Eliminating the Top Causes of Insomnia:

Neurotransmitter Deficiency and Cortisol Excess

I wrote this article in response to a T.L. article, "The Cortisol-Sleep Connection" published in the November 2010 issue and co-authored by Tori Hudson, ND, and Bradley Bush, ND (of Neuroscience.) That article was introduced with informative research-based data, laudably drawing attention to the often critical role of cortisol elevation in sleep disturbance. It also mentioned the role that some neurotransmitters can play in this problem. However, its second section, which focused on clinical recommendations, was riddled with errors and contradictions. I felt compelled to provide more accurate information on the treatment of what amounts to a national epidemic of insomnia, with far reaching physical and emotional consequences. In fact, I assigned an analysis of the Hudson/Bush article to the health professionals in my year-long NeuroNutrient Therapy Certification Program as an exercise in the evaluation of clinical information. What follows is a collective critique, along with clinically relevant suggestions, and case examples.

I have been the director of a holistic clinic in the San Francisco Bay Area for almost 25 years. In that time our clinic has provided nutrient therapy to at least two thousand insomniacs. The careful diagnosis and targeted treatment of the underlying causes of each sleep disorder have led to successful outcomes in

almost every case. At least half of our sleepless clients have responded quickly and well to neurotransmitter precursors such as GABA, tryptophan, and/or melatonin. Others have required very specific cortisol-lowering regimens instead or in addition. These latter cases have tended to involve more severe sleep disturbances and, often, the use of highly addictive benzodiazepines, the only class of pharmaceutical in current use capable of temporarily suppressing cortisol levels.

INITIAL INTERVIEWS OF INSOMNIACS

A detailed sleep function assessment has been crucial for determining the course of successful therapy:

- How long have you had a sleep problem?
- Did it begin during or after a particularly stressful time?
- Does insomnia run in your family?
- What time do you get to sleep?
- How long does it take to fall asleep?
- How long do you sleep?
- How often do you wake up in the night? For how long?
- Do you need to take benzodiazepines such as Xanax, Ativan, or Klonopin to sleep? Or marijuana? Or alcohol? Or carbs?
- Do you have many of the symptoms of any of the following three types of insomnia?

Type One Insomnia: Serotonin/Melatonin Deficiency

This is the most common cause of insomnia in our experience: When levels of the extraordinary antidepressant neurotransmitter, serotonin, are subnormal, there is typically inadequate surplus to use for conversion to melatonin. What results is a difficulty falling asleep (night owl syndrome) more commonly than one of staying asleep (though either or both may be present.) Either way, worries and obsessive thoughts make wakefulness unpleasant. This syndrome is often genetic and longstanding (though the severity may have increased over time.)

The following is a list of the common symptoms of serotonin deficiency, which helps us rule this syndrome in or out as a cause of the particular insomnia being endured. We ask that it be filled out using a severity scale from 1 to 10.

night-owl, hard to get to sleep
disturbed sleep, premature awakening
negativity, depression
worry, anxiety
low self-esteem
obsessive thoughts or behaviors
hyperactivity / tics
perfectionism, controlling behavior
winter blues
irritability, rage (eg PMS)
dislike hot weather
panic attacks; phobias (fear of heights, small spaces, snakes, etc)
fibromyalgia, TMJ, migraine
afternoon or evening cravings for carbs, alcohol, or pot

*The frequent use of benzos is not part of this syndrome.

Re Serotonin Testing: Blood platelet testing for serotonin levels is superior to any but cerebrospinal fluid testing and almost as hard to find. Blood plasma testing gives a rougher idea of actual levels. Research and practice have convinced us that urinary neurotransmitter testing is very unreliable. (See my article on this subject originally published in the TL 10/06 and posted on my website: http://moodcure.com/relarts.html

TREATMENT FOR TYPE ONE INSOMNIA: Tryptophan (500 – 2000 mg for adults--less with children), taken when insomnia occurs, e.g., at bedtime and/or in the night, is the first treatment of choice. 5HTP *raises* cortisol (should hypercortisolism also be an issue) so we avoid it in serious insomnia cases (otherwise nightmares or other sleep deterioration can result.) If tryptophan does not do the whole job, we add melatonin (.5 – 5 mg) as an immediate-release supplement for bedtime-only insomnia, or in a delayed-release form for later-in-the-night awakenings. (We prefer NOW Foods' two-stage release Melatonin.)

