Chronic fatigue syndrome (CFS) and its often simultaneously present cousin, fibromyalgia syndrome (FMS) are common names for an overlapping spectrum of disabling syndromes. It is estimated that FMS alone affects 3 to 6 million Americans, causing more disability than rheumatoid arthritis, and later research suggests a prevalence of CFS/FMS and/or disabling fatigue ranging from 7.3% to 12.9% across different countries.\cite{1,2} The majority of patients I see in clinical practice who have FMS also have CFS.\cite{3} Myofascial pain syndrome (MPS), pain caused by a localized area of muscle shortening, often shares many of the same underlying metabolic processes as FMS\cite{4} and affects many millions more.\cite{5} Structural abnormalities are more of a concern in MPS; however, because this article discusses the metabolic problems often seen in all three processes, I will often refer to the three (CFS/FMS/MPS) together.

Fortunately, two studies (including a recent randomized, controlled trial) done in our research center showed an average 90% improvement rate when using the “SHIN” protocol.\cite{6} SHIN stands for sleep, hormonal support, infections/immune dysfunction, and nutritional support. When a patient has fatigue and insomnia coupled with widespread pain, he or she is seen as having a body-wide “energy crisis.” Treatment with the SHIN approach will help them. A recent editorial in the *Journal of the American Academy of Pain Management* noted that our studies, as well as years of clinical success, have confirmed that subclinical abnormalities are important and that our comprehensive and aggressive metabolic approach to treatment is a powerfully effective part of the standard of practice for treatment of FMS and MPS patients.\cite{7} Fortunately, although we still have much to learn, effective treatment is now available for the large majority of patients with these syndromes.\cite{8,9}

Hypothalamic dysfunction has been implicated as a common denominator in these syndromes.\cite{5,6} This may occur secondarily to mitochondrial dysfunction. Deficiencies of key mitochondrial metabolites such as carnitine have been documented on muscle biopsy studies,\cite{10,11} and improvement of fatigue states with mitochondrial-support treatment (eg, coenzyme Q$_{10}$, D-ribose, Mg-K aspartate, NADH, magnesium, acetyl-L-carnitine) has been reported. Dysfunction of hormonal, sleep, and autonomic control (all centered in the hypothalamus) and energy-production centers can explain the large number of symptoms and why most patients have a similar set of complaints. To make it easier to explain to patients, we use the model of a circuit breaker in a house:

*If the energy demands on your body are more than it can meet, your body “blows a fuse.” The ensuing fatigue forces you to use less energy, protecting you from harm. On the other hand, although a circuit breaker may protect the circuitry in the home, it does little good if you do not know how to turn it back on, or that it even exists.*

This analogy actually reflects what occurs. Research in genetic mitochondrial diseases shows not simply myopathic changes, but also marked hypothalamic disruption. As energy stores are depleted, hypothalamic dysfunction occurs early on, resulting in the disordered sleep, autonomic dysfunction, low body temperatures, and hormonal dysfunctions commonly seen in these syndromes. In addition, inadequate energy stores in a muscle result in muscle shortening (such as in rigor mortis) and pain, which is further accentuated by the loss of deep sleep. Therefore, restoring adequate energy production and eliminating stresses that overutilize energy (eg, infections, situational stresses) restores function in the hypothalamic “circuit breaker” and also allows muscles to release, allowing pain to resolve. Our placebo-controlled study showed that when this is done, 91% of patients improved (vs 36% in the placebo group), with an average 90% improvement in quality of life compared to a 36% improvement in the placebo group. In addition, the majority of patients no longer qualified as having FMS by the end of 3 months.\cite{3}

**Diagnosis**

The criteria for diagnosing CFS, FMS, and MPS are readily available elsewhere. MPS is diagnosed by the presence of trigger points and taut bands. In my experience, there is a simple approach to diagnosing CFS and FMS that is very effective clinically. If the patient has the paradox of severe fatigue combined with insomnia, does not have severe primary depression, and these symptoms do not go away with vacation, the person likely has a CFS-related process. If there is also widespread pain, FMS is probably present as well. Both CFS and FMS respond well to proper treatment, as will be discussed.

