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The Four Hormones Most Adults Need More Of

Analysis by Dr. Joseph Mercola | December 03, 2023

STORY AT-A-GLANCE

- Four hormones most adults can benefit from are progesterone, thyroid hormone T3, DHEA and pregnenolone
- Around the ages of 11 and 12, right before puberty, the hormonal profiles of boys and girls are relatively similar. They produce about the same amounts of pregnenolone and progesterone. This is also the time when thyroid hormone levels are the highest they'll ever be, and it's the time in a person's life cycle when their mortality is the lowest. Most supplementation recommendations are based on these prepubescent levels
- To optimize bioavailability, take T3, DHEA and/or pregnenolone orally, after dissolving them in a long-chain fat (14 carbons or more) such as ghee or butter
- The normal daily output of DHEA by the adrenal gland is about 20 to 50 milligrams (mg), so for most people, the max DHEA dose would be 50 mg, ideally split into several smaller doses. Human studies have shown that once you take more than 50 mg of DHEA per day, you begin to increase estrogen biomarkers
- As a general recommendation, I recommend taking 30 to 50 mg of bioidentical progesterone per a day, taken in the evening before bed, as it can promote sleep. The same dose (30 to 50 mg a day) is recommended for pregnenolone. This is the physiological dose, meaning it's what you need for full replenishment, assuming you're producing nothing

In this interview, repeat guest Georgi Dinkov and I discuss the four hormones most adults need more of if they want to optimize their health. In my introduction I mention

that we will review the benefits and mechanisms of action of carbon dioxide (CO_2), but that will be covered in Part 2 of this interview that will be posted in the next few weeks.

As for hormones, if you're optimally healthy, hormone replacement therapy (HRT) is unnecessary, as your body will make whatever hormones you need. The problem is that very few people, including I, enjoy truly optimal health.

We live in a very polluted world, so "optimal health" is a high bar for all of us. I take four hormones that I believe most adults can benefit from: Progesterone, thyroid hormone T3, DHEA and pregnenolone.

Three of these, progesterone, DHEA and pregnenolone are available over-the-counter. Thyroid hormones, however, require a doctor's prescription. You also need to get routine blood tests done (typically two to four times a year) to make sure your thyroid hormones are maintained at optimal levels. Overtreatment can result in hyperthyroid symptoms, which you clearly want to avoid.

How Hormones Impact Health Span and Life Span

As noted by Dinkov, around the ages of 11 and 12, right before puberty, the hormonal profiles of boys and girls are relatively similar, and they produce about the same amounts of pregnenolone and progesterone.

This is also the time when thyroid hormone levels are the highest they'll ever be, and it's the time in a person's life cycle when their mortality is the lowest. Once puberty strikes, adrenal activity increases. In fact, the old name for puberty was adrenarchy, which tells you that adrenal activity is driving the process.

At this time, boys start producing more testosterone and girls progesterone (depending on where they are in the menstrual cycle). Interestingly, many studies have shown that the later puberty starts, the longer the lifespan and health span of both sexes. Conversely, the earlier the onset of puberty, the shorter the lifespan and the more prone to diseases the individual will be.

"After puberty starts and until the late 20s, people are remarkably resilient to stress," Dinkov notes. *"In fact, stress often seems stimulating for them. This seems to change drastically after they hit 30, and especially after 35. It's basically a very steep decline.*

And if you look at the way the hormonal profile changes, you'll see that whenever young, healthy people are exposed to stress, there's a spike in cortisol release, followed closely by a spike of pregnenolone and DHEA release for males, and pregnenolone, progesterone and DHEA release for females.

That delayed release of these secondary hormones drop off a cliff after the age of about 35. The ranges for pregnenolone, progesterone and DHEA, and even testosterone, change depending on what age group you fall into, but the range for cortisol doesn't change.

So, throughout your lifetime, unless you're critically ill, in which case cortisol drops, or you have Addison disease, which is full on adrenal failure, your cortisol levels do not decline, and that's what keeps you alive because, if you have adrenal failure, unless you take cortisol shots you will die from hypoglycemia or Addison's disease. So, it's lethal.