Re dosing: We start with the lowest dose and have our clients go up as needed. Children under 14 start with a small amount from an opened capsule, mixed with mashed fruit or any other palatable protein-free food. The younger and more sensitive the child, the less provided.

Type Two Insomnia: GABA deficiency

Gamma amino butyric acid is the brain's primary inhibitory (i.e., calming) neurotransmitter. It neutralizes adrenaline as a primary function. A GABA deficiency can accompany a serotonin/melatonin deficiency, or cause sleep problems on its own. Here, muscle tension and other symptoms of overstress interfere with sleep. The following is a list of common symptoms of GABA deficiency which, again, helps us to determine if this syndrome is a significant factor in a particular case of insomnia.

overstressed and burned out
unable to relax/loosen up
stiff or tense muscles
often feel overwhelmed
may experience panic attacks
when resorting to sleep meds, respond best to the benzodiazepines

Re GABA Testing: We are not satisfied with any lab testing for levels of this neurotransmitter. (GABA is not found in the platelets.)

TREATMENT OF TYPE TWO INSOMNIA: 100-500 mg of GABA taken whenever sleep is a problem can be very helpful along with, or instead of, tryptophan/melatonin. The Hudson/Bush article makes the signature Neuroscience (and Senesco) error of, while recommending that levels of the inhibitory neurotransmitter GABA be enhanced, not recommending GABA supplementation itself. GABA is wildly effective (at 100-500 mg, at bedtime

and/or later in the night on awakening) for all over-stressed states, including many cases of insomnia. We do avoid GABA 750 mg, as reverse syndrome (e.g., anxiety) may develop at such high doses. In the few non-responders to GABA, l-theanine often provides a very similar calming effect as they note.

Type Three Insomnia: High Cortisol

Excessive stress always raises our levels of the stress-coping giant, cortisol, the chief of our stress-response team (which also includes adrenaline and endorphin.) Chronic stress can lead to a permanent hypercortisol state—even long after the precipitating events have resolved. When this disturbance occurs at night, when cortisol levels should be at their lowest, the quality of insomnia is typically an alert "ready to get to work" one or an agitated and hyper-vigilant, or even a startled or shocked sensations on sudden nocturnal awakening.

Because, chronically elevated cortisol suppresses serotonin and exhausts GABA, the worried Type One and tense Type Two Insomnia conditions are a regular, but minor, feature here. The balance of this article will concentrate on the less well understood, but often critical, dynamics of Type Three Insomnia.

ASSESSMENT OF NIGHTTIME CORTISOL LEVELS:

In addition to the initial sleep status assessment, salivary cortisol testing is critically important--specifically, salivary collections *in the night at the time(s) that sleep is disturbed*. Without the results of such testing, we cannot be sure if a

particular person's insomnia is high-cortisol related or not, and should be reluctant to suggest therapy. All labs can have lapses, but for the most part we find this to be the most clinically relevant test we've ever recommended. Because we are typically concerned about daytime as well as nighttime adrenal function, our clinic usually recommends the standard four samples: three daytime samples plus a bedtime (10 - 12PM) sample. We add a 1 - 5AM sample, if early awakening is a problem. *Use bedtime reference ranges to evaluate any samples collected between 10PM and 5AM.* Alternatively, you could order one or more single sample cortisol test kit(s) to be used only during the sleepless period(s).

LOWERING CORTISOL LEVELS

We start by providing rich, *basic adrenal support* using high dose multi-vitamins[1], multi-minerals, and extra vitamin C to support a *blood-sugar stabilizing diet* of at least 3 meals, each including 20-25 grams of protein, adequate fat (preferably including saturated fat), and no sugar or other refined carbs. We typically suggest 1000-1500 mg of glutamine between meals to support blood sugar stability. If compliance is a problem, we refer clients to the questionnaire from my book *The Diet Cure,* to identify whether persistent carbohydrate cravings may be due to neurotransmitter deficits, chronic under-eating/dieting, food allergy, yeast overgrowth, or sex hormone dysregulation.

