What Your Endocrinologist Should Know About FMS and CMP

by Devin J. Starlanyl

Please read "What Everyone on Your Health Care Team Should Know About FMS and CMP".

The key to unraveling the Gordian knot fibromyalgia (FMS) is gaining as much control as possible over the perpetuating factors. When those perpetuating factors are metabolic, the patient's hope for symptom relief lies with you. Hormones, peptides, neurotransmitters and other informational substances may be out of balance. These patients may present a seemingly overwhelming challenge. Remember that it's pretty overwhelming to the patient too. They may have seen doctor after doctor who have either dismissed them or passed them on like hot potatoes until they wind up in your waiting room. By then, they are worn out physically, emotionally and financially, and may feel hopeless. You can supply the hope that they need. Often, there may be co-existing conditions, such as myofascial trigger points (TrPs), that have their own set of perpetuating factors. You need to know how to recognize TrPs and their referred pain patterns to make a good differential diagnosis, and because the peripheral stimulation they cause in the form of pain will continue to aggravate the central sensitization of FMS (Borg-Stein 2002). Trigger points may be associated with autonomic concomitants and proprioception dysfunction. They can also cause very real and sometimes intense pain that seems to derive from the viscera and may add to diagnostic confusion (Gerwin R. D. 2002). Nodules, ropy bands and pain at the end of a restricted range of motion signals TrPs, not FMS. *There is no such thing as a fibromyalgia trigger point.*

Metabolic imbalances, such as vitamin and mineral inadequacies, hypothyroid or hypoglycemia states, are very common perpetuators of myofascial TrPs. They are also possible FMS perpetuators. A detailed explanation of them is given in the most recent Trigger Point Manual (Simons, Travell and Simons 1999), along with some therapeutic guidelines.

The standard testing may be insufficient to identify these perpetuating factors. The Trigger Point Manual is clear to state that vitamin and mineral *deficiency* are not required to aggravate TrP symptoms. *Inadequacy* of these nutrients may be the limiting step to important metabolic pathways. Some of these patients have absorption problems or dysfunctions in the metabolic pathways, and levels at the tissue may need monitoring. Standard testing panels may not be reliable indicators. For example, the standard TSH test relies on a healthy, functioning hypothalamus, but the HPA axis is often out of balance in FMS. Standard thyroid panels may come back normal, but if the patient is thyroid resistant, they may

require supplementation with T3 (Lowe, Cullum, Graf Jr., et al. 1997). Even if the FMS patient has low thyroid levels, a combination of T3 and T4 may be more effective than T4 alone (Eisinger 1999). If thiamin levels are low and patients have hypothyroid symptoms, adding adequate thiamine may adequately treat the symptoms (Simons, Travell and Simons 1999, p 102). If the patient is already on thyroid supplementation and yet has inadequate thiamine intake and thiamine supplementation is added, symptoms of hyperthyroid may appear, so it is time to titrate the thyroid dose. Check for hypometabolism and thyroid resistance, which will not show up on standard thyroid panels (Lowe, 2000). Topical (Starlanyl, Jeffrey, Roentsch, et al. 2001-2002) or oral T3 may be of use in FMS patients if hypothyroid symptoms are present. It is important to test free testosterone, and not just total testosterone, to get an accurate picture of this hormone's status (Teitelbaum, 2001).

