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Fibromyalgia

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Fibromyalgia syndrome (FMS) is characterized by diffuse muscle pain, poor sleep, and unrelenting fatigue. Individuals with fibromyalgia may also experience headaches, anxiety, depression, poor memory, numbness and tingling in the extremities, cold hands and feet, irritable bowel syndrome, lowered immune function, and chemical sensitivities. Over 10 million Americans suffer from fibromyalgia; 90% of them are women between the age of 25 and 45.¹

Diagnostic tests are currently unavailable to confirm fibromyalgia. The diagnosis is usually reached after ruling out other conditions including neurological, autoimmune, endocrine, musculoskeletal, immunological, and mental disorders. Patients have typically had the illness at least seven years and have been seen by a dozen different doctors before they're diagnosed with fibromyalgia.

In 1990, The American College of Rheumatology (ACR) first proposed the current criteria for defining fibromyalgia syndrome. The criteria include a history of widespread pain lasting more than three months and the presence of at least 11, out of a possible 18, tender points. Pain is considered to be widespread when it affects all four quadrants of the body; that is, you must have pain in both your right and left sides as well as above and below the waist to be diagnosed with fibromyalgia.²

Fibromyalgia shares several of the same symptoms associated with chronic fatigue syndrome (CFS). One study which compared 50 CFS patients with 50 FMS patients, found that their symptoms of low-grade fever (28%), swollen lymph nodes (33%), rash (47%), cough (40%), and recurrent sore throats (54%) to be the same for both syndromes.³

Another study comparing CFS patients with FMS patients showed that the brain-wave patterns, tender points, pain, and fatigue were virtually identical in both groups.⁴

While there are common characteristics shared by FMS and CFS patients, I've found some distinct differences between the two syndromes. Those with what I call "true fibromyalgia" suffer from fatigue but always list poor sleep and diffuse muscle pain as their primary complaints. They consistently demonstrate symptoms associated with low

serotonin levels; poor sleep, increased pain, irritable bowel, brain fog, anxiety, and depression.⁵

Patients with "true CFS" have a compromised immune system, which is the root of their illness, elevated blood antibodies, intermittent sore throats, and tender lymph nodes. They tend to have chronic sinus or upper respiratory or other infections, which linger for extended periods of time. Unlike those with fibromyalgia, individuals with CFS may have normal serotonin levels. And, unlike those with fibromyalgia, chronic fatigue patients may not have any trouble with their sleep. They usually report they

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sleep all the time, yet never feel rested.

What Causes Fibromyalgia?

Research suggests fibromyalgia may be the result of:

- Trauma⁶, especially whiplash injuries.⁷
- Hypothalamus-pituitary-adrenal axis (HPA) dysfunction.⁸
- Emotional/physical/mental stress.⁹
- Low thyroid function.¹⁰
- Low serotonin states.¹¹
- Adrenal dysfunction.^{12, 13, 14}
- Chronic viral, mycoplasma, and or bacterial infections.¹⁵
- Endocrine disorders.¹⁶
- Sleep disorders.^{17, 18}

The truth is, we really don't know for sure what causes fibromyalgia.

What we do know:

Fibromyalgia is now thought to arise from a miscommunication between the nerve impulses of the central nervous system. The neurons, which supply the brain, become more excitable, exaggerating the pain

sensation. This over-amplification of pain is referred to as "central sensitization."¹⁹ Fibromyalgia patients have a reduction in their pain threshold (allodynia), an increased response to painful stimuli (hyperalgesia) and an increase in the duration of pain after nociceptor stimulation (persistent pain). Individuals with fibromyalgia syndrome have low levels of serotonin, a 4-fold increase in nerve growth factor, and elevated levels of substance P.²⁰ Nerve Growth Factor (NGF) is a member of a family of peptides known as the neurotrophins. The exposure of nociceptive sensory neurons to NGF leads to up-regulation of substance P in sensory neurons.²¹

Substance P, the neuropeptide in spinal fluid, is a neurotransmitter that is released when axons are stimulated. Increased levels of substance P increase the sensitivity of nerves to pain or heighten awareness of pain. Although it's not fully understood, fibromyalgia patients have an imbalance of the hypothalamus-pituitary-adrenal (HPA) axis. This imbalance creates hormonal inconsistencies, which disrupt the body's ability to maintain homeostasis.

