

## HPA-D 3-5 – Part 7

Okay. In this next section, we're going to talk about supplemental nutrients, botanicals, and hormones as part of HPA-D treatment. Remember, a successful treatment must always include diet changes, lifestyle behavior changes, and possibly some of the adjunctive therapies that we just talked about. That said, supplements, botanicals, and, in some cases, even hormones can be necessary and very effective parts of the overall treatment plan.

In the diet section, we talked about nutrients that play an important role in HPA axis function, including vitamin C, B vitamins, potassium, sodium, calcium, zinc, and magnesium. The simplest option is a high-quality multivitamin that provides these if your patient is not getting adequate amounts in the diet, or if you feel he needs additional support. However, I am reluctant to recommend long-term calcium supplementation because of studies that show increased risk for heart disease and cardiovascular disease in both men and women.

Calcium should be in the hard tissues such as the bones and the teeth, and it should stay out of the soft tissues, and the problem with longer-term calcium supplementation is that the calcium likely gets into the soft tissues because the body is not accustomed to dealing with such a large bolus of calcium at one time as you would get in a supplement or in that particular form. Studies have shown that calcium supplements do have a different effect on the body than even an equivalent dose of calcium in food, so given the state of the research right now, I think long-term calcium supplementation is not a good idea. Most of the multivitamins that I would recommend, even for HPA axis support, do not contain calcium for that reason. I do think there is probably less risk if you're using a multivitamin that has calcium in it for a short-term therapeutic period while you're addressing HPA axis function, let's say over a course of several weeks or even a few months, but you would want to make extra sure that you tell your patient to discontinue that multivitamin or anything else with calcium in it over the long term.



### **Vitamin C**

2 grams/d in  
liposomal form



### **Magnesium**

400-600 mg/d in  
glycinate form



### **Pantethine**

450-900 mg/d

If the patient is eating a very nutrient-dense diet, you may not need to supplement with these nutrients at all, but another option is supplementing selectively, which I've always been a bigger fan of than taking a multivitamin, so you can provide higher doses of each nutrient when you do it that way. You could do up to 2 g per day of vitamin C in a liposomal form, which is more bioavailable, 400 to 600 mg per day of magnesium in a glycinate or malate form, and then 450 to 900 mg a day of pantethine, which is the active form of B5.

You also need to consider nutrients that address key activators of the HPA axis. We've talked about glycemic dysregulation, circadian disruption, and inflammatory signaling being three of the four drivers of HPA-D, so if your patient is suffering from one or more of those, then we can think about nutrients and supplements that address those particular drivers.



Let's start with glycemic control. Of course, diet, exercise, sleep, and physical activity are the most important, but if those changes don't regulate blood sugar sufficiently, then we can consider nutrient and botanical blends. I like Metabolic Synergy and GlucoSupreme from Designs for Health. Soluble fibers such as PGX or glucomannan and resistant starch such as potato starch can also be helpful. Some patients with advanced blood sugar issues may even require a medication such as metformin if they are too far down the track to respond adequately to nutritional and supplemental approaches.

For inflammatory signalling, I would consider curcumin, boswellia, skullcap, EPA, and DHA. Starting with curcumin, this is, of course, a compound found in turmeric, and there is quite a lot of research behind it at this point. In addition to reducing inflammation, it also promotes T-regulatory cell production and differentiation, and it reduces oxidative stress. It exerts its beneficial effects by modulating different signaling molecules, including transcription factors, chemokine, cytokines, tumor-suppressor genes, adhesion molecules, and micro-RNA.

It's important to understand that the bioavailability of curcumin varies widely depending on the preparation. In just typical preparations, curcumin and curcumin found in turmeric, the spice, are not particularly bioavailable. This is a pretty confusing area. It seems like there is a new form of curcumin introduced every year with claims that it is the most bioavailable form of curcumin of all time, or certainly every couple of years, and these include liposomes, nanoparticles, polymeric micelles, phospholipid complexes, and microemulsions. It's very controversial because studies don't compare the same variables. Some look at curcumin metabolites, for example, in the blood, while others look at the concentration of actual curcuminoids in the blood. Bioavailability is only

one consideration. You also have to consider the biological action of these various forms of curcumin, so it is not easy to parse it out just by looking at the studies.