Cortisol is really a life-saving hormone. It's proinflammatory, but its primary purpose is to keep blood sugar from dropping too low, because your brain runs predominantly on glucose. So, basically, after the age of 35, cortisol stays the same.

It's a catabolic hormone. It can shred your muscles, soft tissue, bone, you name it. There's no organ that is immune to the effects of cortisol. There is only one that is somewhat resilient, and it's the heart. And the reason the heart is so resilient in both genders is because in males, the heart contains a very large amount of testosterone, and in females it contains very large amounts of progesterone.

> *Both of these happen to be glucocorticoid antagonists. So they're protecting this vital muscle ... but all the other tissues can be shredded and they're considered basically nonessential. So, after the age of 35, you have a stable supply of a catabolic hormone and then a rapidly declining supply of pregnenolone, progesterone and DHEA, all three of which have antiglucocorticoid effects."*

All of that said, if you're taking progesterone, you don't need to worry about the DHEA converting to estrogenic substances because progesterone will block that conversion. Even if there is conversion, progesterone is an antagonist at the estrogen receptors so it will directly block the estrogen as well. Pregnenolone has similar effects. It's a milder aromatase inhibitor than progesterone, but it's still quite good at preventing the uptake of estrogen into the cell.

Cortisol-to-DHEA Ratio Is a Good Predictor of Life Span

One of the take-homes from the above is that when you're young, before puberty sets in, you have high production of T3 thyroid hormone, cortisol and anti-cortisol steroids. After age 35, there's a gradual decline of thyroid function and a rapid decline in the synthesis and release of the anti-cortisol hormones, some of which also happen to be anti-estrogenic.

As a result, you enter a state of relative glucocorticoid and estrogen excess, both of which have detrimental effects on health. Dinkov explains:

> *"The state of glucocorticoid excess is not very well known. It's easily measurable though by the ratio of cortisol to DHEA, or cortisol to progesterone, or cortisol to pregnenolone. Studies demonstrate that the cortisol to DHEA ratio is the best predictor we have for how long you're going to live and for any diseases that you're going to develop throughout your lifetime."*

DHEA Influences Your Immune Function

One of the reasons for this is because DHEA is an immune booster, and your immune system is your first line of defense against both acute and chronic diseases, including cancer. And the amount of DHEA produced is about the same in both sexes, regardless of age. Dinkov suspects an ideal ratio of cortisol to DHEA is 0-to-3 or lower.

As for DHEA by itself, he recommends aiming for a level in the upper 50th percentile for the upper range of a 20-year-old, which is around 600 nanograms per deciliter (ng/dL). So, ideally, if you're older than 35, you'd want your DHEA to be somewhere between 300 and 600 ng/dL.

As for the daily dosage, the normal daily output of DHEA by the adrenal gland is about 10 milligrams (mg), so for most people, the max DHEA dose would be 5-10 mg and mixed with a long-chain fat. According to Dinkov, human studies have shown that once you take more than 10 mg of DHEA per day, you begin to increase estrogen biomarkers, which is something you don't want.

> *"Anything less than [10 mg], which happens to be a physiological dose, doesn't really cause that much of a problem, but I would still take it with progesterone because blood levels are not always indicative of tissue levels,"* Dinkov says.
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> *"In fact, [DHEA] is not always reflected on the blood test ... If you look at the studies, they show you that cells have a very high uptake of pregnenolone and DHEA. They accumulate them at levels 100 times higher than what they are in the bloodstream. So if you're very DHEA deficient, it will take a while to fill up your reserves and then for the extra to spill over. About six months.*
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> *There's a study with Italian women. They took 10 mg for a full year. Eventually that restored their levels back to normal, but not until the six-month mark did they see significant change. So it really depends on how deficient you are, for how long you've been deficient, and the state of your adrenal gland.*
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> *Another study demonstrated that the DHEA starts working immediately. You don't see it in the blood test, but they started measuring downstream metabolites of DHEA and found that taking just 10 mg of DHEA drastically*

increased the metabolites of the dihydrotestosterone such as 3-alpha androstane diol and metabolites of testosterone, such as testosterone glucoronate and sulfate.

So, DHEA starts working immediately and converting to downstream hormones, but it's going to take a while to see that in the biomarkers that are usually measured, which is DHEA and DHEA sulfate. What they really should be doing is measure all of the other things that DHA can convert into.