Many of the most common fibromyalgia symptoms including widespread muscle pain, fatigue, poor sleep, gastrointestinal problems, and depression regularly occur in people with various neuroendocrine disorders, including those manifested by HPA dysfunction.²²

Researchers believe suppression of the HPA (quite likely from chronic stress), which results in lowering human growth hormone (HGH), dehydroepiandrosterone (DHEA), cortisol, and other hormones, is aggravated by the chronic pain and poor sleep associated with fibromyalgia.^{23, 24}

Hypothalamus-Pituitary-Adrenal Axis (HPA) Dysfunction

The main function of the hypothalamus is homeostasis, or maintaining the body's status quo. The hypothalamus receives and transmits messages from the nervous system and hormonally through the circulatory system. Because of its broad sphere of influence, the hypothalamus could be considered the body's master computer. The hypothalamus receives continuous input about the state of the body and must be able to initiate compensatory changes if anything drifts out of line.

The Hypothalamus regulates such bodily functions as:

1. Blood pressure: often low in those with fibromyalgia.
2. Digestion: bloating, gas, indigestion, and reflux are common in FMS patients.
3. Circadian rhythms (sleep/wake cycle): which is consistently disrupted in FMS.
4. Sex drive: loss of libido is a common complaint for FMS patients.
5. Body temperature: often low in FMS patients.
6. Balance and coordination: FMS patients have balance and coordination problems.
7. Heart rate: mitral valve prolapse (MVP) and heart

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arrhythmias are a common finding in FMS patients.

8. Sweating: it's not unusual for FMS patients to experience excessive sweating.
9. Adrenal hormones: consistently low in FMS patients.
10. Thyroid hormones and metabolism: hypothyroid is a common finding in FMS patients. Recent studies show that over 43% of FMS patients have low thyroid function. It's estimated that those with FMS are 10 to 250,000 times more likely to suffer from thyroid dysfunction.²⁵

A Vicious Cycle

1. Chronic stress disrupts HPA homeostasis, leading to allodynia.
2. Chronic pain disrupts the circadian rhythm.
3. Dysfunction in the circadian rhythm results in poor sleep.
4. Poor sleep reduces growth hormone production, leading to poor repair of damaged muscle fibers, poor memory, fatigue, suppressed immune function, and more pain.²⁶
5. Increased pain further disrupts sleep and leads to depletion of stress-coping chemicals including serotonin.^{27, 28}
6. A reduction in serotonin causes an increase in the neurotransmitter, substance P. Substance P enhances pain receptors, creating even more pain.
7. Poor sleep and ongoing stress lead to fatigue, mood disorders, and IBS, and may cause thyroid dysfunction.²⁹
8. Chronic stress contributes to adrenal fatigue, decreased DHEA, and lowered resistance to stress. Decreased stress-coping abilities then lead to lowered immune function.³⁰
9. Lowered blood volume from adrenal dysfunction (and resultant hypotension) leads to further fatigue.³¹

Stress and Fibromyalgia

A survey by The Fibromyalgia Network reports that 62% of their respondents list physical or emotional stress as the initiating factor in their acquiring fibromyalgia.³²

I believe chronic stress is the underlying catalyst for the onset of HPA dysfunction and fibromyalgia. Several studies have demonstrated how chronic stress undermines the normal hypothalamic-pituitary-adrenal axis (HPA) function.³³

When explaining the role of stress in fibromyalgia, I find the following analogy helps put stress and fibromyalgia into perspective.