Inadequate energy production (as is seen in mitochondrial myopathies) and energy needs greater than the body’s production ability (as in “Female Athlete Triad” or some viral infections) have been shown to trigger hypothalamic dysfunction. I suspect that the same occurs in many other “energy stressors,” such as infections and inflammation, disrupted sleep, pregnancy, hormonal and nutritional deficiencies, toxin exposures, and other physical and/or situational stresses.

**Treatment**

As mentioned earlier, using the SHIN acronym will facilitate the effective treatment of CFS (Figure). Let’s begin with “S” for sleep.

*S: Disordered Sleep*

A foundation of CFS/FMS is sleep disorder. Using medications that increase deep restorative sleep so that the patient gets 7 to 9 hours of solid sleep without waking or hangover is critical. Start...
treatment with natural therapies or with a low dose of sleep medications that do not decrease stage 3 or 4 sleep. Continue to adjust the treatments each night until the patient is sleeping 8 hours a night without a hangover.

Due to next-day sedation and each medication having its own independent half-life, CFS/FMS patients respond better to a combination of low doses of several medications than to a high dose of one. The natural remedies I recommend starting with include the following:

1. Herbal preparations containing a mix of valerian root, wild lettuce, Jamaican dogwood, passionflower, hops, and theanine. These six herbs can help reduce muscle pain, increase libido, and improve sleep;12-16
2. melatonin: .5 mg to 1 mg at bedtime;
3. 5 Hydroxytryptophan: 200 mg to 400 mg at night; and
4. calcium and magnesium at bedtime to promote sleep.

If natural remedies do not result in at least 8 hours a night of sleep, consider these medications:

- zolpidem: 5 mg to 20 mg each night at bedtime;
- gabapentin: 100 mg to 900 mg at bedtime for sleep and pain,
as well as restless leg syndrome (RLS);
- cyclobenzaprine: 10 mg; clonazepam: 5 mg; and/or carisprodol: 350 mg (use one of these first if myalgias are a major problem); or
- trazodone: 50 mg (use 0.5 to 6 tablets each night at bedtime).

Some patients will sleep well with natural therapies and/or synthetic ones. Others will require a surprisingly large amount of sleep support because the malfunctioning hypothalamus controls sleep.

Although less common, three other sleep disturbances must be considered and treated if present. These are sleep apnea, upper airway resistance syndrome, and RLS, which is also fairly common in fibromyalgia.17

H: Evaluation and Treatment of Associated Hormonal Dysfunction

Hormonal imbalances are associated with FMS. Sources of imbalance include hypothalamic dysfunction, adrenal exhaustion from chronic stress, environmental toxins, and autoimmune processes, such as Hashimoto's thyroiditis.

It is important to understand the limitations of testing and the normal ranges. Many blood tests use two standard deviations to define blood-test norms. By definition, only the lowest or highest 2.5% of the population is in the abnormal (treatment) range. This

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**Figure 1. Effective Treatment of Chronic Fatigue Syndrome**

- **Sleep deprivation unresolved by natural means**
- **Unresolved myalgia**
- **Disordered sleep**
  - zolpidem, gabapentin, cyclobenzaprine
- **Hormonal dysfunction**
  - Hypothyroidism: treat based on symptoms, not lab tests.
  - Adrenal insufficiency: vitamins B6 & C; physiologic doses of hydrocortisone DHEA
  - Perimenopause: estradiol/estradiol progesterone
  - Testosterone: as indicated
- **Alleviate pain** Willow bark, Boswellia
- **Stress type A personality** Stress management
- **Support immune function. Treat infections** Optimize hydration with pure water, eliminate sugar and caffeine, high-potency vitamin-mineral, iron, as needed, vitamin B12 coenzyme Q10, D-ribose
- **Resolve nutritional deficiencies** Thymic hormone support, probiotics, antifungals: grapefruit seed extract, caprylic acid, fluconazole

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**Teitelbaum—Chronic Fatigue Syndrome**

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Suboptimal thyroid function is very common, and I find it reasonable to treat all chronic myalgia patients with thyroid-hormone replacement if their free T₄ blood levels are below even 50% of normal. Many CFS/FMS patients also have difficulty in converting T₄, which is fairly inactive, to T₃, the active hormone. Additionally, T₃ receptor resistance may be present, requiring higher levels. In most CFS/FMS patients, I give an empirical trial of a thyroid glandular supplement, .5 grain to 3 grains every morning, adjusted to the dose that feels best to the patient, as long as the free T₄ is not above the upper limit of normal. Many other alternatives, such as compounded combinations of T₄ and T₃, are also reasonable.

