
# Episode 294: Using Targeted Nutrition to Alleviate Hormone Related Issues With Dr. Chris Masterjohn

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Katie: Hello and welcome to the Wellness Mama Podcast. I'm Katie from wellnessmama.com and this episode is a much requested round two with Dr. Chris Masterjohn. Like our first episode, we go deep on various aspects of nutrition and Chris is one of the smartest people I know when it comes to most of these topics. He earned a PhD in Nutritional Sciences from the University of Connecticut and served as Assistant Professor of Health and Nutrition Sciences at Brooklyn College. He has a really amazing guide called "The Ultimate Cheatsheet" which helps you decode your own body's nutritional needs as well as a really informative website and podcast I highly recommend both and I know that you are going to love this episode as much as I did. Chris, welcome back. Thanks for joining us again.

Chris: Thanks for having me, Katie. It's good to be here.

Katie: Well, your first interview was so helpful. We went deep on a lot of nutritional topics, and I've heard from a lot of the audience how some of your tips on like pantothenic acid helping skin has been really amazing for them. And I knew I had to have you back to go deeper on different nutrients and to learn more.

And, on this episode, I'd really love to talk a little bit more women-specific because I think women potentially deal with a bunch of symptoms that men may not face because of all the hormone changes that we go through, whether it be monthly, whether it be during pregnancy. We just have a lot more going on. I think than guys do, and I know if you look at the chart, like, you guys have hormone fluctuations, but women is almost like a roller coaster every month just because we have all these hormones coming into play.

So I'd actually love to start with just, like, an overview of things that you've found that seem to be nutrient deficiencies related to those hormone changes each month that come with the monthly period, with ovulation. What are some things we need to know and be aware of when it comes to that?

Chris: Yeah. So my interest in this first peaked when I was talking to a consulting client of mine who was having real, bad problems with headaches. And she hadn't identified any triggers, and so we talked about food triggers as nothing. And she didn't offer the fact that it correlated with her menstrual cycle maybe because she didn't think it would make any sense until I asked. And then she was like, "Yeah. They always occur on day 13. That's when they're the worst." And then a couple of days before I have my period, they often occur, and they're not quite as bad."

And so I looked at the chart and, you know, sure enough, that corresponds to the big estrogen peak around ovulation and then the smaller estrogen peak that happens to also be balanced with more progesterone in the days leading up to menstruation. And so, you know, at the time, I was researching histamine a lot, and so the first thing I think is, "Well, let me see what estrogen does to diamine oxidase activity." Diamine oxidase or DAO is an enzyme that you need a number of nutrients for, including B6 and copper especially, and vitamin C.

So diamine oxidase is one of the main ways that you clear histamine. And so, sure enough, estrogen massively down-regulates diamine oxidase activity. And so, I suggested to my client she should try supplementing with diamine oxidase proactively around those times of her menstrual cycle, and it works. So, you know, that was the first place that got me interested in this. But, you know, once you look into this a little bit more deeply, I think we can paint a little bit of a broader picture and one that applies to several different contexts. So one area that's been of quite a bit of interest, I think, for years at this point has been the fact that, for reasons that no one has really identified that well, high dose vitamin B6 supplementation has been at least promising, if not often effective, in treating morning sickness associated with pregnancy.

And so it seems like the morning sickness of pregnancy must be tied in some way to something that has to do with B6. So one hypothesis that came out a couple of years ago that I think is a very compelling argument is that estrogen increases hydrogen sulfide production, and hydrogen sulfide can generate sulfite, which is toxic, and which happens to be something that's added to a lot of medications, cosmetics, and processed foods as a preservative that a lot of people don't tell. You know, some people, like certain wines give them really bad headaches, and it's because of the sulfites in the wine.

Well, when you're pregnant, you're making sulfite. And you're not making sulfite to make sulfite. You're making hydrogen sulfide gas, which, although like we would typically associate it with the smell of rotten eggs at high doses, has been discovered in recent years to be a very important signaling molecule that is, among other things, a vasodilator. So hydrogen sulfide gas falls into a very small category of things that can dilate blood vessels, along with nitric oxide, which has been known about for a much longer period of time.

And hydrogen sulfide is particularly important in delivering blood to the placenta when you're pregnant. And it also has other activities related to pregnancy. For example, it suppresses preterm labor. And it's necessary to keep hydrogen sulfide levels higher than they would be when you're not pregnant or for probably anytime if you're a man, in order to prevent you from going into labor early, but also just to keep the blood flow, the placenta going to nourish the growing baby.

And now it so happens that a small portion of hydrogen sulfide is going to be turned into sulfite, which is a toxic compound. And sulfite, we all generate sulfite in the course of normal metabolism from any of the sources of sulfur in our diet, especially the sulfur-containing amino acids that are in the protein we eat. And in order to neutralize that sulfite, we use a mineral, molybdenum, to convert the sulfite, which is toxic, to sulfate. Sulfate is both not toxic and is also highly useful. We use it for detoxification. We use it for regulating hormones. We use it to synthesize structural things that are protective against cardiovascular disease, highly protective against arthritis in our joints, and so on.