The Importance of a Good Night's Sleep

Studies have shown that individuals who were prevented from going into deep sleep for a period of a

week develop the same symptoms associated with FMS and CFS; diffuse pain, fatigue, depression, anxiety, irritability, stomach disturbances, and headaches.^{34, 35}

Sleep deprivation markedly increases inflammatory cytokines (pain causing chemicals)- by a whopping 40%.³⁶

Serotonin

Serotonin helps regulate sleep, digestion, pain, mood, and mental clarity.³⁷

Serotonin helps:

1. Raise the pain threshold (have less pain) by blocking substance P.
2. You fall asleep and stay asleep through the night.
3. Regulate moods. "The happy hormone" reduces anxiety and reduces depression.
4. Reduce sugar cravings and over eating.
5. Increase a person's mental abilities.
6. Regulate normal gut motility (transportation of food-stuff) and reverse irritable bowel syndrome (IBS). Surveys have shown that as many as 73% of FMS patients have irritable bowel syndrome. You have more serotonin receptors in your intestinal tract than you do in your brain.

Emotionally stressful situations cause the body to release adrenaline, cortisol and insulin. These stress hormones stimulate the brain to secrete serotonin. Long-term stress and poor dietary habits can deplete the body's serotonin stores.³⁸

Tryptophan, 5 Hydroxytryptophan (5HTP), and Serotonin

Tryptophan is one of eight essential amino acids. Tryptophan is absorbed from the gut into the bloodstream and then dispersed throughout the body. 90% of tryptophan is used for protein synthesis, 1% is converted to serotonin, and the balance is used to make niacin. In the formation of serotonin, tryptophan is hydroxylated to 5-hydroxy-tryptophan (5-HTP) by tryptophan hydroxylase.

5-HTP is converted to serotonin by the decarboxylase enzyme, which is vitamin B6 dependent. Tryptophan is transported across the blood-brain barrier via a transport molecule, which also carries leucine, isoleucine, and valine, and prefers leucine.

However, 5-HTP easily crosses the blood-brain barrier and does not utilize this transport mechanism; thus, it does not compete for passage through the blood-brain barrier with these amino acids.³⁹ And unlike tryptophan, which is made from bacterial fermentation (and hence subject to contamination), 5HTP is derived from the West African plant *Grifonia simplicifolia*.

In the body, 5-HTP is converted directly into serotonin. It is not broken down by tryptophan pyrrolase and does not have to compete for transport across the blood-brain barrier. Individuals with fibromyalgia have low levels of tryptophan³⁸, serotonin³⁹, and 5-HTP.⁴⁰ Studies show that fibromyalgia patients have higher levels of metabolites in

the kynurenine pathway, which diverts tryptophan away from serotonin production.⁴¹

Selective Serotonin Reuptake Inhibitor (SSRI) Medications

Prescription antidepressants can be helpful. However, antidepressant drugs have potential side effects including anxiety, depression, fatigue, decreased sex drive, and disruption of normal circadian rhythms.⁴² SSRI's are supposed to help a patient hang onto and use their naturally occurring stores of the brain chemical serotonin. It's like using a gasoline additive to help increase the efficiency of your car's fuel. Most of the patients I see with fibromyalgia are running on fumes, and a gasoline additive won't help. Please keep in mind that several studies show that between 19-70% of those taking antidepressant medications do just as well by taking a placebo or sugar pill.⁴³

I recommend my patients boost their serotonin levels by taking 5HTP.

5HTP and Depression

Studies (including double-blind) comparing SSRI and tricyclic antidepressants to 5HTP have consistently shown that 5HTP is as good, if not better, than prescription medications in supporting mood. Furthermore, 5HTP doesn't have some of the more troubling side effects associated with prescription medications.^{44, 45}

5HTP and Sleep

5HTP has been shown to improve sleep quality by increasing REM sleep, and increases the body's production of melatonin by 200%.^{46, 47}

5HTP and Fibromyalgia

Double-blind, placebo-controlled trials have shown that patients with FMS were able to see the following benefits from taking 5HTP:⁴⁸

- decreased pain
- improved sleep
- less tender points
- less morning stiffness
- less anxiety
- improved mood⁴⁹
- increased energy

Irritable Bowel Syndrome, 5HTP and Serotonin

There are more serotonin receptors in the intestinal tract than there are in the brain. This is one reason people get butterflies in their stomach when they get nervous.⁵⁰

The brain and gut are connected through the neuroreceptors 5-hydroxytryptamine-3 (5-HT₃) and 5-hydroxytryptamine-4 (5-HT₄). These serotonin receptors regulate the perception of visceral pain and the gastrointestinal (GI) motility. Serotonin controls how fast or

how slow food moves through the intestinal tract.^{51, 52}

It's common for the symptoms associated with IBS, diarrhea and constipation to disappear within one-two weeks once serotonin levels are normalized with 5HTP replacement therapy.

