

Fibromyalgia & Thyroid Disease

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The clinical features of fibromyalgia syndrome (FMS) and hypothyroidism are virtually the same (1,2,3,4,5,6,7,8,9,10). The most common symptoms of FMS are also common symptoms of hypothyroidism, and the objective abnormalities of FMS are also objective abnormalities of hypothyroidism. The symptoms and objective abnormalities of hypothyroidism are mediated by inadequate thyroid hormone regulation of cell function. Inadequate thyroid hormone regulation also plausibly mediates the documented features of FMS (11).

Hypothyroidism in FMS

Primary Hypothyroidism. The estimated incidence of hypothyroidism in FMS is higher than in the general public. The reported incidence of primary hypothyroidism in the general non-elderly USA population varies between 1% (12) and 5% (13). Laboratory thyroid function testing suggests that the incidence of primary hypothyroidism in FMS is 10% to 13% (14, 15, 16, 17, 18).

Anti-thyroid Antibodies. Aarflot and Bruusgaard measured thyroid microsomal antibodies in 737 men and 771 women who ranged in age from 40-to-42 (19). Subjects with chronic widespread musculoskeletal complaints had a significantly higher incidence of antibodies than did subjects without such complaints (16.0% versus 7.3%, $p < 0.01$). The prevalence of antibodies was significantly higher in women than men (20.4% versus 11.6%, $p = 0.02$). It is noteworthy, however, that laboratory thyroid function test results did not differ significantly between the two groups. The investigators wrote that their results suggest that patients with microsomal thyroid antibodies may have symptoms due to subnormal thyroid hormone regulation of cell function before thyroid gland dysfunction is detectable by tests of thyroid hormone and TSH levels. The researchers implied that many patients diagnosed with FMS may in fact have chronic, widespread pain due to impaired thyroid gland function revealed only by increased titers of thyroid microsomal antibodies. If this is true, then the incidence of primary hypothyroidism among FMS patients may be higher than the 10% to 13% suggested by measures of TSH and thyroid hormone levels.

Central Hypothyroidism. The incidence of central hypothyroidism, involving hypothalamic or pituitary dysfunction, in the USA population at large is about 0.00021% (12). Our research group has found that of 92 sequential unselected FMS patients, 40 patients (43.5%) had laboratory test results consistent with central hypothyroidism (16, 18). Other researchers have also reported high incidences of test results consistent with central hypothyroidism (20,21).

Thus, the incidence of primary hypothyroidism among FMS patients may be 2 to 10 or more times higher than in the USA population at large. The incidence of possible central hypothyroidism, however, may be 250,000 times higher. If we trust that thyroid function test results are reliable, we are compelled to reach a conclusion: If 10% of FMS patients have primary hypothyroidism, and 44% have central hypothyroidism, the total percentage of FMS patients with hypothyroidism is 54%.

Thyroid Hormone Resistance

Many researchers and clinicians consider the term "thyroid disease" to include only pathological processes that occur 1) within the thyroid gland itself, or 2) in other tissues, such as the pituitary gland, and indirectly result in subnormal function of the thyroid gland. However, this definition may be too narrow. In 1967, Refetoff et al. provided convincing evidence of partial cellular resistance to thyroid hormone in humans (22). Since then, a great volume of studies of human thyroid hormone resistance has accumulated. Also, mutations in the *c-erbA β* gene on chromosome 3 (which codes for the $\beta 1$ T3-receptor) have been shown to be the underlying mechanisms of general resistance to thyroid hormone (23). (The mechanisms of resistance in most afflicted patients remain unknown.) In some thyroidology textbooks, thyroid hormone resistance is grouped under "Special Topics in Thyroidology." However, it can be argued that thyroid hormone resistance should be classified as a subset of thyroid disease. As in central hypothyroidism, which is classed as a thyroid disease, thyroid gland function is indirectly altered in two classifications of thyroid hormone resistance. Also as in primary and central hypothyroidism, patients with symptoms and signs caused by thyroid hormone resistance can be effectively treated with thyroid hormone (albeit in higher than physiologic dosages, called "supraphysiologic" dosages).