So, you basically have this balance between sulfite, which is toxic, and sulfate, which is extremely necessary and useful. And the more sulfite you generate, the more you need to convert it to sulfate. Even if you don't need extra sulfate, you still need to get rid of sulfite because it's toxic, and you do that with molybdenum. So that would imply that during pregnancy, because of increased hydrogen sulfide, you are going to generate more sulfite. Your molybdenum needs will increase to make sulfate.

Now, what happens to molybdenum intakes during pregnancy? Well, by far and away, the best source of molybdenum is beans. And in pregnancy, a lot of women develop aversions to beans and other molybdenum-rich foods just because they're more difficult to tolerate digestively and, you know, maybe as well as taste aversions and things like that. So in someone who's pregnant, molybdenum intakes tend to go down just because they're less tolerant of molybdenum-rich foods. And then, at the same time, molybdenum needs to go up because of the increased sulfite generation. Now, why would that relate to vitamin B6? Well, it turns out that sulfite binds to B6 and essentially destroys it, basically eliminates it from the body.

So sulfite can induce a B6 deficiency, and high doses of B6 can be used to clear away sulfite that you were not able to convert into the non-toxic sulfate using molybdenum. So, basically, this hypothesis is that molybdenum needs would go up. But since most pregnant women aren't meeting those needs for molybdenum, high doses of B6 can act as a...I want to say Band-Aid solution, but it's not really Band-Aid because it's not like you're just managing the symptoms. You are clearing away the sulfite, but sort of like...you can't... So, like, the doses of B6 used in morning sickness would be like 100 milligrams a day, completely impossible to get from food, so I

don't even want to call it a backup mechanism. Like, molybdenum at nutritional doses would be really, really useful here and would be most related to the root cause.

High doses of B6 are very natural, very safe, and effective, but they're one step removed away from the root cause. It's like because you didn't have the molybdenum, you're more reliant on the B6. And who knows exactly what that's doing? You know, maybe the sulfite, because it's giving you a B6 deficiency, that itself is taking away from important things that B6 would do to prevent morning sickness, or it might just be that the extra B6 is mopping up the sulfite, and the sulfite is what's causing morning sickness.

Now, sulfite does a bunch of toxic things, but one of the things that it does is it can cause mast cells to release histamine. And histamine in the gut can give you all kinds of gut-related issues like diarrhea, for example, make you feel nauseated, you know, things that could be possibly related to morning sickness, especially if because of B6 deficiency. And actually, I think sulfite also inhibits diamine oxidase, and diamine oxidase requires B6 that's needed to clear histamine from foods.

She might, on top of everything, become more intolerant to histamine, certain foods maybe. So who knows what the mechanisms are, but the sort of like takeaway point is that because sulfite is going up, your needs for molybdenum are going up. And if you don't have enough molybdenum, your needs for B6 are going to go up, but they're not going to go up within the nutritional range. They're going to go up like ridiculously high. So, you know, maybe on a ridiculously high B6 intake from natural foods, you could hit 10 milligrams of B6, but you might need 100 milligrams to mop up all that sulfite. So it's not insane amounts, but it's way out of what you could get from natural foods.

And now, looking at that, I'm like, "Well, what about outside of pregnancy? You know, what's regulating this? Is it estrogen?" And, yes, it's estrogen that's regulating sulfite. I don't know what the effect of progesterone is, so I had trouble finding direct research on it. But it can't be the case that progesterone is effective at countering the effect of estrogen because progesterone rises in pregnancy alongside estrogen, and none of this would be an issue in pregnancy if progesterone was really protective.

The other thing is if you look at, like, Plan B has some side effects that are very similar to the morning sickness of pregnancy, and Plan B doesn't have any estrogen. It's an emergency post-sex contraceptive that only has a synthetic form of progesterone in it. So I don't know what progesterone does to this, but I wouldn't be surprised if progesterone was actually acting in concert with estrogen here and maybe augmenting its effects just because this seems to be like a highly pregnancy-related thing. But in any case, you can tie this to the estrogen peaks in the menstrual cycle, especially...

You know, the big peak is around ovulation. The more moderate peak is in the days leading up to menstruation. And then you can also tie it to other supplemental estrogens. So most birth control patch or pill has estrogen in it, and then, you know, hormone replacement therapy that women would typically go on after menopause has estrogen in it. And so, any of these sources of estrogen are going to affect diamine oxidase

and possibly make you histamine intolerant, and they're also going to increase sulfite production, increase your needs for molybdenum, and possibly increase your needs for B6.

I think those are the things that are most related to headaches, nausea, you know, any other form of digestive complaints, feeling queasy or just like general GI distress, and any kind of allergy-like symptoms, so itching, hives, etc. And, you know, we could branch off from there in numerous directions, but I think that's the sort of most interesting thing I've been synthesizing lately related to this stuff.

Katie: That's so fascinating. And it seems like a vicious cycle. Once you're in that, it will be difficult to pull out of it without, like you said, supplementation. So if I'm understanding correctly, would this be maybe something if people have symptoms more so around ovulation when that estrogen spike is, or they're taking an estrogen-based birth control, this would be something they could look at and try?