And some of those things are estrogens. Chances are, at least based on studies, that either prolactin or estrone will rise if you're taking too high of a dose long before there will be changes in the blood levels of DHEA or DHEA sulfate."

Caveats and Warnings

There are a few important caveats here. Taking too high a dose of DHEA can cause unwanted hair growth in women, and breast growth in men,[1] so be sure to monitor your symptoms. DHEA is also banned in sports. It's classified as a doping agent by the World Anti-Doping Agency, so athletes must take their competitive status into account before taking supplemental DHEA.

Also, never take DHEA without progesterone. They need to be taken together. Another point to optimize the therapy and not derail it is that if you take T3, DHEA and/or pregnenolone orally, you need to dissolve them in a long-chain fat (14 carbons or more) first.

If you don't do that, they'll be metabolized by your liver, which significantly lowers their effectiveness. According to Dinkov, the bioavailability of oral hormones can be as low as 10%. Dissolving the supplements in a little ghee or butter will bypass liver metabolism and allow you to get the most out of your supplements.

Olive oil is also a long-chain fat, but I don't recommend it in this case, as it can have 20% linoleic acid (LA) and a flavor that many don't like. According to Dinkov, at least one

study has demonstrated that LA binds directly to estrogen receptors and acts like estrogen.

So, LA not merely promotes the effects of estrogen but also acts as an estrogen directly. Since estrogen is a potent carcinogen, you want to avoid things with estrogenic activity.

Progesterone Works Best With Vitamin E

Progesterone, meanwhile, needs to be mixed into vitamin E for optimal bioavailability. Health Natura sells a progesterone in vitamin E product. Alternatively, you can make your own by dissolving pure USP progesterone powder in one capsule of a high-quality vitamin E. The difference in bioavailability between taking progesterone orally without vitamin E and taking it with vitamin E is 45 minutes versus 48 hours.

Another good reason for taking progesterone with vitamin E is because it binds to red blood cells, which allows the progesterone to be carried throughout your body and be distributed to where it's needed the most. What's more, Dinkov cites recent research showing that when you dissolve a substance in vitamin E, it specifically targets sites with the highest inflammation.

Other Important Benefits of Vitamin E

Another important benefit of vitamin E is that it prevents LA stored in your tissues from being oxidized into toxic byproducts. Since most people are walking around with LA stores that are 10 times higher than normal, and since excess LA is likely one of the primary contributors to chronic disease, it can be a good idea to take vitamin E regularly until you get your LA down to healthy levels, which may take up to six years for most people.

> **"Vitamin E also prevents LA stored in your tissues from being oxidized into dangerous toxic byproducts."**

Vitamin E can almost miraculously prevent most of the damage done by LA. It can also reverse or prevent many of the issues associated with excess estrogen. This is important because LA has remarkable parallels to excess estrogen in terms of its metabolic and anti-health effects.

When you eat excess PUFA or LA, you increase your body's production of estrogen. So, when you increase LA, estrogen levels go up — and that's not a good thing. Both LA and estrogen interestingly increase the flow of calcium from outside the cell to inside because the concentration of calcium outside as well is 50 times higher than inside. So, the excess as LA will cause the influx of calcium inside the cell, which causes nitric oxide and superoxide to increase inside the cell.

Nitric oxide and superoxide combine almost instantaneously to form a very pernicious reactive nitrogen species called peroxynitrite, which causes pervasive damage to tissues in your body.

Both LA and estrogen also increase a potentially dangerous process in your body called lipolysis, which is simply the liberation of fatty acids from your fat cells into your bloodstream where they are mobilized. This then increases the oxidation of LA, which is precisely what you want to avoid as ideally you want to keep LA in your fat cells until they metabolize it with peroxisomes.

Fortunately, vitamin E can also help neutralize this damaging effect of LA. Vitamin E also directly inhibits the activity of an enzyme called aromatase. This is an enzyme that converts the male hormones like testosterone and DHEA into estrogens.

Even better, it serves as an estrogen antagonist, meaning it binds to the estrogen receptor to block it from binding to estrogen. This dramatically lowers the damage from excess estrogen.