My 5HTP and Sleep Restoration Protocol

I instruct my patients to take 50mg of 5HTP 30 minutes before bed on an empty stomach (90 minutes after or 30 minutes before eating), with 4 ounces of grape juice. I know 5HTP doesn't have to compete with other amino acids to cross the blood-brain barrier, but this routine seems to heighten the effect of 5HTP. One of three things will happen when taking 5HTP.

Starting with 50 mg. of 5HTP:

1. The patient falls asleep within 30 minutes and sleeps through the night. If so, they stay on this dose until their next scheduled visit with me (typically 2 weeks).
2. Nothing happens. This is typical response to such a low dose. The patient should add an additional 50 mg. each night (up to a max of 300 mg.) until they fall asleep within 30 minutes and sleep through the night.
3. Instead of making the patient sleepy, the first dose makes them more alert. This occurs more often in CFS and chemical sensitivity patients who have a sluggish liver. If this happens, they're to discontinue taking 5HTP at bedtime and instead take 50 mg. with food for 1-2 days. Taking 5HTP with food seems to help slow down its absorption, allowing the liver to process it more effectively. Taking 5HTP with food will not (usually) make you sleepy. After 1-2 days on 5HTP with no further problems, they should increase to 100 mg. of 5HTP with each meal (300mg a day).

Melatonin

Melatonin is the primary hormone of the pineal gland and acts to regulate the body's circadian rhythm, especially the sleep/wake cycle. One percent of serotonin turns into melatonin, which then promotes deep restorative sleep. Melatonin is an extremely important hormone which plays a vital role in the circadian rhythm.

Normally, melatonin levels begin to rise in the mid-to-late evening, remain high for most of the night, and then decline in the early morning hours.

Natural melatonin production is partly affected by light. During the shorter days of the winter months, melatonin production may start earlier or, more often, later. This change can lead to symptoms of seasonal affective disorder (SAD) or winter depression.⁵³

Natural melatonin levels decline gradually with age. Some older adults produce very small amounts of melatonin or none at all.

When administered in pharmacological doses (1-6 mg. before bed), melatonin acts as a powerful sleep-regulating

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Malabsorption in Fibromyalgia: Nutritional Supplementation to Improve Overall Well-Being

Dr. Ronald Klatz and Dr. Bob Goldman

Fibromyalgia syndrome (FMS) is a rheumatic disorder characterized by chronic aching muscular pain that has no obvious physical cause. The most distinctive feature of FMS is the existence of certain "tender points," 18 specific spots where the muscles are abnormally tender to the touch, and are clustered around the neck, shoulders, chest, knees, elbows, and hips.

Research has demonstrated that the axis connecting the three glands primarily responsible for the stress response (hypothalamus, pituitary, adrenals) may be dysfunctional in people with fibromyalgia. Contrary to previously held notions, inflammation of the involved structures is generally absent in fibromyalgia.

Scientists have discovered that malabsorption problems are common in people with FMS, and consequently specific supplemental nutrients may be of benefit. In this article, we highlight some of the key nutritional agents for FMS and review the scientific literature supporting supplementation.

B-Complex: Vitamin B complex is needed by the body to improve energy and normalize brain function. In particular, Dr. Eisenger and colleagues from Centre Hospitalier Intercommunal Toulon (France) have found that vitamin B1 (thiamine) levels and thiamine-dependent enzymes are reduced in people with FMS.

Coenzyme Q-10 and Ginkgo biloba: Coenzyme Q-10 is needed by the body to oxygenate tissues, improve immune function, and protect the heart, whereas Ginkgo improves circulation and brain function. In a 3-month long study, Dr. Lister and colleagues in the United Kingdom found that 200 mg Coenzyme Q-10 and 200 mg Ginkgo biloba extract resulted with progressive improvement in the quality-of-life scores over the study period. At the end of the study, 64% claimed their symptoms improved (whereas only 9% reported feeling worse).