Chris: Yeah. In fact, I'd go a little bit further than that. So another thing that has been known for decades to happen when women are on birth control is that the amino acid, tryptophan, which is used to make serotonin, and is used to make melatonin, and is also used to make niacin, which is vitamin B3, estrogen increases the production of niacin, vitamin B3, from tryptophan. And in so doing, there's a neurotoxic compound that kind of spills out of the pathway called kynurenine. And there are studies...this has been known for a long time and yet no one knows it because what happened was they tested different doses of B6 to see what could normalize tryptophan metabolism.

And I would imagine this to be beneficial for insomnia and headaches in particular. Anyway, so what they did was they tested a couple of low doses, up to 2 milligrams, and they tested 20 milligrams. And they found that 20 milligrams of B6 completely made tryptophan metabolism totally normal, but all of the doses that they considered reasonable to get from food didn't. And so, they basically dismissed their own finding, about 20 milligrams, and said like...because there's this bias in mainstream nutrition where they don't want everyone running around taking supplements.

So they looked at that, and they said like, "That effect can’t be, like, a real effect." Like, B6 obviously isn't doing something here because 20 milligrams is a ridiculous dose, and we're not going to tell people to take 20 milligrams, even though it's well under what the Institute of Medicine has set as the dose that would have no safety concerns, which is 100 milligrams. So the reality is that the data have said, for decades, that 20 milligrams of B6 normalizes the negative effects of birth control on tryptophan metabolism, and there are no reviews that say that.

I have to go back and look at the original papers because all the reviews from people that I would expect about this...sorry, not expect, that I would respect and that would be considered prestigious, they just cite these people citing their own data saying that B6 didn't fully normalize tryptophan metabolism. And you have to go back to the paper and see that 20 milligrams does. So I would go more than that to say that anyone

who's on supplemental estrogen should, by default, take 20 milligrams of B6 and tweak from there, but I would do it as a precautionary measure.

Katie: Wow, that's amazing. And the safety data, just to reiterate what you said, is up to 100 milligrams that can be safely taken based on what they've demonstrated? Is that also during pregnancy?

Chris: Yeah. There's no alteration to the safe limit in pregnancy for B6 or for molybdenum, which is the other nutrient we were talking about before. And, you know, there are people anecdotally who believe that they've developed problems from taking high doses of B6 that are in that range, but there's no published data of case reports showing that. And the published data of case reports shows that B6 can have neurotoxic effects at very high doses. All of those studies have used pyridoxine, and I actually think pyridoxal 5-phosphate is the ideal for P5P.

All of those studies also showed that the consequences went away as soon as you removed the supplement. And the minimum dose of B6 in any of those studies was 500 milligrams a day. Nothing below that has been shown to have negative effects. So when the Institute of Medicine set the tolerable upper intake level or TUIL, which is...you know, a lot of people are familiar with the RDA.

The TUIL, the upper intake level, is always set alongside the RDA, And the definition is basically, this is the dose that we would expect to have no risk of adverse effects in the general population. And that doesn't rule out that someone might have a hypersensitivity disorder or something like that. But, you know, if you take 100 people and you put them all on 100 milligrams of B6, you would expect approximately zero people to develop any problems from that.

You know, what they did with that was they took the lowest observed adverse effect at 500 milligrams, and they applied a safety factor of five-fold to that. So they said, "We don't have any evidence of this occurring at less than 500 milligrams, so we'll take 500 milligrams as the dangerous dose and say that, you know, even if there's 1,000 things that we don't know, 100 milligrams should be like the mega safe dose." And then 20 milligrams has been shown to normalize tryptophan metabolism, which is five times under that. So it's 25 times under what we have case reports showing problems of.

And so, you know, there's, like, dramatic windows of safety applied to get down to 20 milligrams. You know, and it's not well-studied, like, maybe the ideal dose that you need is 10 milligrams. I don't know. But there's some studies suggesting that 5 to 10 milligrams are not enough to normalize markers of B6 status in pregnant women, which suggests, to me, that the ideal dose for, like, minimizing risk of B6 deficiency symptoms during pregnancy and during any conditions of supplemental estrogen is probably at least 10 milligrams. And, you know, 20 has been shown to be effective in studies, so I'm happy with that, and I'm content that it's not a safety risk.

Katie: When especially that's a water-soluble vitamin. So, like you said, as soon as you stop taking it, your body should be okay, even if you had a high dose.

Chris: Yeah, I mean...so I actually think that's a myth that has been propagated very widely and doesn't have that much basis that the solubility of a nutrient is related to its toxicity profile. So, like vitamin E, although it might have some negative effects at high doses by interfering with the function of other fat-soluble vitamins, it doesn't actually have a toxicity syndrome at all, and vitamin B6, which is water-soluble, does. So even though...I mean, like yes, what the case reports showed is that it's reversible. I have no idea if that relates to its water solubility or not.

So, like niacin has a serious toxicity profile at very high doses, totally water-soluble, you know. So, like niacin and B6, both have toxicity profiles at very high doses. Thiamine, which is water-soluble doesn't. Riboflavin, which is considered a water-soluble vitamin, but it's actually, like, 50% fat-soluble. It's just, like, halfway in between water and fat solubility on a chemical solubility level, and at hundreds of times the normal intake has produced no safety concerns whatsoever.

So I actually think that the solubility really is, like, largely unrelated to the safety of nutrient. But, yeah, it appears to be completely reversible on the basis that the case reports showing, like, tingling in the hands and feet on it that when you remove it, it goes away.