Vitamin E works very similarly to the drug tamoxifen, which is used to treat estrogen receptor-positive breast cancers. For these reasons, I firmly believe nearly everyone needs to be getting vitamin E in their diet. However, due to the high LA burden, very few

people can get enough vitamin E from their diet to suppress this oxidative destruction unless they're supplementing with vitamin E.

The good news is that since the supplementation is short term, you're not going to need it the rest of your life. If you can keep your LA intake to below 5 grams a day for three years, it's likely you may not even need it at all, or at most, only a few times a month.

However, if for whatever reason, during this time, or when the LA in your tissues are low or normal, and you go out and binge on a meal that's very high in LA, I would strongly recommend taking a vitamin E capsule to protect yourself from this exposure.

Vitamin E also protects against free radical damage and the normal effects of aging. It's particularly important for brain health, and studies have found it can help delay the loss of cognitive function in people with Alzheimer's disease by preventing cell membrane damage and neuronal death.[2]

How to Pick a Good Vitamin E Supplement

Most vitamin E supplements are synthetic, and you want to steer clear of those. Studies have demonstrated that synthetic vitamin E has the opposite effect of natural vitamin E, such as increasing the risk of certain cancers rather than lowering it, for example. So, it's important to make sure you're getting a natural version.

Synthetic vitamin E is called alpha tocopherol acetate. The acetate indicates that it's synthetic. Next, you need to pay attention to the orientation of the optical isomer. Most vitamin supplements are racemic, or they have left- and right-hand isomers. This is a problem as most biological molecules have optical isomers that are right-handed.

They're usually called D and L isomers, which stands for right and left. When you have both left and right isomers present, it's called racemic. Biologically, there's usually only one optical isomer that works well, and with vitamin E it is the D isomer that works in your body, while the L isomer is useless. Yet in synthetic supplements, 50% of the vitamin E in the supplement is the useless L isomer.

To make matters even worse, many synthetic versions use an ester of vitamin E, which only has about 50% of the activity of the natural product. So, the total activity of many vitamin E supplements is reduced by 75%.

So, the first step in identifying healthy good vitamin E supplements is to make sure you're getting real vitamin E and not synthetic. What you're looking for is "d alpha tocopherol." This is the pure D isomer, which is what your body can use.

Many vitamin E brands will use vitamin E from sunflower oil, which has a very high percentage of LA. However, the LA in the capsule is an insignificant amount, probably less than 50 or 100 mg, so in this case it's not a problem. Your goal is to keep LA intake under 5,000 mg, and even better under 2,500 mg, so it really won't negatively impact your LA intake at all.

As for dose, you don't need more than 100 mg a day. There are also other vitamin E isomers, and you want the complete spectrum of tocotrienols, specifically the beta, gamma, and delta types of vitamin E, in the effective D isomer. It's important to get this right, which is why I'm going into this much detail.

Most People Can Benefit From Bioidentical Progesterone

So, to tie up the discussion about progesterone, bioidentical progesterone (not synthetic progestin) is probably the most important hormone that most adults need. Conversely, I believe estrogen — including bioidentical estrogen — should never be used, as estrogen is carcinogenic.

As noted by Dinkov, virtually all cancers respond to hormones and estrogen is a primary growth factor in all of them. So, there's really no such thing as a nonendocrine cancer. To learn more about this, see our previous interview, where we dove deeper into the **hazards of estrogen**.

Unfortunately, most people who use progesterone use it transdermally, which could be problematic. As explained by Dinkov, your skin expresses high levels of 5-alpha reductase enzyme, which causes a significant portion of the progesterone you're taking

to be irreversibly converted primarily into allopregnanolone and cannot be converted back into progesterone.

If you're taking it orally with vitamin E as the solvent, a significant portion will be non-metabolized, that non-metabolized progesterone has potent pro-thyroid effects. It's also a thermogenic steroid. It induces uncoupling, so you'll be producing more heat, which is one of the effects of taking T3. While not as potent as taking T3, it can raise your metabolic rate by about 10%.

Progesterone also blocks cortisol and helps protect against excess cortisol production, but not to the point of causing cortisol deficiency (Addison disease), and it helps deactivate adrenaline.

