continually monitored from the perspectives of the individual patient, the care centre, and the cystic-fibrosis population as a whole. Such effort should help in bringing the management of *Pseudomonas aeruginosa* infection close to the ideal, while a cure for cystic fibrosis is awaited.

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Thyroid (neuro)myopathy

There has been a longstanding clinical suspicion that muscular complaints are common symptoms of thyroid disease—muscle stiffness being especially so in hyperthyroidism and muscle weakness in both hypothyroidism and hyperthyroidism. This suspicion has been confirmed by Ruurd Duyff and colleagues[1] in their prospective study in which they recorded objective measures of muscle and nerve function. They found that over 75% of hypothyroid patients and 67% of hyperthyroid patients have neuromuscular symptoms. Most notable was the observation that proper diagnosis and appropriate treatment led to resolution of these symptoms.

The investigators comment that the muscle weakness in hyperthyroidism, although traditionally viewed as being myopathic, could not be confirmed by electromyographic studies. This conclusion is correct from an electrodiagnostic point of view but does not acknowledge the regulatory role of thyroid hormone on the transcription of numerous muscle genes encoding both myofibrillar and calcium-regulatory proteins (panel).[2] Although this regulatory effect is best documented in the heart, many studies of skeletal muscle have shown changes in expression of myosin-heavy-chain gene that accompany thyroid disease states.[3] Such phenotypic changes would not necessarily be expected to alter electromyographic studies, but their effects on muscle-function tests and symptoms would be reversed with restoration of normal serum concentrations of thyroid hormone. Duyff and colleagues' finding that the myopathic changes resolved with treatment over 5–6 months is consistent with the inherent latency of other actions of thyroid hormone on the cell nucleus.[4] In addition to the long half-life of thyroxine (7 days) changes in protein synthesis and degradation must occur to restore the euthyroid myocyte phenotype.

Thyroid-hormone-responsive muscle genes

- Na^+/K^+ ATPase
- Myosin heavy chain isoforms
- Sarcoplasmic reticulum Ca^{2+} ATPase (SERCA2)
- Phospholamban (PLB)
- Adenylyl cyclase
- Voltage-gated K^+ channels (Kv 1·5, 4·2, 4·3)
- β_1-adrenergic receptors
- Guanine nucleotide regulatory protein (G_s)
- Na^+/Ca^{2+} exchanger (NCX)

β-adrenergic blockade can rapidly reverse a substantial part of the muscle weakness in hyperthyroidism.[5] This response indicates that reversible changes in calcium handling and cyclic-AMP-mediated contractile function contribute to the thyroid myopathy. Changes in diameter of type 2A fibres and a decline in oxidative capacity have been shown in thyrotoxic human skeletal muscles.[6] These changes occur acutely and perhaps at the neuromuscular junction or other cell-surface receptors (β-adrenergic), which suggests that the myopathy may in fact be a neuromyopathy.

Not to be overlooked in the understanding of thyroid hormone action on skeletal muscle is the positive inotropic effects that thyroid hormone exerts on the heart.[2] These effects contrast with the characteristic and well-documented impairment resulting from excess thyroid hormone on skeletal muscle function.[1,5] Although the reason for this organ-specific difference remains unclear, different myosin isoforms and, more importantly, different pathways for calcium cycling and the associated regulatory proteins probably underlie these findings.[2,3] The ability of thyroid hormone to promote phospholamban phosphorylation as well as regulate its expression in the heart[4,7] is further evidence of its selective cardiac inotropic action.

Whatever the mechanism by which the thyroid affects muscles, prompt diagnosis and restoration of normal thyroid function leads to resolution of most neuromuscular symptoms (such as weakness, fatigue, stiffness, and cramps). The implication of this finding is that all patients being assessed for neuromuscular disease could benefit from routine testing of serum thyrotropin.

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