Katie: That's a really interesting point and good to know because that's definitely something I have heard quite a bit, is that if it's water-soluble, it's fine, and you have to be really careful with fat-soluble vitamins. Since there's an estrogen component here, is it also logical to suggest that maybe people with, for instance, PCOS or other things that lead to estrogen dominance or have an estrogen dominant component could benefit from experimenting with this as well?

Chris: Yes, I think so. And actually, I think there's quite a lot of unanswered questions here. So, for example, in males, testosterone also increases hydrogen sulfide production in certain cells. And so it's, like, what does the increased androgens do in PCOS to this? I have no idea, you know. I'm highly confident in what estrogen is doing here. I'm rather confused about what testosterone is doing. And, I really have no idea what progesterone is doing.

So I'm highly confident that anything where you're approaching estrogen levels seen at the peaks during the menstrual cycle, pregnancy, birth control, and hormone replacement therapy are highly relevant. I think PCOS has a complex hormonal profile that I don't really understand exactly how it would relate to this. But I would definitely consider it because, if you think about the recommendations that I would make to compensate for this, basically molybdenum, you know, the average dose that you would try to get by default every day is like 45 micrograms.

The safe upper intake level is 2,000 micrograms or 2 milligrams. And the safety profile from that, I couldn't find any reliable human data suggesting problems with excess molybdenum, so they actually took fertility problems in female rats at the body weight-adjusted equivalent of 50 milligrams a day and applied this extraordinarily huge safety factor to wind down to 2 milligrams a day as the safe upper limit for humans.

So, you know, to go from a normal...like, imagine a pregnant woman is reducing her molybdenum intake just sort of by, you know, food aversions, and maybe getting down to 30 micrograms a day. There's a lot of room to go up between 30 and 2,000 micrograms. And so I'm guessing that, you know, 300 to 500 micrograms would be more than enough and way within the upper limit for molybdenum.

And like I said before, 20 milligrams of B6 should be more than enough. In most cases, you could go up to 100 and still way within the upper limit. And I would say that, you know, anything that seems sex hormone-related could plausibly relate to these things. My confidence being really high if estrogen being high is the main thing, and then the more complexities you add to that of hormonal imbalance, I'm less and less sure exactly what it means.

But if the symptoms of headaches, of insomnia, of queasiness or nausea, of GI distress, or of anything that seems related to allergies like hives, and itching, and redness, any of that cluster of symptoms that go along with definitely high estrogen and maybe other abnormalities in hormone metabolism, I would say, would be something where trying this completely safe thing of adding some extra 300 to 500 micrograms of molybdenum and 20 milligrams of B6 to, like, try and see if it works.

Katie: That makes perfect sense. To circle back on histamine for a minute, this is something I'm hearing a lot more about from the audience increasingly, so I'm wondering if it's something that's on the rise. Is this something that is universally worth trying for anyone suffering from histamine issues, and are there other things that come into play as well when we're just talking about histamine?

Chris: Yeah, okay. So I think that there are some complexities when you get to histamine. And, it depends where it's coming from, and it depends whether, for example, it's a food-based thing or it's more than that. So let's, like, sort of start with the gut and work our way inside. So, in the gut, there's histamine that you encounter in your food, and you can also have gut bacteria producing histamine. And if the gut bacteria are producing it, I don't know exactly what to do about that. But, you know, shifting the microbiome with prebiotics and probiotics would be the thing that really fits the bill.

But anyway, let's just assume the histamine is coming in from your food because there's plenty of histamine in foods. And if the histamine is coming in your food, then nausea and diarrhea are probably the big things you would expect at the gut level, but then histamine can get inside your blood. And when it's systemic, then that's where you can start to get more allergy-like symptoms like hives, itching, or redness, flushing. That's also when you could get changes in blood pressure.

By default, histamine lowers blood pressure, but sometimes you get an adrenaline response to that that causes secondary increase in blood pressure above normal. So any changes in blood pressure could be plausibly related. And then histamine can increase the permeability of the blood-brain barrier generally and let stuff in, including itself. And if histamine gets into the brain, histamine in the brain usually, by default, is produced inside the brain in a highly regulated fashion to regulate your wakefulness and alertness.

And this is why if you take Benadryl, for example, you get sleepy, and it might knock you out because it's antagonizing the histamine in your brain. On the flip side of that though, too much histamine in the brain could cause insomnia, or cause generalized anxiety, or could cause panic attacks. So, you know, trace it from the gut through the brain, and you're getting nausea, diarrhea, then you get inside, hives, itching, redness flushing, then blood pressure changes, and you get into the brain, insomnia, anxiety, panic attacks.

So, any of those things, the first line of defense is the production of diamine oxidase in the gut. So you can think of histamine as having two main defenses. Diamine oxidase is the extracellular defense. Methylation is the intracellular defense. When you're eating food, that's outside your cells, and it's going through your gut, which is actually literally everything from your mouth to your anus is outside your body because we're all sort of, like, a cylindrical tube, where the inside surfaces, mouth, the anus, that's outside the body. The skin is the outside surface outside the body, and things get absorbed to get inside the body.