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[1] We prefer True Balance by NOW or GlucoBalance by Biotics for their strong blood sugar regulating inpact, stable blood sugar spares the adrenaline- and cortisol-raising impact of hypoglycemia.

Providing nutrient supplements that specifically lower cortisol: Perhaps 15% of cases of chronically elevated nocturnal cortisol respond well to GABA and/or tryptophan or melatonin. The rest require the nutrients I'll mention next.

The use of phosphatidyl serine to lower cortisol is advocated by Hudson/Bush and many others. However, we have found that the phosphorylated form of serine (e.g., Seriphos[2]) has a much stronger cortisol-lowering impact. DiagnosTechs' comparison trials demonstrated this years ago. Our clinic has used both forms and can attest to the superiority of the phosphorylated form. It is, in fact, one of a very few substances that can permanently subdue really stubborn cortisol elevation after only a few weeks or months of use. Hydrolyzed casien (Lactium[3]) is another. We often combine the two. Seriphos usually needs to be given 4-6 hours prior to an elevated-cortisol sleep disturbance, while (1-2) Lactium 85 mg. works immediately. Only (3) Seriphos per day may be used, while Lactium may be used more freely. (See the case studies that follow.)

Cortisol-lowering Herbs. Holy basil can be helpful, as can reishi and magnolia bark. We use them for sensitive people who do not tolerate Seriphos or Lactium well. Acupuncture/Chinese herbs for kidney/adrenal treatment should always be considered, especially when cortisol is elevated during the day as well as at night.

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[2] Contact InterPlexus.com for information on its use and contraindications.
[3] Supplements of Lactium/hydrolyzed casein are made by Swanson Health Products (Women's Stress Formula), Biotics (De-Stress), and others.

Avoid *supplementation with stimulating, cortisol-elevating nutrients.*
For example, insomnia caused by high cortisol is not eliminated, but, rather, exacerbated by the use of the stimulating amino acid, *l-tyrosine* (l-tyrosine converts to noradrenaline and adrenaline.) The Hudson/Bush article recommends tyrosine, but also mentions that elevated noradrenaline is part of sleep disturbances along with excessive cortisol...? If indicated by the noradrenalin deficiency symptoms of fatigue or poor concentration, we might recommend tyrosine in the AM only. Typically we forgo such treatment until after cortisol levels are lowered, and often find that the resulting improved sleep alone restores energy and focus.

The *"adaptogenic" herbal mixture*s recommended by Hudson/Bush and others typically contain ashwaganda and licorice, which *elevate* cortisol. Their article actually mentions that ashwaganda has proven to be energizing (and licorice certainly is.) We have found these herbs, even when combined with more calming herbs, to be too stimulating for many of our already hyper and sleepless high-cortisol clients. (We like them for clients who need help raising low cortisol levels, but we prefer Isocort.)

Other Cortisol-Normalizing Considerations. Stress reduction/management needs, the use of caffeine, alcohol, and other cortisol-elevating drugs as well as excessive dieting or exercise (which also elevate cortisol) may need to be evaluated and addressed.

Where benzodiazepines have been used as regular sleep aids and addiction has resulted, a gradual taper, supported by all of the above nutrients, as needed, guided by the Ashton Manual[4] may be required. IVs emphasizing vitamin C (15-25 grams) and taurine are helpful on taper days to reduce or eliminate withdrawal symptoms. (IV-administered GABA sometimes has adverse effects, but taurine strongly and benignly supports GABA fubnction in the brain.)

Stress and Disrupted Sleep Associated with Elevated Cortisol: Two Successful Cases

With the proper use of the right tools, the stubborn insomnia caused by neurotransmitter deficiency and/or chronically elevated cortisol can be cured very quickly. Here are two examples from cases written up by health professionals who are candidates for certification in my current NeuroNutrient Therapy Institute's (NNTI) training process.