In FMS, multiple neuroendocrine pathways are disturbed, but we aren't sure if these are a result or a cause of FMS (Crofford, 1998). The hypothalamic-pituitary-adrenal (HPA) axis seems to be one of the first axes to become dysfunctional. This axis affects the immune system, the gonadal axes, the growth hormone axes, and the thyroid axes, which all in turn exert influence back on the HPA axis. This can work to your patient's advantage, and yours, but you must proceed very slowly and carefully. All of these axes can be profoundly influenced by insulin resistance, which is an extremely common perpetuator of both FMS and chronic myofascial pain. The "fibromyalgia fat pad" over the belly is often an early warning flag, even in people who are not obese. Unless excess carbohydrates are removed from the equation, there is a high risk of developing metabolic syndrome (Peters, Schweiger, Fruwald-Schultes. et al. 2002) or at least insulin resistance (Farias-Silva, Sampaio-Barros, Amaral et al.2002). Up to 80% of patients with metabolic syndrome die from cardiovascular complications, so it is vital that the insulin resistance component of this condition be treated aggressively (Lombard, Augustyn, Ascott-Evans 2002). The metabolic syndrome is highly prevalent and associated with a dysfunctional HPA axis (Tsigos, Chrousos 2002) often overlooked, and may have far-reaching health implications. Many researchers consider FMS to be a form of dysautonomia (Raj, Bruillard, Simpson 2000). If the ANS is chronically stimulated, there "is a prevalent and potent risk factor for adverse cardiovascular events, including mortality" (Curtis, O'Keefe. 2002). Fibromyalgia must not be taken lightly.

Some of the dysfunctions that are commonly associated with FMS are:

Altered functioning of both somatotropic and lactotropic axes during sleep Landis, Lentz, Rothermel 2001).

Cognitive dysfunction (Park, Glass Minear et al. 2001; Grigsby, Rosenberg, Busenbark 1995).

Fragmented sleep (Drewes, Gade, Nielsen et al. 1995).

Growth hormone and prolactin imbalances (Bennett, Clark, Walczyk. 1998; Griep, Boersma de Kloet. 1994).

Neurally mediated hypotension (Bou-Holaigah, Calkins, Flynn et al. 1997).

Orthostatic intolerance (Martinez-Lavin, Hermosillo, Mendoza et al. 1997).

Raynaud's syndrome (Bennett 1991).

Sensory dysfunctions (Kosek, Ekholm, Hansson 1996).

Tissue resistance to a variety of hormones (Tsigos, Chrousos 2002).

These are but a few samples of a large body of research in related fields. Yet there are still some doctors who refuse to believe that fibromyalgia even exists.

Fluid retention syndrome is common in women with FMS. Its range of symptoms is wide, and it may add to fatigue, weakness and pain (Deodhar, Fisher, Blacker et al. 1994). A diffuse bloated feeling and variable weight are flags that warn of possible insulin resistance. Edema can start with the release of sensitizing substances such as histamine, bradykinin or prostaglandins) during times of trauma (including repetitive use). In cases of central sensitization such as FMS, nociceptors keep firing after the sensitizing substances are gone. Resulting edema may compress blood and lymph vessels. This contributes to local microcirculation problems, which, in turn, causes the release of more sensitizing substances. This cycle will also contribute to myofascial TrPs.

Check for malabsorption if oral supplementation does not appear to be effective. Look upstream in metabolic pathways. For example, if the amount of available inositol is insufficient, thyroid supplementation may not be effective. [If your patient has bipolar disorder as well, avoid inositol, as it reverses the action of many common medications given for this condition (Williams Cheng, Mudge et al. 2002]. In a patient who has uncontrolled FMS for a long time, or who has both FMS and chronic myofascial pain or other co-existing conditions, a "...combination of multiple, mild impaired responses may lead to more profound physiologic and clinical consequences as compared with a defect in only one system..." (Adler, Manfredsdottir, Creskoff 2002).

Inadequate pain control may also influence endocrine balance. Never underestimate the effect of myofascial TrP pain augmented by FMS amplification. "Significant knowledge deficits regarding currently accepted principles of pain management practice as well as beliefs that could interfere with optimal care, mandate a need for educational interventions....Unwarranted fear of addiction is a misunderstood and important concept that needs to be addressed" (Lebovits, Florence, Bathina. et al. 1997). Add that to the misery the patient may feel if s/he

has been disbelieved, untreated, and/or mistreated, and there may be iatrogenic depression. Chronic pain itself can cause depression (Hendler 1984). Reassure your patient that the key to dealing with these conditions is identifying and controlling the perpetuating factors, and that you can help. Hope is a great medicine. These conditions are complex, and they take time, a good diagnostic eye, and may require education of the patient and the patient's insurance carrier as well.