Thyroid Hormone Resistance and FMS. As far back as the late 1980s, I (JCL) was puzzled as to why euthyroid FMS patients (those with normal thyroid test results) had identically the same hypothyroid-like symptoms and signs as did hypothyroid FMS patients. In searching for an answer, I came into communication with thyroid hormone resistance researchers. One of these, Steve Usala, had established a link between the c-erbA β gene and thyroid hormone resistance (24). He was also first to discover a mutation in the gene (25). (More than 100 different mutations in the gene have now been discovered (11).) Based on communication with Usala and other thyroid hormone resistance researchers, in 1990, my colleagues and I treated 77 euthyroid female FMS patients with T3 (as part of comprehensive metabolic treatment).

This treatment was based on our hypothesis that the patients had partial cellular resistance to thyroid hormone (26). Of the 77 patients, 19 (25%) did not feel that T3 had improved their status. They were withdrawn from use of the hormone. The remaining 58 patients (75%) reported that their symptoms were improved to varying degrees. For the group, the difference between pre- and post-treatment algometer scores (mean of the pressure/pain threshold of 18 tender points) was highly significant ($p < 0.0005$). The mean pressure/pain threshold of the 18 tender point sites was significantly higher (improved) after T3 treatment. Effective dosages of T3 ranged from 75 μ g. to 150 μ g.

Most patients improved with dosages between 81.25 μ g. and 100 μ g. (Normal replacement dosages were reported to be from 25-to-75 μ g.) Since that early open trial, we have continued to treat euthyroid FMS patients on the assumption that they have thyroid hormone resistance. We find that approximately 75% of euthyroid FMS patients markedly improve or completely recover when treated with what we term "metabolic rehabilitation." The treatment involves the use of T3, exercise to tolerance, wholesome diet, nutritional supplements, physical treatment, and cessation of the use of metabolism-impeding medications.

Most euthyroid patients improve only with supraphysiologic dosages of T3. We are convinced that the patients who improve or recover with supraphysiologic dosages of T3 have cellular resistance to thyroid hormone. We conclude that a patient has thyroid hormone resistance when four criteria are met. The patient:

- (1) is euthyroid before beginning the use of T3, according to thyroid function test results, including a TRH stimulation test;
- (2) markedly improves or completely recovers from hypothyroid-like FMS symptoms and signs with supraphysiologic dosages of T3;
- (3) after beginning T3 therapy has an extremely high free T3 blood level;
- (4) has no evidence of tissue thyrotoxicosis due to the high free T3 level, according to the results of serial ECGs, serum and urine biochemical tests, and bone densitometry.

Most of our euthyroid patients who improve or recover with metabolic rehabilitation involving T3 therapy meet these four criteria. Clearly, this set of findings in many treated euthyroid FMS patients shows that they meet Refetoff's definition of thyroid hormone resistance: "reduced responsiveness of target tissues to concentrations of thyroid hormone that under normal conditions would be excessive" (23). According to the four criteria, we have documented the presence of thyroid hormone resistance in FMS patients in [several double-blind, placebo-controlled, crossover studies](#) (27, 28, 31). Also, in a [case-control study](#), we found that the results of the treatment lasted long term (29). Throughout a 1-to-5 year follow-up period, 10 hypothyroid FMS patients maintained their improvement compared to untreated FMS matched control patients. Also, 10 euthyroid FMS patients treated with T3 maintained their improvement compared to control patients.

Criticisms

Eisinger (rheumatologist) and Fontaine and Rinaldi (thyroid specialists) have given several criticisms of the hypothesis we present here (30). We agree with most of the criticisms. For example, we know that a small amount of the available evidence contradicts the hypothesis. Despite this, the hypothesis is supported by far more of the available evidence than is any competing hypothesis of the etiology of FMS. Also, rigorous logical analyses show that the hypothesis is the most useful at this time for stimulating further fruitful theoretical and experimental exploration of FMS.

