Structural Pathology in the Muscles of Subclinical Hypothyroid Patients: Another Call for Early Treatment

Dr. John C. Lowe*

*Fibromyalgia Research Foundation
drlowe@FibromyalgiaResearch.org www.drlowe.com

A study report we published in *Thyroid Science* this past week is well worth announcing.[1] It stirs a hope in us—that the report will motivate more clinicians to provide subclinical hypothyroid patients with early thyroid hormone treatment. Early treatment is likely to relieve the patients' suffering, enable them to maintain normal function, and reduce their overall costs for health care services. In addition, early treatment will—if assertively engaged in—halt incipient functional and structural abnormalities, or reverse the frank pathology that has already developed, such as the muscle abnormalities reported by the authors of the report we published this week.

Four of the researchers and authors of the report (Drs. Michael Dunn, Arthur Cosmas, Linda Lamont, and Thomas Manfredi) are from the Department of Kinesiology, University of Rhode Island. The fourth (Dr. James Hennessey) is from the Division of Endocrinology, Rhode Island Hospital, Brown University School of Medicine.

To qualify a patient to enter their study, Dunn et al. used the conventional criteria for the diagnosis of subclinical hypothyroidism, the mildest form of hypothyroidism. The criteria included an above-range TSH level and an in-range free T_4 level.

Their study shows that among subclinical hypothyroid patients, muscle symptoms may be underlain by objectively verifiable structural muscle abnormalities. The study is the first to document with light and electron microscopy, pathological structural changes in the skeletal muscles of subclinical hypothyroid patients. The researchers note that their findings indicate a progression of such changes from subclinical to overt hypothyroidism.

The structural muscle pathology that Dunn et al. report is consistent with other researchers' reports of other muscle-related abnormalities in subclinical hypothyroid patients. (To read the specific findings of Dunn et al., detailed on pages 4 through 6 of their paper,[1,pp.4-6] must be compelling to clinicians who are committed to the well-being of their patients.) Hekimsoy and Oktem,[2] for example, reported elevated creatine kinase levels in subclinical patients. The patients' levels were not significantly elevated. Overall, however, the TSH and creatine kinase levels were positively correlated; that is, the higher the TSH levels, the higher the creatine kinase levels. Conversely, creatine kinase levels and free T_3 and free T_4 levels were inversely correlated; higher creatine kinase levels were associated with lower free T_3 and free T_4 levels.

Monzani et al. reported that during exercise, the average blood lactate level of subclinical hypothyroid patients was significantly higher than in controls "from the third exercise step onward."[3] The researchers wrote that the patients' mean increase of blood lactate during exercise was positively related to the duration of their subclinical hypothyroidism. "We conclude," they wrote, "that muscle energy metabolism is impaired in [subclinical hypothyroidism] in rough proportion to the known duration of the disease." This finding has an important practical implication: among subclinical hypothyroid patients, the energy-related biochemical abnormality of elevated blood lactate may progressively worsen when patients fail to undergo early therapy hormone therapy.

As Dunn et al. point out,[1] the muscle pathology they found is among a range of possible adverse health consequences when hypothyroid patients go untreated. They note that some of the adverse effects ("coronary heart disease, osteoporosis, atrial fibrillation, cognitive impairment, and depression") are among the nation's most common causes of illness, death, and diminished quality of daily life among older adults.[1,p.1]

But older adults aren't the only people adversely affected by untreated hypothyroidism. In more than two decades of working clinically with

hypothyroid patients, I've regularly seen subclinical hypothyroid patients—ranging in age from the teens through the fifties—in an unfortunate circumstance: their clinicians cavalierly denied them thyroid hormone therapy, preferring to wait until the patients' subclinical condition progressed to an overt and, in some cases, disabling stage.

The delayed treatment was, to me, patently unjustified. The patients had multiple classic hypothyroid symptoms. These included different combinations of fatigue, depression, cognitive dysfunction, cold intolerance, constipation, dry skin, hair loss, depression, cognitive dysfunction, exercise intolerance, chronic muscle pain and tension. The patients also had test results consistent with hypothyroidism, such as high cholesterol and LDL levels despite wholesome diets and regular exercise. Many patients had high thyroid peroxidase and thyroglobulin antibodies. The first of these subclinical hypothyroid patients I worked with suffered from treatment-resistant myofascial pain syndromes. The patients had failed to get more than palliation, even with high-quality physical treatment.

Most of my patients—perhaps because they were younger than the more commonly afflicted older adults—responded quickly, often dramatically, to thyroid hormone therapy; they had either complete or nearly-complete recovery from their symptoms and signs. On the other hand, I observed that in general, when clinicians had allowed their patients' hypothyroidism to progress from subclinical to overt, the patients' health problems had become compounded and complicated. As a result, more time and greater effort were needed for them to recover their health. Observing the results of delayed treatment were troubling to witness and worse for the patients. Hence, I'm especially appreciative of the report of the muscle pathology found by Dunn et al. in that it may lead to earlier treatment for many subclinical hypothyroid patients.