It may be difficult to sort out all the symptoms and medications. Often, new meds have been added, and supplements as well, and they may be interacting and causing more symptoms. For example, the combination of Zoloft, melatonin and a high protein diet (such as for metabolic syndrome) can cause toxic neuropathy (Lehman, Johnson 1999). This may seem overwhelming, but be patient. Start with those symptoms that are perpetuating the cycle, such as lack of restorative sleep (Meerlo, Koehl, van der Borght et al. 2002). Anything that may impact on the wind-up and central sensitization, such as pain control, must be addressed (Staud, Vierck, Cannon et al. 2001), so you may be calling in a variety of medical care team members to help. The simple addition of Estrace vaginal cream may activate abdominal TrPs, causing symptoms such as menstrual cramps (even in patients without a uterus) and diarrhea. Discontinuing the therapy is not sufficient to remove the symptoms. The TrPs must be treated as well. Dealing with complicated diagnoses such as fibromyalgia and chronic myofascial pain is a challenge, but the difference you can make in the lives of these chronic pain patients is priceless.

References

Adler G. K, Manfredsdottir V. F., Creskoff F.W. 2002. Neuroendocrine abnormalities in fibromyalgia. *Curr Headache Rep* 6(4):289-98.

Bennett, R. M., S. C. Clark and J. Walczyk. 1998. A randomized, double-blind, placebo-controlled study of growth hormone in the treatment of fibromyalgia. *A J Med* 104(3):227-231.

Bennett, R. M. 1991. Symptoms of Raynaud's syndrome in patients with fibromyalgia. A study utilizing the Nielsen test, digital photopleysmography, and measurements of platelet alpha 2-adrenergic receptors. *Arth Rheum* 34(3):264–269.

Borg-Stein J. 2002. Management of peripheral pain generators in fibromyalgia. 2002. *Rheum Dis Clin North Am* 28(2):305-17.

Bou-Holaigah, I., H. Calkins, J. A. Flynn et al. 1997. Provocation of hypotension and pain during upright tilt table testing in adults with fibromyalgia. *Clin Exp Rheumatol* 15(3):239–246.

Crofford, L. J. 1998. Neuroendocrine abnormalities in fibromyalgia and related disorders. *Am J Med Sci* 315(6):359-366.

Curtis B.M., O'Keefe J.H. Jr. 2002. Autonomic tone as a cardiovascular risk factor: the dangers of chronic fight or flight. *Mayo Clin Proc* 398-9; 77(1):7-9.

Deodhar, A. A., R.A. Fisher, C.V. Blacker and A.D. Woolf. 1994. Fluid retention syndrome and fibromyalgia. *Br J Rheumatol* 33(6):576-582.

Drewes, A.M., K. Gade, K.D. Nielsen et al. 1995. Clustering of sleep electro-encephalographic patterns in patients with the fibromyalgia syndrome. *Brit J Rheumatol* 34(12):1151–1156.

Eisinger, J.B. 1999. [Hypothyroidism treatment: one hormone or two?] *Myalgies* 2(Suppl 2):1-3. [French]

Farias-Silva E., Sampaio-Barros M.M., Amaral M.E. et al. 2002. Subsensitivity to insulin in adipocytes from rats submitted to foot-shock stress. *Can J Physiol Pharmacol* 80(8):783-9.

Gerwin R.D. 2002. Myofascial and visceral pain syndromes: visceral-somatic pain representations. *J Musculoskel Pain* 10(½)"165-175.