Magnesium and Malic Acid: These nutrients are involved in energy production in muscle cells, and both are needed by the body for sugar metabolism. Researchers at the University of Texas Health Science Center (USA) found that a combination of up to 600 mg of elemental magnesium and 2,400 mg of malic acid per day positively supported muscle function.

5-HTP: People with fibromyalgia often have low serotonin levels in their blood, thus supplementation with 5-HTP may increase serotonin synthesis in these cases. Dr. Puttini and colleagues from L Sacco Hospital (Italy) found that administration of 5-HTP improved the number of tender points, anxiety, pain intensity, quality of sleep, and fatigue in FMS patients, with clinical improvement in nearly 50% of the patients during the treatment period.

S-adenosylmethionine (SAME): The body needs SAME to relieve stress, depression, pain. In a study conducted by Dr. Volkmann and colleagues from Frederiksberg Hospital (Denmark), study participants who took oral SAME (600 mg for 10 days) reported improvements in the subjective perception of pain at rest, pain on movement, and overall well-being. A previous study by the same team found, conducted for 6 weeks, found that SAME (800 mg per day) successfully reduced pain, fatigue, and stiffness, and improved mood.

Melatonin: Most people with fibromyalgia also suffer from alpha-EEG anomaly, a sleep disorder in which the individual's deep sleep periods are interrupted by bouts of waking-type brain activity, resulting in poor sleep quality. In a trial conducted by Dr. Citera and colleagues at the Universidad de Buenos Aires, Argentina, 3 mg of melatonin at bedtime was found to reduce tender points and to improve sleep.

In addition to nutritional supplementation, simple lifestyle changes

can help to improve fibromyalgia symptoms. A low salt, vegan diet may be helpful. In a controlled clinical trial involving women with FMS who followed a raw food diet (fruits, vegetables, nuts, seeds, legumes, cereals, and fermented foods) for three months, the study participants experienced a significant reduction in pain, morning sickness, use of painkillers, depression, and the number of sore fibromyalgia points. Additionally, some research suggests that it is important for those suffering from FMS to eliminate monosodium glutamate (MSG) or MSG plus aspartame from their diets. Finally, low-intensity exercise may improve fibromyalgia symptoms. Dr. Gowans and colleagues at the University of Toronto (Canada) found that a long-term aerobic exercise regimen caused improvements in physical function, mood, symptom severity, and aspects of self-efficacy in FMS patients that lasted at least 12 months.

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agent that controls the circadian rhythm. In a recent study, volunteers were either given a .3 mg. or a 1mg. dose of melatonin or a placebo. Both levels of melatonin were effective at decreasing the time needed to fall asleep.⁵⁴

Delayed Sleep Phase Insomnia

Patients with altered circadian rhythms often find it hard to fall asleep before the early morning hours. They then end up sleeping through the day. This causes a further disruption to normal circadian rhythms. It can be hard to get these patients' rhythms normalized. Studies have shown that 5 mg. of melatonin given at 11 p.m. helps advance and reset circadian rhythms.⁵⁵

What Can Decrease Melatonin Levels?⁵⁶

- exposure to bright lights at night
- exposure to electromagnetic fields
- NSAIDs (Celebrex, Vioxx, Mobic, Alleve, Bextra, etc.)
- SSRIs yes, the very same antidepressants that many take for FMS, including Prozac, Zoloft, Celexa, Paxil, and Lexapro.
- anxiety meds (benzodiazepines) like Klonopin, Ativan, Xanax, Restoril, etc.
- anti-hypertensive meds (beta-blockers, adrenergics, and calcium channel blockers) including, Inderal, Toprol, Tenormin, Lorpessor, etc.
- steroids
- over 3 mg. of vitamin B12 in a day
- caffeine
- alcohol
- tobacco
- evening exercise (for up to three hours after taking it)
- depression

Foods High in Melatonin:⁵⁷

- | | |
|-------------------|------------|
| ■ oats | ■ tomatoes |
| ■ sweet corn | ■ barley |
| ■ rice | ■ bananas |
| ■ Japanese radish | |

Drugs That Raise Melatonin Levels:⁵⁸

- fluvoxamine (Luvox)
- desipramine (Norpramin)
- most MAOIs
- St. John's Wort (acts as an MAOI and may help raise melatonin levels)

Although adequate levels of melatonin are essential for a good night's sleep, fibromyalgia patients should initially try boosting their serotonin with 5HTP.⁵⁹

Questions:

What if my patient is taking a prescription sleep medication and sleeping through the night?