So, in the gut, you're outside the body, you're outside your cells. You're producing massive amounts of diamine oxidase or DAO for the purpose of completely neutralizing all the histamine in your food. And the diamine oxidase could be missing from the gut due to nutrient deficiencies, or due to intestinal damage. Nutrient deficiencies, the ones that are most relevant are B6 and copper. There's some possible...and actually manganese is also important there, possible roles for vitamin C and possible role for riboflavin, although that hasn't been shown with the human enzyme.

Now, on top of that, you could just have intestinal damage that's damaging the cells that produce diamine oxidase. That kind of unravels a whole another area that I'm not really an expert in. My expertise is really in the micronutrients, the vitamins and minerals. For example, if you have an autoimmune condition like celiac disease that's destroying the intestinal cells, or you have some pathogen in there that's, you know, your immune system is trying to defeat the infection and is causing damage to your intestinal cells, possibilities like that are reasons for having low diamine oxidase activity.

And then, of course, I don't really know anything about how to modify this, but you could also have gut bacteria that are producing histamine as well. Then when you get inside...and actually this isn't just inside. So, inside your body, or even in the gut, you can have increased mast cell burden. Mast cells are those cells that produce histamine. And now we're getting into the area where we're not talking about the histamine in foods, we're talking about the histamine that you produce yourself. And so the normal way that you would think about this, like, the kind of conventional thing that would happen is in an allergy.

And in a traditional conventional allergy, you have your immune system reacting to some allergen, produces IgE antibodies that then activate a cascade of things that leads ultimately to the release of histamine by mast cells. You can also have things that cause mast cells to release histamine that you're not allergic to, and that's what sulfite does that we were talking about before. So sulfite will just act on the mast cell to make it release histamine, but it's not an allergy because there was no antibody made by your immune system.

It looks like an allergy because you get itching, hives, you know, redness, any of the traditional allergic symptoms that are caused by histamine, and it kind of walks and talks like an allergy because you might get it in response to certain specific foods if those are foods that have histamine in them or have sulfites in them that cause histamine release or whatever, but it's not an allergy because, in the case of sulfite or dietary histamine, there's no antibody-mediated response. So it looks, talks, walks, smells like an allergy, but it's not.

And in the mast cell, there's two categories of things that we should care about. One is antioxidants because oxidative stress increases histamine release from mast cells, and the other is methylation. And those two things are both, like, big cans of worms that we could each spend an hour talking about just on its own. But to briefly summarize, antioxidants, I think, a lot of people think about is like, "Oh, those are the things that are in berries, and fruits, and vegetables, and stuff like that," which I think is a misleadingly simplistic way to think about it. Your antioxidant defense is very much based on minerals and protein-related things that you make yourself. And I don't mean you make the minerals. I mean, you eat the minerals and you make enzymes that require the minerals.

So very briefly, protein, zinc, copper, selenium, iron, and manganese, vitamin E, and vitamin C, and all those colorful things in fruits and vegetables that people call antioxidants, those things together are the things we care about in terms of antioxidant defense. And then, on the second category, methylation, that's where we get into B12, folate, and choline as the top nutrients, and then we can peel layers away to get at many minerals and B vitamins working underneath those as the main support.

You know, so that is, I think, a pretty broad view of histamine generally and all the potential things that you could work on related to it. And then you want to ask questions like, where is histamine coming from? Because it might be primarily hormonal, like we were talking about before, or you might have, you know, a rare condition like mast cell activation disorder, mast cell activation syndrome, which might require finding a very good specialist to start digging away at.

Katie: That was an amazing overview. Thank you for that. I think you're right. There's so much at play there, but I think so much of what you just said is probably going to be really helpful to a lot of people. And, for my own curiosity, I wonder if there's a difference or any other considerations for women who tend to have their symptoms right around their periods or not at ovulation when estrogen strikes, but they have things like migraines, or PMS, or other symptoms right about when their period begins? Are there other nutrients that come into play in that scenario?

Chris: Yeah. So, first of all, I look specifically at this once to look at water retention. And, in general, I think that the other symptoms of PMS kind of go hand in hand here, but I didn't look at them as much as I was looking at water retention. And I was actually surprised to find that the key difference between women who have PMS symptoms, including water retention, which I was more focused on, and those who don't is that they actually have higher progesterone levels in the days leading up to menstruation. So the progesterone should be like an ovulation-related sort of, like, post-ovulation spike during the breakdown of everything produced during ovulation, but it should be cleared effectively by the time you get into menstruation.

And the women who have PMS-related symptoms, especially where I was looking at in water retention, they basically produce the same levels of all the hormones, but the primary difference is the clearance rate of progesterone is a lot lower. And my suspicion is the water retention issue is driven by the fact that one of the ways that you can get rid of excess progesterone, it's... Actually, this isn't really a way of getting rid...it shouldn't be a way of getting rid of progesterone. But progesterone, if it's elevated and not cleared through the normal ways, can spill over into aldosterone production, which can cause retention of sodium and loss of potassium, and with retention of sodium comes retention of water.

I don't know if that would cause some of the other symptoms, although I could imagine it would because if you retain water, you're going to get swelling everywhere. And if your blood volume is increasing, and you're getting generalized swelling in extracellular space, you're going to put pressure in a lot of places that wouldn't otherwise have pressure. And, in your head, I think that would cause a headache. I'm not saying that's the only thing, but it just might be a contributor there.