TSH testing is not reliable since hypothalamic dysfunction with hypothyroidism (based on symptoms and response to thyroid hormone) is common in fibromyalgia, and in hypothalamic hypothyroidism, the patient’s TSH can be low, normal, or high. The inadequacy of thyroid testing is further suggested by studies that show:

- most patients with suspected thyroid problems have normal blood studies
- when patients with symptoms of hypothyroidism and normal labs were treated with a thyroid supplement, a large majority improved significantly.

In addition, remember that thyroid supplementation can increase a patient’s cortisol metabolism and unmask a case of subclinical adrenal insufficiency. If the patient feels worse on low-dose thyroid replacement, he or she may need adrenal support as well.

Adrenal Insufficiency. The hypothalamic-pituitary-adrenal axis does not function well in CFS/FMS. Because early researchers were not aware of physiological doses of cortisol, they treated with high doses and their patients developed severe complications. William Jefferies, MD, author of Safe Use of Cortisol, helped us to understand the difference between physiological and pharmacological dosing. He found, in his experience with thousands of patients and years of use, that adrenal suppression and significant toxicity (besides gastrointestinal upset, weight gain, and fluid retention) were very uncommon with physiological dosing of hydrocortisone (ie, up to 20 mg a day). Twenty mg of hydrocortisone is approximately equivalent in potency to 4 mg to 5 mg of prednisone.

Our study did not show adrenal suppression using lower hydrocortisone dosing. Dr Jefferies, with thousands of patient-years’ experience in using low-dose hydrocortisone, recommends an empirical trial of 20 mg a day of hydrocortisone for all patients with severe, unexplained fatigue and has found this to be quite safe for long-term use. Confirming this, our research and clinical experience suggest that using hydrocortisone at 20 mg a day or less in CFS and FMS patients is safe and often helpful. Although this has not been subjected to controlled research, clinically, many patients find it to be extremely helpful.

Symptoms of an underactive adrenal gland include hypoglycemia/irritability when hungry, weakness, hypotension, dizziness, and recurrent infections—all of which are common in CFS/FMS. Although a baseline morning cortisol of >6 mcg/dl is often considered “normal,” most healthy people run approximately 16 mcg/dl to 22 mcg/dl at 8:00 AM.

My treatment guidelines are that if the baseline cortisol is less than 16 mcg/dl or if the patient’s symptoms suggest inadequate adrenal function, I treat with a therapeutic trial of 5 mg to 15 mg hydrocortisone in the morning, 2.5 mg to 10 mg at lunchtime, and 0 to 2.5 mg at 4:00 PM (maximum of 20 mg a day). After 9 to 18 months, the patient can often taper off the hydrocortisone. Remember, more is not better.

In addition to supplying very low-dose cortisone, it is important to supply nutritional support for the adrenal gland, as well as teaching the patient mind-body approaches that can decrease worry and increase relaxation, thus taking stress off the adrenals. I teach my patients to ask themselves this simple question when they start getting worried or stressed out: “Am I in imminent danger?” The answer is almost always “no,” which seems to help patients to “stand down” from their “fight or flight” reaction. Nutritional support should include vitamin C and pantothenic acid, as well as adrenal glandulars. Herbs such as ginseng and licorice can also be helpful.

Dehydroepiandrosterone. Dehydroepiandrosterone (DHEA) is a major adrenal hormone that has recently been getting a lot of attention in the press for its role as a “fountain of youth” hormone. DHEA is stored as DHEA-sulfate (DHEAS), and levels of the activated free DHEA fluctuate throughout the day. Because of this, I recommend checking serum DHEA-S levels rather than DHEA levels.