Case #2 from the practice of Julian Isaacs, PhD, Marin County, California:

VA is a forty one year old single woman with a history of childhood familial psychological abuse. She presents as an intelligent individual who is under considerable stress. She is working a demanding job as well as training to be a nurse. She contacted this office with reference to her sleep disorder in late 2010. Her diet was reported as being of good quality and she was not taking any kind of stimulant food or drinks, nor

[4] Benzodiazepine tapering protocols by UK physician-specialist Heather Ashton are available at http://www.benzo.org.uk/manual/index.htm

does she drink alcohol. She exercises and lives a stable if very demanding and busy life. She reported highly disturbed nocturnal sleep patterns. Surprisingly, despite disturbed sleep she reported normal energy levels. She was not depressed or significantly anxious in the day. She had trouble with sleep onset, the sleep latency period often being up to an hour or more. But she would also awaken every night in the very early morning (2 – 3 am) and usually be unable to get back to sleep. She described awakenings as being accompanied by "adrenalin rushes", with accelerated heartbeat, anxiety and hypervigilance. However she denied cognitive awareness of external threats or fears for body integrity or anxious ruminative content. She had tolerated this condition for two years until being informed by a friend of my amino acid activities.

Her first neurotransmitter deficiency questionnaire suggested needs for tryptophan and GABA for stress, sleep onset and sleep stability. Accordingly she was advised to take one 500 mG Tryptophan capsule at 4 hour intervals during the day, starting at noon, for stress and three at night, half an hour before retiring, for sleep onset. By her report this reduced stress and shortened sleep onset somewhat. However, the adrenaline rush at nocturnal awakenings continued unabated. She was then advised to take one GABA sublingual tablet (125 mg) prior to going to sleep and immediately after each nocturnal awakening. She did this for a week and then the GABA dose was increased to two tablets after nocturnal awakening, which reduced the anxiety after awakenings somewhat but did not prevent the awakenings nor subsequent insomnia.

It was then determined that her nocturnal awakenings were due to high nocturnal cortisol levels and a trial of Seriphos (1000 mg capsules of Phosphorylated Serine) as a cortisol antagonist at night time. She was carefully warned of the dangers of overuse of Seriphos,

and warned of the long latency (up to 6 hours) prior to its taking effect. She was advised to take a single capsule at 8pm at night. She found this process effective the very first night, but asked to modify the dosage to be at bedtime rather than before. This worked even better. She tried doubling the dose for three nights but decided that a single capsule was enough. She continued taking the Seriphos for a total of three weeks. She then reported that she spontaneously felt sleepy at night at 10.30pm before taking the Seriphos. She was advised to stop taking the Seriphos immediately and a few days later to try gradually withdrawing the tryptophan, which she did. Happily, she found that both her sleep onset insomnia and awakenings had resolved and have not returned as of our last contact, three months after we began meeting.

Case #2 from the practice of Sabrina Nioche, Director of "Le Centre" pilates and movement therapy studio, Mammoth Lakes, CA.

M is a 53 year old male. His sleep problems started when the real estate crisis joined forces with a three year divorce. This lasting stress took it out of him. He could not stay asleep, plus he felt constantly agitated and his blood pressure was very high. I had suggested GABA several years previously and he had experienced great relief from it then.

This time we combined tryptophan with the GABA in the late afternoon to help prepare for sleep. He repeated the same protocol 30-60 minutes before bedtime. We did not get the desired result so I chose to test his nighttime cortisol levels. At 1:30Am his cortisol was through the roof. So we implemented a new protocol of the Seriphos and Lactium

combination. He takes 3 Seriphos at bedtime with 2 Lactium capsules. Because Lactium takes effect more quickly, he takes more Lactium if he wakes up in the night. He has not slept this well in years. He texted to thank me after sleeping for 11 hours more recently. He is no longer as tired because he is sleeping. His agitation and blood pressure are problems of the past as well.

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