Eisinger, Fontaine, and Rinaldi also argued that the hypothesis applies only to a subgroup of FMS patients. We maintain that the subgroup is large—close to 90%. We agree with them, however, that patients should be treated with precaution. We also agree with an astute observation of theirs: that when the peripheral cellular effects of thyroid hormone can be normalized by agents such as selenium (which may increase the monodeiodination of T4),

this therapy is preferable to the use of exogenous thyroid hormone. (The American FMS/thyroid researcher Richard Garrison has made a similar argument.) We should rigorously study the treatment of FMS patients with agents such as thiol and selenium to learn whether some of the patients benefit more from these agents than from the use of T3. Even when patients do benefit from such agents, however, the benefits are mediated by an improvement in thyroid hormone regulation of cell function. This outcome further supports the hypothesis that in the involved patients, inadequate thyroid hormone regulation of cell function underlies their FMS.

Conclusions

If cellular resistance to thyroid hormone is accepted as a subset of thyroid disease not directly involving the thyroid gland, then our findings suggest that most FMS patients have thyroid disease. About 10% have laboratory test results consistent with primary hypothyroidism, and about 45% have results consistent with central hypothyroidism. This is a total of 55% of FMS patients who may have hypothyroidism.

Of the remaining 45% who have test results consistent with euthyroidism, 75% on average improve or recover when treated on the assumption that they have thyroid hormone resistance. This 75% is about 34% of our total sample of FMS patients. For a total percentage of FMS patients with possible thyroid disease, we can add this 34% of patients with thyroid hormone resistance (according to the four post-treatment criteria) to the 55% of hypothyroid patients (according to thyroid function test results). The result is 89% of FMS patients with putative thyroid disease. (See Table 1.)

This estimate is consistent with previous findings such as glycolysis abnormalities and T3-induced improvement in FMS patients with the polymyalgia-hypothyroid intractability syndrome described by Eisinger (11,14). In fact, as I (JCL) recently argued (11), virtually every symptom and abnormal finding in FMS is plausibly explained by inadequate thyroid hormone regulation. This proposed mechanism is unique in this respect.

Table 1. Percentage of FMS patients with thyroid disease.

Class of Thyroid Disease	% of Patients
Primary hypothyroid	10%
Central hypothyroid	45%
Thyroid hormone resistant	34%
Total % with thyroid disease	89%

The remaining 11% of FMS patients also have symptoms and signs that resemble those of hypothyroidism. Our conjecture is that these patients' symptoms and signs result from pathophysiological processes not related directly to thyroid hormone. However, we believe the pathophysiological processes in these patients impede metabolism in a set of tissues that generate symptoms and signs resembling those of hypothyroidism or thyroid hormone resistance.

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A Follow-up to Our Trip To France

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We had three objectives in visiting France. One was to personally meet Prof. J.B. Eisinger, who had invited us. Over the last several years, we've had prolific and enriching communications with Prof. Eisinger. We were delighted to spend time with him and his wife, André. They were very gracious and hospitable.

Prof. Eisinger is the leading fibromyalgia researcher in France. We can't overstate his importance to the advanced understanding of fibromyalgia as a metabolic disorder. Some of his studies helped reveal the bankruptcy of the "serotonin deficiency hypothesis" of fibromyalgia. By so doing, his studies have been strong leavening for the incipient rise of the "metabolic" paradigm of fibromyalgia.

The second objective of our trip was to announce our finding that some 90% of fibromyalgia patients have thyroid disease. We've posted our [text of the announcement](#) on another page of [drlowe.com](#).

Our third objective was to meet French clinicians, researchers, and fibromyalgia patients, and to establish a dialog with them about our work. We succeeded at these objectives. At the same time, we began some friendships and had a wonderful time.

The Grenoble, France Conference

On May 6, 2000, in Grenoble, we gave our presentations to the audience at the Congrès de l' Association des Fibromyalgiques de la Région Rhône-Alpes. I (JCL) presented our findings on the relation of fibromyalgia to thyroid disease. I (GH-L) presented information on the special use of ultrasound in the treatment of fibromyalgia patients as a part of metabolic rehabilitation. We gave our presentations in English. Only about a of the audience spoke English. So, after each of us spoke, French researchers read the main points of our presentations in French.