Many CFS/FMS patients have suboptimal DHEA-S levels, and the benefit of treatment is often dramatic. Most women need 5 g to 25 mg per day, and most men need 25 mg to 50 mg per day. I use the middle of normal range for a 29-year-old patient, keeping the DHEA-S level at 150 mcg/dl to 180 mcg/dl in women and at 350 mcg/dl to 480 mcg/dl in men. Although DHEA and testosterone levels normally drop with age, many practitioners feel this is not necessarily healthy. For example, studies show that low testosterone and low DHEA may be associated with insulin resistance and glucose intolerance.

Low Estrogen and Testosterone. Although we are trained to diagnose menopause by symptoms such as cessation of periods, hot flashes, and elevated follicle-stimulating hormone and luteinizing hormone levels, these are late symptoms. Estrogen deficiency often begins many years before and may coincide with the onset of CFS/FMS.

The initial symptoms of estrogen deficiency are poor sleep, poor libido, brain fog, achiness, and especially worsening of CFS/FMS symptoms in the days to a week before the period. I prefer to have the pharmacist make a combination of estriol and estradiol (Bi-Est)
2.5 mg plus progesterone, 30 mg to 50 mg plus testosterone 4 mg—
all in 1/10 or 2/10 of a CC of cream (which can be applied to the
mucosal surface of the labia each evening).

**Testosterone Deficiency.** Among my CFS/FMS patients, 70% of
men and many women have free testosterone levels in the lowest
quartile, while their total testosterone levels are normal. I therefore
recommend blood testing for “free testosterone.” A recently com-
pleted study (not yet published) found that treating low testosterone
in women decreases FMS pain. As noted above, supplementation
can be done easily by adding 4 mg of testosterone to the estrogen
cream. Testosterone supplementation also decreases sex hormone-
binding globulin, thus making more free hormone available.

Testosterone supplementation can also cause elevated thyroid
hormone levels in men taking thyroid supplements. In addition,
despite the concerns about athletes using very high levels of syn-
thetic testosterone, it is important to remember that research shows
that raising a low testosterone level in men using natural testoster-
one actually results in lower cholesterol, decreased angina and
depression, and improved diabetes.34

1. **Immune Dysfunction and Infections**

   Immune dysfunction is part of the process for CFS/FMS
   patients. Opportunistic infections present in CFS/FMS include
   yeast/Candida, chronic upper respiratory infections and sinusitis,
   bowel infections, and chronic, low-grade prostatitis, all of which
   need to be treated.

   Chronic sinusitis responds poorly to antibiotics but responds
   well to antifungals.36 Bowl infections with alterations of normal
   bacterial flora, fungal overgrowth, and parasitic infections are also
   frequently present, as is reflected by the patient’s bowel symptoms.
   Because of the lack of a definitive test for yeast overgrowth, there is
   little research published in this area, and treatment is controversial;
it is empirical and based on the patient’s history. Yeast vaginitis,
onchomycosis, sinusitis, a history of frequent antibiotic use (such as
tetracycline for acne), or gas, bloating, diarrhea, or constipation war-
rant an empirical, therapeutic antifungal trial. Many CFS/FMS
patients who have not responded to other therapies for spastic colon
or sinusitis have responded dramatically to antifungal treatments. I
give an empirical trial of antifungal therapy in most CFS/FMS/MPS
patients. I treat with sugar avoidance, a mix of antifungal herbs (eg,
grapefruit seed extract and caprylic acid), and acidophilus for 5
months. After 4 weeks on the herbs and acidophilus, I add 200 mg
daily of fluconazole for 6 weeks.

Parasitic, occult infections such as chlamydia, mycoplasma
incognitus, human herpesvirus 6, cytomegalovirus, and Epstein-
Barr virus are also sometimes active in CFS/FMS patients. In these
cases, I often use thymic hormone mimics, which are excellent
immune stimulants for acute infections as well.

Restoring normal gut flora and eliminating bowel infections are
a critical part of treatment for many reasons, including improving
digestion and nutrition. This brings us to the “N,” perhaps the most
important part of the SHIN acronym of treatment.