Griep, E.N., J.W. Boersma and E.R. de Kloet. 1994. Pituitary release of growth hormone and prolactin in the primary fibromyalgia syndrome. *J Rheumatol* 21(11):2125–2130.

Grigsby, J., N.L. Rosenberg and D. Busenbark. 1995. Chronic pain is associated with deficits in information processing. *Percept Mot Skills* 81(2):403–410.

Hendler, N. 1984. Depression caused by chronic pain. *J Clin Psychiatry* 45(3 pt 2):30–38.

Kosek, E., J. Ekholm and P. Hansson. 1996. Sensory dysfunction in fibromyalgia patients with implications for pathogenic mechanisms. *Pain* 68(2-3):375–383.

Landis C.A., Lentz M..J., Rothermel J. 2001. Decreased nocturnal levels of prolactin and growth hormone in women with fibromyalgia. *J Clin Endocrinol Metab* 86(4):1672-1678.

Lebovits A.H., Florence I, Bathina R. et al. 1997. Pain knowledge and attitudes of health care providers: practice characteristic differences. *Clin J Pain* 13(3):237-243.

Lehman N.L., Johnson L.N. 1999. Toxic optic neuropathy after concomitant use of melatonin, zoloft, and a high protein diet. *J Neurooptha lmol* 19(4):232-234.

Lombard L., Augustyn M.N., Ascott-Evans B.H. 2002. The metabolic syndrome — pathogenesis, clinical features and management. *Cardiovasc J S Afr* 13(4):181-6.

Lowe J. 2000. *The Metabolic Treatment of Fibromyalgia*. Boulder, CO: McDowell Publishing Company.

Lowe, J.C., M.E. Cullum, L.H. Graf Jr. et al. 1997. Mutations in the c-erbA beta gene: do they underlie euthyroid fibromyalgia? *Med Hypo* 48 (2):125-135.

Martinez-Lavin, M., A.G. Hermosillo, C. Mendoza et al. 1997. Orthostatic sympathetic derangement in subjects with fibromyalgia. *J Rheumatol* 24(4):714–718.

Meerlo P., Koehl M., van der Borght K. et al. 2002. Sleep restriction alters the hypothalamic-pituitary-adrenal response to stress. *J Neuroendocrinol* 14(5):397-402.

Park D.C., Glass J.M., Minear M. et al. 2001. Cognitive function in fibromyalgia patients. *Arthritis Rheum* 44(9):2125-33.

Peters A., Schweiger U., Fruwald-Schultes B. et al. 2002. The neuroendocrine control of glucose allocation. *Exp Clin Endocrinol Diabetes* 110(5):119-211.

Raj S.R., Bruillard D., Simpson C.S. 2000. Dysautonomia among patients with fibromyalgia: a noninvasive assessment. *J Rheumatol* 27(11):2660-5.

Simons D.G., J.G. Travell, and L.S. Simons. 1999. Travell and Simons Myofascial Pain and Dysfunction: the Trigger Point Manual: Volume I, edition 2: The Upper Body. Baltimore: Williams and Wilkins.

Starlanyl DJ, Jeffrey JL, Roentsch G et al. 2001-2002. The effect of transdermal T3 (3,3′,5-triiodothyronine) on geloid masses found in patients with both fibromyalgia and myofascial pain: double-blinded, N of 1 clinical study. *Myalgies* 2(2):8-18.

Staud R., Vierck C.J. Cannon R.L. et al. 2001. Abnormal sensitization and temporal summation of second pain (wind-up) in patients with fibromyalgia syndrome. *Pain* 91(1-2):165-75.

Teitelbaum, J. 2001. From Fatigued to Fantastic. New York: Penguin Putnam Inc.

Tsigos C., Chrousos G. 2002. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *J Psychosom Res* 53(4):865.

Williams R.S., Cheng L., Mudge A.W. et al. 2002. A common mechanism of action for three mood-stabilizing drugs. *Nature* 417(6886):292-295.