Prescription drugs that promote deep restorative sleep include Ambien, Elavil, Trazadone, Flexeril, and Lunesta. These medications can be helpful. However, these medications have potential side effects that may cause the very symptoms associated with fibromyalgia. Ambien may cause short-term memory loss, fatigue, depression, and flu-like aches and pains.

Other common sleep-inducing drugs, including benzodiazepines (Klonopin, Ativan, etc.), muscle relaxants (Zanaflex), Neurontin, and Lyrica don't promote deep delta wave sleep and therefore are not recommended. Remember, the reason they're taking these prescription drugs is because they have a serotonin (and perhaps a melatonin) deficiency, not a drug deficiency. You want them to build up their serotonin levels so that eventually they may not need prescription sleep medications. You should have them add 5HTP (50 mg.) three times daily with food. If no problems arise after 2-3 days, they should then increase to 100 mg. with each meal.

What if someone has a serotonin syndrome reaction?

A serotonin syndrome reaction may occur if a person gets too much serotonin. This can cause rapid heartbeat, increased pulse rate, elevated blood pressure, agitation, and, in its worst-case scenario, life-threatening irregular heartbeats (arrhythmia). I've recommended 5HTP to thousands of individuals over the last 7 years. Rarely have I encountered a problem. I always start with a low dose (50 mg.) and warn the patient to stop taking it at bedtime if he/she has a funny reaction.

What are some of the other potential side effects of 5HTP?

Other than some patients becoming more alert when taking 5HTP at bedtime, I have had very few complaints from patients. The literature reports that individuals may have transient headaches and nausea from taking 5HTP. I have had less than half a dozen patients have one of these side effects. The headaches and any nausea usually go away after a couple of days.

When should I increase my patient's 5HTP dose?

If your patient is taking 100mg of 5HTP and is sleeping through the night and dreaming, then I would leave him/her at that dose. However, if the patient continues to have IBS symptoms, sugar cravings, low moods, or a lot of pain, I have them continue to take the night dose that is putting them to sleep, along with taking additional 5HTP with food during the day (up to a total of 300 mg. daily).

What do you do when your patient still can't fall asleep and sleep through the night even when taking 300mg of 5HTP?

If after two weeks, someone is not falling asleep and staying asleep through the night, I add melatonin. First, I make sure she is taking 5HTP as she should be and at the maximum dose of 300mg.

Melatonin Replacement Therapy

I have patients who aren't able to fall asleep within 30 minutes (while taking 300mg. of 5HTP) take 3-9mg of sublingual (dissolves under tongue for rapid absorption) melatonin 30 minutes before bed, along with the 300 mg. of 5HTP.

What if your patient falls asleep within 30 minutes but can't stay asleep?

If a patient is falling asleep but has trouble staying asleep, I'll add 3mg of timed-release melatonin to their normal bedtime dose of 5HTP and regular melatonin.

Can patients take 5HTP, melatonin, and prescription sleep medications at the same time?

If they don't consistently fall asleep and stay asleep while combining their prescription sleep medication (preferably one that puts them into deep sleep, see list above) with 300mg. of 5HTP, then you need to add melatonin as well.

The Bottom Line

Although I've found sleeping well to be the essential first step, there are several hormonal, nutritional, and biochemical deficiencies that must be corrected before a patient can truly realize a benefit. Unfortunately, space doesn't permit me to address these potential deficiencies at this time. I encourage you to check out my books where you'll find much more detailed information. In this newsletter I've explored the relationship of serotonin, deep restorative sleep, and fibromyalgia because I've consistently found that many of the most troubling symptoms associated with fibromyalgia, such as poor sleep, fatigue, chronic pain, IBS, mood disorders, and brain fog, are diminished (sometimes dramatically) when serotonin levels are boosted and normal circadian rhythms are restored.

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