And so, specifically, in the case of water retention, salt is controversial. So there are some cases that I think are the exception to the rule where sometimes you can reduce water retention by increasing salt, but that's not normally the case. And I think for most women in that case, probably reducing salt and increasing potassium is going to be the thing that's best going to help the water retention. In terms of both, and I don't know the mechanisms here, but in terms of both the water attention and the other symptoms of PMS, magnesium and B6 have been the top things that have been helpful.

I think the doses... I'm blanking here. I don't have 100% confidence on this, but I believe that the papers I was looking at, the doses are around, like, 40 milligrams of B6. I would use P5P for the form of B6, and somewhere around 200 or 300 milligrams of magnesium, so higher doses of B6 and people are usually using lower doses of magnesium that a lot of people are using. But both of those seem to have some positive benefits in a number of human trials.

And then for PMS symptoms, the data is less good for manganese, but low manganese levels correlate with PMS symptoms. And it's possible that manganese supplementation would help, but no one has clearly shown that. But notably, manganese along with B6 are co-factors for diamine oxidase, so it could all come back to

histamine metabolism in some way in terms of some of those symptoms. But I don't think histamine would be related to the water retention, but headaches and mood disturbances, maybe.

Katie: That's really interesting. And I'm definitely gonna plug your book, "Testing Your Nutritional Status," because I think that's a great place for people to delve in and try to figure out what they specifically need to take.

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Katie: But I am curious, when it comes to women and hormone fluctuations, either during pregnancy or just during normal monthly cycles. Are there nutrients in general in any amounts, that you would say, on average most or all women should be taking or it's safe to take than not take?

Chris: Can you go over the context again? You were talking about pregnancy, or you were talking about through the menstrual cycle.

Katie: I would say they need to be separate answers. During pregnancy, are there things that women need to be especially cognizant of and then also hormones?

Chris: Yeah. So, pregnancy, the nutritional recommendations are generally made around birth defects. And I think those are... I mean, I would reinforce those. So, like, the typical pregnant woman is going to get put on prenatals to have extra folic acid in them, for example. I would say you want to make sure you're getting full...I would prefer using methyl folate as a supplement. But I think making sure you're getting the RDA for folate through that is really important. I mean, that's mainly used to prevent neural tube defects, which are mainly spina bifida, and then another rare one that is just fatal.

It's, quantitatively, like, the likelihood of that happening is very small, but the consequences are so devastating that, you know, it's just worth it to reinforce those recommendations. One nutrient that I haven't talked about yet, but it applies across the board to all estrogen-related things here. And actually, this is a good bifurcation between pregnancy and other estrogen conditions. So, estrogen increases copper absorption from the gut, and the placenta during pregnancy causes all that extra copper to go to the baby.

So I don't think that you need extra copper during pregnancy because you hyper absorb copper and you hyper transport it to the fetus. But estrogen outside of pregnancy causes you to hyper absorb copper just as much, and you don't have a placenta. So, there's nowhere to put it. It just accumulates. Now, in most cases, probably what happens is the woman's liver just makes more proteins that bind copper such as ceruloplasmin to protect the copper from causing problems. But if the woman does not make enough ceruloplasmin and other copper-binding proteins, the free copper can cause a lot of problems. It can cause serious problems in the eyes. It can accumulate in the brain and contribute to neurodegenerative diseases later in life.

It can generally cause oxidative stress. So, what I would suggest is, normally, I would say the upper limit for what you really want to steer clear of copper is, like, 10 milligrams. I would cut that down to 5 milligrams for anyone who is on supplemental estrogen. You know, during the estrogen peaks in the menstrual cycle, if the menstrual cycle is normal, I'm not too worried about it because it just goes up for a couple of days, comes down, goes up for another couple days, comes down. It's not a major...you're gonna hyper absorb copper during that time, but, you know, more days than not, you just have normal estrogen levels for a woman and so it all kind of evens out.

But when you're on birth control, or when you're on hormone replacement therapy, those are essentially the only other conditions where you'd have chronic exposure to estrogen like you would in pregnancy. So, you're going to hyper absorb copper and not have any place to put it. So I think it's best to cut the upper limit for copper in half, down to 5 milligrams, and then just more generally not go out of your way to increase the 5 milligrams. So, I'm not too worried about foods. Copper-rich foods include liver, mushrooms, seaweed, shellfish.

You know, those other foods have things that balance copper and protect copper from causing problems like zinc, for example. So I'm not saying, you know, micromanage your fruits and don't hit 5 milligrams. But I'm

saying like, you know, if you're taking supplements, don't use supplements to go above 5 milligrams total intake. And, you know, don't go out of your way to try to hit 5 milligrams or higher with your foods.

But for pregnancy, I would say, you know, the copper is just sort of, like, you want to get your minimum requirement for copper, and you don't have to alter it because you are going to absorb it better, and you are going to do something with that copper. So another concern with pregnancy is vitamin A. And I don't think the evidence is strong on this, but there is some very limited evidence that I think is very shaky that vitamin A intakes over 10,000 IU during the first eight weeks of pregnancy could cause birth defects.

