to your intestines. Serotonin has been incorrectly dubbed the "happy hormone." It's not.

Selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressants that raise your serotonin levels, but contrary to popular belief, this can cause significant problems. The easiest solution for depression, anxiety and insomnia is GABA, with or without progesterone.

> *"Even 100 mg of oral GABA was enough to lower the assessment scores of patients with anxiety and depression disorders. The Beck's Depression Inventory is for depression, and there's another one for anxiety. Just 100 mg of GABA was sufficient to lower significantly in the score on both scales.*
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> *Combining it with another GABA agonist amino acid known as L-theanine, which is founding in tea, drastically increased the effects. And L-theanine lowers the*

levels of serotonin in the brain. It's perhaps the most direct evidence that serotonin in the brain is not good at elevated levels.

So for people who 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 antiserotonergic. One is called mepirzapine, also known as mirtazapine.

If you look at the structure, it's very similar to a drug called cyproheptadine, which is a known selective serotonin antagonist. Mepirzapine 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 an antiserotonin drug is approved for depression, considering that all the other proserotonin drugs are also approved for depression. Something doesn't add up there."

Cyproheptadine also acts as a sleeping pill, so if you do not have insomnia, don't go over 2.5 mg. Cut it in half or even a quarter. It's also a potent histamine blocker and can be used for acute allergic reactions. It is a prescription and think it would be wise to have it on hand, but Benadryl could also be used.

It also might have benefit for those who are on SSRIs, sleeping pills or anti-anxiety agents. However, I think high dose GABA therapy is likely a far better, safer, and less expensive approach. Georgi and I discuss this in the podcast.

Just be careful about combination products as they may contain magnesium. While magnesium is very helpful if you push the GABA to high doses you will get far too much magnesium and it will have a laxative effect.

The other drug Georgi recommends is tianeptine, which is a selective serotonin reuptake enhancer (SSRE), basically the converse of an SSRI, and it too is a potent antidepressant.

If you don’t want to go the pharmaceutical route, you can use GABA, at a dose of 500 mg to 2,000 mg (2 grams) daily. This range has been shown to relieve anxiety and insomnia in people who are already taking SSRI drugs, Georgi notes, adding, "I've seen people in very severe cases of anxiety and depression plateau it about 3 to 4 grams. After that ... the mental effects usually plateau."

Interestingly, if you take too much GABA, some of it will get deaminated and convert into succinic acid, an intermediate of the Krebs cycle. As such, GABA also helps boost mitochondrial function at high doses. So from a toxicity perspective it appears to be very safe.

Elevated Serotonin Has Devastating Psychological Effects

Ironically, while many doctors blame insomnia on depression caused by low serotonin, it may actually be the other way around. Georgi explains:

> *"Every single antiserotonin drug ever tested ... 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. How?*
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> *If serotonin is a precursor to melatonin, how can it actually cause problems with the sleep? It’s because serotonin is the most potent activator in the body of the release of cortisol through ACTH. In fact, the first antidepressant drug, Prozac, is a partial serotonin antagonist. It specifically blocks the serotonin receptor responsible for the release of cortisol, serotonin receptor 2C5-HT2C.*
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> *Prozac is a potent inhibitor of that receptor while maintaining the rest of its serotonergic effects. So, it's the perfect coverup, right? You can claim that serotonin is great for your depression, while in reality you're giving a drug that’s blocking the effects of serotonin and lowering cortisol, but that’s unknown to most people, even doctors that I've discussed it with.*

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 levels of both. So people that are high in GABA are usually low in serotonin. They're very calm, they're very gregarious.

Serotonin is not a happiness hormone. Multiple studies, even a court case recently agreed that serotonin actually destroys empathy, love and wisdom. Those are specific quotes from the court study. Another animal study found that crabs exposed to very low levels of SSRIs because of sewage being dumped into the ocean ... 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 also a metabolic inhibitor ... The primary role of serotonin is metabolic, and the evolutionary role of serotonin is probably for numbing pain when you're under stress.

It turns off your pain reaction, even your grief reaction, but at the expense of turning off all the other emotions as well. Multiple studies have 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."

Other Adverse Effects of Serotonin

High serotonin can also cause serotonin syndrome and contribute to fibrosis (including cardiac and pulmonary fibrosis), impaired thyroid function, reduced metabolism due to excessive glycolysis and high lactic acid production, and reductive stress. High serotonin is also responsible for bizarre, recurring nightmares and may play a role in PTSD as well.

Serotonin also inhibits pyruvate dehydrogenase, cytochrome c oxidase and Complex 2 of the electron transport chain (succinic acid dehydrogenase, which also participates in

the Krebs cycle).

> *"The evolutionary reason is probably that in times of stress and injury, these things rise in order to help you repair. But it should be acute only,"* Georgi says.
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> *"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 in order to conserve energy, which means your high metabolism (which means you're gaining weight), your good mood (which means you're going to be depressed).*
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> *Then eventually, if things go down that route, the body will start turning off 'nonessential' organs by turning them into fibrotic clumps so that they don't have to waste energy on repairing them. That's how you get fibrosis. Ultimately, the end stage of fibrosis is cancer, unless you die from the organ failure before that."*

In closing, the take-home from all of this is that you really want to minimize estrogen and keep your serotonin level as low as possible, and increasing progesterone, pregnenolone and GABA will help lower both and appear to be useful, inexpensive, nonprescription modalities if you use them correctly. For even more details, be sure to listen to the interview in its entirety.

Sources and References

- [1] Science Daily December 13, 2002
- [2] Women's Health Initiative
- [3] Smithsonian August 7, 2023
- [4] Health Natura LLC