Following our presentations, we talked individually with French fibromyalgia patients, clinicians, and researchers. We were privileged to spend time with Michel Nicollet, M.D., of Toulouse, France, a physical medicine and rehabilitation specialist. I (GH-L) spent time with G. De Bisshop, M.D., author of several books on electrotherapy. He is working with ultrasound and transcutaneous electrical nerve stimulation as fibromyalgia treatments. We discussed the use of ultrasound to treat fibromyalgia patients.

We discussed our finding that some 90% of fibromyalgia patients have underlying thyroid disease with others at the conference. When Dr. Lowe presented the finding before the whole audience, reactions were mixed. The surprise and disbelief of some rheumatology fibromyalgia researchers were expected. Many patients, however, were encouraged to learn that an effective treatment is available.

Delegation from Switzerland. After we spoke to the audience in Grenoble, a delegation from Switzerland asked to speak with us. The delegation represented the Federation Suisse, Fibromyalgie: Groupe Genevois d'Entraide centre la Fibromyalgie. (Their website URL is < Madame Thérèse Jaquier-Seguin, Président of the Federation, was present.

Among other subjects, we talked with them about Professor Garth Nicolson's work in the USA. We were saddened to hear that in Switzerland, the medical community generally considers fibromyalgia a psychiatric illness. As I (JCL) showed in [The Metabolic Treatment of Fibromyalgia](#), labeling fibromyalgia as a psychiatric illness is a mixed bag of metaphysics, pseudo-science, and medical quackery. I'm slowly reaching the repugnant conclusion that this reprehensible practice knows no national limits.

Visit to Annecy

After the conference in Grenoble, we visited a warmly hospitable family, the Claveaus, in Annecy. Their daughter has fibromyalgia, and we are working on arrangements with her to translate some of [drlowe.com](#) into French. This is important to us; we want to make the information on our website available to patients in France who don't speak English. The Claveaus generously helped us with our schedule and plans and made the visit as special and memorable as could be. As Céline Claveau and we walked about Annecy, I (GH-L) took photographs. We've [posted some to a page](#) so you can see how beautiful this old city is.

Toulon, France Teleconference

When we left Annecy, we traveled by train to Toulon. There, we were hosted by Mme. Michèle Iltis, Editor of the French fibromyalgia publication *Myalgies*. We spent time with Mme. Iltis, Prof. Eisinger, and his wife André. The following day, May 11, we took part in a teleconference at the Centre Hospitalier Intercommunal. The main subject of discussion during the conference was physical treatment for fibromyalgia, such as ultrasound.

Afterward, still at the hospital, we participated in the examination of a fibromyalgia patient, and discussed differences in approaches to making diagnostic and treatment decisions. This meeting occurred in the examining room of Kamel Mechtouf, M.D., staff rheumatologist. Also present were Dr. Isabelle Berreder, physician and nutritionist, J. Mollines, M.D., anesthesiologist, and Francois Bonneville and Fanny Zaluski, microkinesiotherapists. Afterward, we had further discussions with Prof. Eisinger, Dr. Mechtouf, Dr. Berreder, and Mme. Iltis.

This was the conclusion of our activities in France. We left for home the next day, hopeful that over time, further dialogue with French clinicians, researchers, and patients will benefit fibromyalgia patients both in that country and ours.

Final Note: We learned on our trip that French physicians are prohibited from prescribing T3 except in "picogram" dosages. A picogram is one trillionth of a gram---too little to regulate the metabolism of fleas. The prohibition is based on a decision of a consensus panel of conventional thyroidologists. This French panel thus contributes to conventional thyroidology's 30-year legacy of illogical, scientifically-unjustifiable, and patient-harming conclusions.

In the USA, pharmacists provide patients with a leaflet when they fill their Cytomel (T3) prescriptions. It reads: "No known adverse effects when used properly." Yet French physicians can't prescribe therapeutic amounts of this harmless and extraordinarily useful hormone. This consensus opinion consigns incalculable numbers of French citizens to a poor quality of life, continuing illness, and premature death. Learning of this tragically unwise and harmful consensus opinion strengthens my (JCL) belief that conventional thyroidology is a worldwide public health menace. On humanitarian grounds, something simply must be done to free the public from its adverse influence.