The muscle pathology that Dunn et al. report add to other types of muscle abnormalities that researchers have previously reported. Together, the different research groups' findings make clear to us ominous possibilities for subclinical hypothyroid patients whose clinicians deny them early treatment. If treatment is delayed, some of the patients are highly likely to undergo more advanced muscle pathology with associated worsening of their muscle symptoms and signs. It's highly likely that early treatment will prevent the proliferation of muscle pathology, reverse incipient muscle abnormalities, and relieve the patients' suffering from muscle tension, cramps, energy-deficiency contractures, and treatment-resistant myofascial pain.[10]

Early treatment for subclinical hypothyroidism will prevent clinicians from diagnosing some patients as having "fibromyalgia." Nowadays this diagnosis leads to FDA-approved "fibromyalgia" drug therapies (Cymbalta and Lyrica) that are inappropriate, unnecessary, and "effective" only in the most liberal sense of the term. We regularly hear complaints of adverse effects from patients who have undergone treatment with the drugs. The muscle abnormalities Dunn et al. report are similar to those of patients with a diagnosis of fibromyalgia.[4,5,6,7,8] The muscle abnormalities among fibromyalgia patients, along with other similarities to hypothyroidism, led Eisinger et al. in France[7,8] and me in the U.S., separately but almost simultaneously in the early 1990s,[10,11,12] to conclude that fibromyalgia is a metabolic disorder; in most respects, it is virtually identical to hypothyroidism. The hypothyroid-like muscle abnormalities of fibromyalgia patients were among the research findings that led my colleagues and me to conclude that the main underlying mechanism of fibromyalgia is inadequate thyroid hormone regulation.[9,10] The findings of Dunn et al. add carbon to our already-steel hard conclusion about the etiology of fibromyalgia.[9,10]

When Monzani et al. reported high lactate levels in subclinical hypothyroid patients, they concluded, "Early [thyroid hormone] therapy may be useful not only to provide specific treatment for such metabolic changes, but also to avoid progression to frank hypothyroidism." This humane proposal—early thyroid hormone treatment—is echoed by Dunn et al.[1,pp.7-8] For emphasis, I quote their conclusion:

"Establishing consistent morphological markers of subclinical hypothyroidism prior to disease progression could justify an earlier, more efficacious treatment with thyroid hormone. This treatment strategy may diminish morbidity by preventing disease progression from subclinical to overt hypothyroidism. Earlier initiation of this therapy may ultimately translate into an improvement in patients' lifestyle."[1,pp.7-8]

At *Thyroid Science*, we *earnestly* concur with Dunn et al.

References

1. Dunn, M.E., Hennessey, J.V., Cosmas, A.C., Lamont, L.S., and Manfredi, T.G.: Clinical Case Report: Ultrastructural Evidence of Skeletal Muscle Mitochondrial Dysfunction in Patients With Subclinical Hypothyroidism. *Thyroid Science*, 4(6):CLS1-8, 2009.
2. Hekimsoy, Z. And Oktem, I.K.: Serum creatine kinase levels in overt and subclinical hypothyroidism. *Endocr. Res*., 2005;31(3):171-175, 2005.
3. Monzani, F., Caraccio, N., Siciliano, G., et al.: Clinical and biochemical features of muscle dysfunction in subclinical hypothyroidism. *J. Clin. Endocrinol. Metab*., 82(10):3315-3318, 1997.
4. Kalyan-Raman, U.P., Kalyan-Raman, K., Yunus, M.B. and Masi, A.T.: Muscle pathology in primary fibromyalgia syndrome: a light microscopic, histological and ultrastructural study. *J. Rheumatol*., 11:808-813, 1984.
5. Awad, E.A.: Pathological changes in fibromyalgia. First International Symposium on Myofascial Pain and Fibromyalgia. Minneapolis, Minnesota, May 9, 1989.
6. Awad, E.A.: Histopathological changes in fibrositis. In *Advances in Pain Research and Therapy*, Vol.17. Edited by J.R. Fricton and E.A. Awad, New York, Raven Press, Ltd., 1990, pp.249-258.
7. Eisinger, J., Plantamura, A., and Ayavou, T.: Glycolysis abnormalities in fibromyalgia. *J. Am. Coll. Nutr*., 13:144-148, 1994.
8. Eisinger, J., Clairet, D., Zakarian, H., and Ayavou, T.: ATP érythrocytaire et apparel locomoteur: action de la calcitonine. *Lyon Méditerranée Med*., 26:326-328, 1990.
9. Lowe, J.C.: *The Metabolic Treatment of Fibromyalgia*. Boulder, McDowell Publishing Co., 2000.
10. Lowe, J.C. and Yellin, J.: Inadequate Thyroid Hormone Regulation as the Main Mechanism of Fibromyalgia: A Review of the Evidence. *Thyroid Science*, 3(6):R1-14, 2008.
11. Lowe, J.C.: Improvement in euthyroid fibromyalgia patients treated with T3 (tri-iodothyronine). *J. Myofasc. Ther*., 1(2):-16-29, 1994.
12. Lowe, J.C.: T3-induced recovery from fibromyalgia by a hypothyroid patient resistant to T4 and desiccated thyroid. *J. Myofasc. Ther*., 1(4):21-30, 1995.