> *"There are human studies demonstrating that you administer progesterone, even in its nonoptimal form — such as just the powder without the long-chain fatty acids and definitely without the tocopherols — even in that form, 100 to 200 milligrams orally.*
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> *A single dose is sufficient to drop cortisol and adrenaline by about 60%. As a side effect of that, the blood pressure also dropped in both sexes,"* Dinkov says. *"So, we know that progesterone has a very potent antistress effect by acting specifically on the two sides of the stress system, cortisol and adrenaline.*
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> *One of the explanations is that progesterone has shown some ability to directly activate the alpha receptors, which are negative feedback. In other words, if you activate the alpha adrenal receptor, you basically send in the signal that there's too much adrenaline, so the body will produce less adrenaline ..."*

The dose of bioidentical progesterone I recommend is 30 to 50 mg a day (again, mixed with a long-chain fat), taken in the evening before bed, as it can promote sleepiness. The same dose (30 to 50 mg a day) is recommended for pregnenolone. This is the physiological dose, meaning it’s what you need for full replenishment, assuming you're producing nothing.

Important Caveat for Menstruating Women

Women who still menstruate need to be careful with the timing of their progesterone supplementation. Progesterone is crucial for successful pregnancy, and you can severely inhibit your ability to get pregnant if you take it at the wrong time. (During pregnancy, progesterone actually skyrockets. In the third trimester, women produce about 600 mg a day.)

If your menses are regular, start taking the progesterone on the 14th day after your menstrual flow begins, and take it for 14 days straight (until cycle day 27). If your cycles are short, start on day 12 and continue for 14 days. Always take the progesterone for the full 14 days even if your menses begin before the 14 days are over. Start the next progesterone 14 days after the flow began.[3]

There's no toxicity to progesterone, unlike estrogen and testosterone, neither of which I recommend. Progesterone, T3, DHEA and pregnenolone are the only hormones you really need. Supplementing progesterone also will not lower your natural production, so you don't need to be concerned about that. In fact, it enhances your natural production.

Thyroid Hormone Supplementation

When it comes to your thyroid, most people only need T3. That said, desiccated thyroid contains both T3 and T4 and can be a good option for some. Here, unless you're treating a specific thyroid problem, the generally recommended dose is 10 micrograms two to three times a day. Dinkov comments:

> *"The thyroid gland produces about 100 micrograms in a healthy person — 100 micrograms of T3 over 24-hour period. If you take more than 25 micrograms, even that is a very high dose because it has such a potent thermogenic effect, and in higher doses can be catabolic.*
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> *The body has deiodinase enzymes, and they very quickly convert the excess T3 into something called T2 and even T1 ... So, in other words, you're going to be*

wasting most of it. Interestingly, the same type of enzymes, T3 deactivating, are highly overexpressed in cancer cells, and cancer cells just happen to be very hypometabolic, as we've discussed previously.

So the thyroid gland produces T3 and T4 in a ratio of about 1 to 4 in favor of T4. T4 is actually a prohormone, it by itself does not have a very high activity directly at the thyroid receptors T3. So, it circulates and about 80% of it in the liver, in a healthy person, should get converted to T3. The other 20% can get converted to T3 peripherally, or if the dosage of T4 is too high, the excess very quickly gets converted to something called reverse T3.

This is a very dangerous state because reverse T3 acts as a thyroid hormone antagonist ... Most doctors don't take these things into account, so if they prescribe you, let's say, 100 or 200 micrograms T4 daily. You better be praying that this will get properly converted because if it doesn't, and gets converted to reverse T3, you'll end up in a more hypothyroid state than if you did not take the T4 at all ...

T4 is almost never a good option by itself unless the person is very young. But even then, if a person is hypothyroid, that by definition already means that the liver will be burdened, because one of the primary functions of the liver is the detox mechanisms and one of the primary things that liver detoxifies are polyunsaturated fats and estrogens.

But the detoxification mechanisms themselves depend on thyroid function. So hypothyroid means sluggish liver by definition. So, if you give a hypothyroid person T4 only, especially if the dose is higher, you're asking for trouble. Some of that will get converted to reverse T3."

Sources and References

- [1] Medical News Today June 14, 2018
- [2] Medical News Today April 14, 2015
- [3] Cemcor Cyclic Progesterone Therapy