And I want to reiterate here, like, triple reiterate here, the data is not good, the data is not good, the data is not good. However, most women have no need to go over 10,000 IU of vitamin A. I mean, yes, if you have signs of vitamin A deficiency because you're poorly absorbing it, or there's some other thing that is causing your needs to go up, and you're monitoring blood levels, and you're working with someone who's sort of managing your nutrition with you, fine.

But if you're planning on getting pregnant, and you don't have any symptoms of vitamin A deficiency, and you don't have any reason to think you have higher than normal needs of vitamin A, then, even though the data is not good, the data is not good, the data is not good, it's prudent to not supplement with vitamin A to bring your intakes of retinol, which is the animal form of vitamin A that we're most concerned with here, to not bring those over 10,000 IU per day.

After eight weeks, it doesn't matter. So I think that's one concern that women will encounter, and that's basically, like, if they hear it. They might hear it put another way by someone who's looked at the data less, like, "Vitamin A is toxic to your baby. Don't take vitamin A when you're pregnant." So what I just said I think is the way to say that that actually sticks to the kernel of truth that's there. And then, like we said before, managing morning sickness and just being proactive with, I would say, maybe like 100 to 300 micrograms of molybdenum on a proactive basis and 10 to 20 milligrams of B6 on a proactive basis as P5P.

And then, you know, I mean, for women who are philosophically natural-minded and don't want to take extra supplements, I would say, like, you know, try to hit your targets for those foods. But honestly, like, telling a woman to eat a lot of beans when she's pregnant might not go over very well. So taking 100 to 300 micrograms of molybdenum, taking 10 to 20 milligrams of P5P form of B6, and then... Well, one thing I didn't mention before is that, folate, all the emphasis is on folate, but choline is very important to methylation, helps conserve folate.

And although we don't have data in pregnant human women, we have data from rats suggesting that, if we were to extrapolate to humans, suggesting that if a woman got three times the basal requirement for choline during pregnancy, and during nursing, and then supported the growing child with three times the minimum recommendations for the first four years of life, that that could have extremely profound benefits to the brain, especially as an increase in audio spatial memory dealing with, you know, sounds and visual perception of

space, preventing interference memory, which is the kind of memory loss where you forget where you parked your car when you go to the grocery store because you parked at that grocery store, you know, 350 times before, and you're mixing all the 350 memories of where you parked your car.

And then, also, in these rats, it basically fully protects them from age-related senility at the end of life. So we're talking about choline during pregnancy, nursing, and first four years of the child's life, conferring brain benefits at, you know, 70, 80, 90 years old. So, I think, I actually have a good thing to link in the show notes would be my choline database. You can also Google "Masterjohn choline database," and you can go see my recommendations there of how to get choline from foods. And if you could make a mix of choline and betaine that gets up around 1,200 or 1,300 milligrams a day from those foods, then I think that would be great to do. And you can make up the balance of supplements. I have specific recommendations for how to get choline supplements on there as well.

And I would summarize those by saying phosphatidylcholine is the best form of choline to take, and it's the form that's predominant in food. And you just have to be careful that, usually, when you take a supplement, the dose of phosphatidylcholine and not the dose of choline is mentioned on there. So you have to multiply it by...excuse me, you have to divide the dose on the bottle by eight to know the amount of choline you're getting. And then trimethylglycine or TMG, you could just sort of like take that alongside the phosphatidylcholine half and half to get that.

And then the last thing I would mention is biotin. So about one-third of women spontaneously become biotin deficient during pregnancy, and biotin deficiency can cause a lot of skin problems and mood problems. So depression is a major risk of biotin deficiency as is dermatitis, which can affect a number of areas around the face and also the perineum, which is between the vagina and the anus. Particularly dermatitis in that area, like, being in the perineum would be kind of a red flag for biotin deficiency.

But also the fact that just with good markers, we know that a third of women just become biotin deficient when they're pregnant because of their pregnancy, and it goes away after pregnancy. But, you know, how many women develop skin problems and depression during or after pregnancy? So, there, getting a few eggs a day would be your best bet. And honestly, if you try to meet the choline requirements I was just talking about, you will, by accident, meet the biotin requirements. But it's also perfectly safe to put, you know, as much as 1, 2, 3, 4, 5 milligrams of biotin in your food, which is actually way higher than what you would need.

What you're getting for food if you shoot for, like, four egg yolks a day is going to be more on the order of 30, 40, 50 micrograms, and a microgram is a thousandth of a milligram, you know. Basically, with a supplement, if you add like 1 milligram of biotin in there, you're getting completely safe amount of biotin that is definitely in excess of what you need. That's my general view of pregnancy.

Katie: That was super helpful. And the last one I'll ask you about today, but I think I'm just gonna have to keep asking you back is vitamin D because I know I've seen studies on vitamin D deficiency, and like low birth

weights, or premature labor, and there seem to be some really big implications, but also it is one that can store in the body for at least from what I've read. So I know it's one that you want to test and you want to know what your levels are. Do you have any data that you've seen or guidelines you would give about what target vitamin D level to aim for and what form is best to get that from?