**N: Nutritional Deficiencies**

CFS/FMS patients are often nutritionally deficient. In addition
to bowel infections, which result in potential nutrient losses
and increased needs secondary to illness, the standard American
diet is nutritionally inadequate. People often ask, “Which vitamin
am I low in?” when they tend to be deficient in many nutrients.
For example, B vitamins, magnesium, iron, D-ribose, coenzyme
Q10, malic acid, glutathione, and carnitine are essential for mito-
chondrial function35,37 and energy production. Inadequate energy
production, for instance, can result in muscle shortening (think
“rigor mortis”) with associated pain, poor immune and liver
(detoxification) function, cognitive dysfunction, etc. Optimal
nutrient support is also critical for many other processes.
Although blood testing is not reliable or necessary for most nutri-
ents, I do recommend that B12, iron, total iron-binding capacity,
and ferritin levels be checked. I begin CFS/FMS patients on the
following nutritional regimen.

1. A quality multivitamin suited for their needs. It should
   contain at least a 50 mg B-complex, 150 mg magnesium (as the
glycinate), 900 mg malic acid, 600 IU vitamin D, 500 mg vita-
   min C, 15 mg zinc, 200 mcg selenium, 200 mcg chromium, and
   amino acids. Because there are dozens of important nutrients
   and patients get tired of taking handfuls of tablets, I now use a
   powdered multivitamin so that one capsule plus a single drink
   replaces more than 35 tablets or capsules of supplements each
day. This should be taken longterm.

2. Supplement with iron if the iron percent saturation is
   under 22% or the ferritin is under 40 mg/mL. Iron should be
taken on an empty stomach and at least 6 hours away from
thyroid hormones.

3. If the B12 level is under 540 pg/mL, I recommend B12 injec-
tions, 3000 mcg intramuscularly three times a week times for 15
   weeks, then as needed based on the patient’s clinical
   response.38-41

4. Coenzyme Q10: 100 mg to 200 mg a day.

5. Acetyl-L-carnitine: 500 mg twice daily for 4 months.

6. D-ribose: one scoop three times daily for 3 weeks, then
twice daily.

7. The patient should avoid sugar and caffeine, and water
   intake should be increased as well. Most patients find that a
   high-protein, “whole foods” diet feels best, but it is important to
   remember that there is a broad range of biological individuality,
   so I encourage patients to “check in with their bodies” a few
   hours after eating to see what foods help them to feel the best.

**General Pain Relief**

Although many kinds of pain will often resolve within 3 months
of simply using the SHIN treatment as discussed above, it is also
critical to eliminate pain directly. Several studies show a marked
analgesic and antiinflammatory effect from adequate doses of two
herbals: willow bark (containing at least 240 mg of salicin) and
boswellia (900+ mg). Willow, for example, has been shown to be as
effective as ibuprofen and rofecoxib (Vioxx).42,43 These herbals
are excellent for arthritic, inflammatory, and other pains. The herbs
discussed earlier as sleep remedies can also help muscle pain.
Clinically, gabapentin, tramadol, and metaxalone are also far more
effective for CFS/FMS/MPS pain than nonsteroidal antiinflam-
matory drugs.
Psychological Wellbeing

Many illnesses are associated with various psychological profiles. In CFS/FMS, a common profile is a “megetype-A” overachiever who, because of low self-esteem in childhood, overachieves to get approval. They tend to be perfectionists and have difficulties protecting their boundaries—that is, they say “yes” to requests when they feel like saying “no.” Instead of responding to their bodies’ signals of fatigue by resting, they redouble their efforts. Taking time to rest and getting and staying out of abusive personal and work environments is critical to psychological well-being. A simple approach is to teach patients (and yourself) to only do and keep their attention on things that, from a centered place, feel good. Joseph Campbell put it beautifully and succinctly when he said, “Follow your bliss.”44

REFERENCES


34. Viltet EL. Screaming To Be Heard: Hormone Connections Women Suspect...and Doctors Ignore. New York, NY: M. Evans and Company; 1995.