What I can tell you from having looked at the studies and having used just about every form of bioavailable curcumin is that at the time of this recording the two that I prefer and use most regularly are the Longvida form, which has a decent amount of research behind it. It may have particularly positive effects for the brain, as it has been shown to improve mood and cognitive health in the elderly, and it may suppress tau oligomers and correct molecular chaperone deficits in the brain, so it may actually help to prevent against Alzheimer's. The Longvida form is one form that I find myself using, particularly in cases of neurodegenerative disease, and the other form that I like is the liposomal form, which is relatively new. There is not a ton of research on liposomal curcumin bioavailability, but generally, liposomes are quite bioavailable as a means of oral delivery, whether you're talking about glutathione, curcumin, or anything else. We've seen good response clinically to liposomal curcumin.

Next is boswellia, also known as frankincense, another botanical with anti-inflammatory properties. It's a gum resin extract from a tree that grows in the dry mountainous regions of India, northern Africa, and the Middle East. It inhibits tumor necrosis factor  $\alpha$ , interleukin-1  $\beta$ , nitric oxide, and mitogen-activated protein kinases, or MAP kinases. Data suggests that of the various boswellic acids, 3-acetyl 11-keto  $\beta$ -boswellic acid, or AKBA, is considered the most powerful. Some newer products on the market contain only boswellia AKBA, and they are much more expensive. The dose of standard boswellia is about 400 mg per day, while the more concentrated or isolated AKBA is 100 mg per day.

There is some logic to taking curcumin and boswellia together because they work with complementary mechanisms or pathways. Curcumin primarily inhibits cyclooxygenase-2, or COX-2, that pathway, which is what the same pathway that ibuprofen inhibits, whereas boswellia is a 5-lipoxygenase, or LOX-5, pathway inhibitor, so they have a complementary mechanism of action, and if you use them together, it often has a better effect than using either one of them apart.

The next botanical to talk about is *Scutellaria baicalensis*, which is Chinese skullcap, not American skullcap. There is a very important difference, so just be aware of that. Chinese skullcap reduces the expression of nitric oxide; inducible nitric oxide synthase, which is one of the more inflammatory forms of NO; cyclooxygenase-2, again it's a COX-2 inhibitor just like curcumin is; prostaglandin E2; and nuclear factor kappa beta as well as other inflammatory cytokines such as interleukin-1  $\beta$ , interleukin-2, interleukin-6, interleukin-12, and TNF $\alpha$ . It's neuroprotective. It reduces neuroinflammation, supports memory and learning, reduces anxiety, and can improve blood glucose. I like the tincture form of Chinese skullcap from Woodland Essence, and the dose would be one full dropper twice a day.

Finally, EPA and DHA have been shown to reduce inflammatory markers in a wide variety of conditions such as rheumatoid arthritis, diabetes, and pain conditions. I believe, as we've discussed elsewhere, that eating a pound of cold water, fatty fish is the best way to get a sufficient amount of

EPA and DHA into your diet. You may be aware that there has been a lot of research that has come out over the past few years suggesting that high doses of fish oil aren't as beneficial as was once believed, particularly for cardiovascular conditions, and may even increase the risk of certain diseases, which makes sense if you think about it because they are polyunsaturated oils. They are highly susceptible to oxidative damage. Eating fish is, I think, a safer strategy and one that is more in alignment with an ancestral framework.

When we're talking about fish consumption, there are always a variety of questions that come up about mercury and other toxins that are in fish. Without going into detail here, since we're covering that in different parts of the program, I think just aiming for lower-mercury species of fish is probably a good use of the precautionary principle, and people who can't eat fish or won't for any reason, then supplementing with cod liver oil or wild salmon oil can provide some of the benefits of EPA and DHA.

Okay, now let's talk about supplements for circadian disruption. There are a number of botanicals that have been shown to assist with circadian regulation such as valerian, passionflower, jujube, and hops, and these can be effective. They are usually best taken in low to medium doses, particularly valerian, which can be really sedating and cause a hangover effect, so you want to start slowly with that one in your patients. Bedtime Tea from Yogi Tea is a great blend with some of these botanicals that can be purchased over the counter, and there are other similar blends that are good options. Tranquility from Natura Health Products is a good oral supplement blend of these nutrients.