Chris: Yeah. So, you know, vitamin D is interesting because there has been so much enthusiasm and research on vitamin D promoting high levels of it that we kind of have this...you know, which was genuinely merited by the fact that there has been and still is widespread inadequate vitamin D levels. Like, there was a study in the UK a couple of decades ago that showed that in a third trimester of pregnancy, women in the UK, on average, would have their vitamin D levels dropped to zero.

That's, like, you know, ridiculously in need of a Vitamin D, right? And yet, we have, like, this bifurcation between kind of the general population where they probably need more vitamin D, and then we have health-conscious populations where everyone's supplementing. And the funny thing that...you know, the majority of those people are probably getting too much, even though they, you know, certainly are people with very high needs that are minorities but are important to include here.

And so, yeah, it's fat-soluble. But, you know, more importantly, it does have a toxicity profile, and it does increase the risk of soft tissue calcification. And I also think we always have a danger when people are told to avoid vitamin A and to take vitamin D. The risk of soft tissue calcification is going to increase because vitamin A protects against soft tissue calcification caused by too much vitamin D. So, I think, on a background for vitamin D supplementation, you don't want to get into the hype around paranoia about vitamin A because that in and of itself is going to make vitamin D less safe.

But in pregnancy, the vitamin D needs are very similar to a non-pregnant woman for the first two trimesters. And then, in the third trimester, the fetal skeleton starts to get mineralized. And when that happens, there's, like, a massive mobilization of calcium, phosphorus, and vitamin D all going towards the mineralization, the fetal skeleton. And that's when you see 25(OH)D levels, which is the marker that we use for vitamin D nutritional status drop in women's blood.

Now, vitamin D is also complicated by the fact that the levels of the markers change during pregnancy. And so, it's actually, like, it makes things difficult because the way that they change are not... It's well-characterized what happens, but it's not well-characterized what it means in terms of how to re-interpret the markers to know whether women need more or less. And, as a result, I think that the reason that makes things difficult is that we have this voluminous data on, you know, thousands of studies of tens or really hundreds of thousands of people on how to interpret those markers, and they just don't apply to pregnant women.

So what happens in pregnancy is that 25(OH)D, which is the traditional marker that is mostly used to assess vitamin D status, goes down, calcium levels go down, and parathyroid hormone levels go down. Parathyroid hormone or PTH is generally a marker of...like, the higher it is, the more you need vitamin D and calcium. And

meanwhile, calcitriol, which is the active hormonal form of vitamin D goes up. And I think these are probably adaptations to supply calcium to the fetus while simultaneously minimizing the risk of bone loss to the mother because PTH, which rises when you have deficient calcium and vitamin D, helps mobilize calcium to get into your blood by taking it out of your bones.

So, basically, what pregnancy is doing... And calcitriol, the active hormonal form of vitamin D, it does take calcium out of your bones, but it also increases absorption of calcium from your food. So, basically, PTH and calcitriol are two different ways that you can mobilize more calcium into the blood, which, in the case of pregnancy, you're trying to get it to go to the fetus. And what pregnancy is doing is, and I don't know what mediates this, estrogen, progesterone or, you know, chorionic and...I don't know what it is. Something in pregnancy is shifting the balance to a calcitriol dominant state to take more calcium out of your food and less calcium out of your bones. That way, overall, you get net more calcium moving to the fetus, but to the degree you're not taxing the mother's bones.

You can support that system by supplying more vitamin D to the mother, and that's going to funnel in to bring 25(OH)D levels back up, which we measure as the main marker of nutritional status. It's also the precursor to calcitriol, so it's going to spill into calcitriol production. The more calcitriol you get and the less PTH you get, the more you're going to protect the mother's skeleton, while also simultaneously maximally extracting calcium from food to shift towards the fetus. At the same time, you can support that by getting more calcium in the diet.

We talked about this last time. I think the calcium requirements, the official calcium requirements are not changed during pregnancy if I remember that right, but, I think they clearly are, physiologically. And more to the point, I think a lot of women who are, you know, maybe altering what they eat because of pregnancy and their food aversions and so on, and then, on top of that, women in our audiences who are health conscious are often...especially like in the Paleo world, this is also true in the vegan world. A lot of people are worried about calcium supplements.

And I would say that in pregnancy, especially in the third trimester, to support mineralization of the fetal skeleton with minimal risk to the woman's bones, you at least want to hit the RDA for calcium, and I would say go a little bit above it. So consistently hitting like 1,200 or 1,300 milligrams of calcium I think would be the ideal thing, alongside taking whatever vitamin D will keep your 25(OH)D levels up into the normal range, which, you know, to me, you're looking at 30 to 40 nanograms per milliliter, in my opinion. And then, you know, it's perfectly safe to take an extra 1,000 or 2,000 IU of vitamin D if you're not measuring your blood level, but it'd be ideal to measure your blood levels.

Katie: Amazing. That is so practical and helpful. And, once again, our time has completely flown by, and you're just gonna have to come back at some point.

Chris: I would be happy to.

Katie: Thank you so much for the time today. I know how busy you are. And I'm so grateful for you coming back again to share even more, and I look forward to more episodes in the future.

Chris: Awesome. Can't wait.

Katie: And thanks to all of you for joining us and listening today, and I hope that you will join me again on the next episode of the "Wellness Mama Podcast."

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