

# Hyperthyroidism: progress in last two decades research papers examples

[Technology](#), [Development](#)



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The complexity of managing hyperthyroidism is largely attributable to the multi systemic effects, a diverse range of symptoms and a wide clinical spectrum ranging from subclinical to severe disease. This work briefly touches on the trends in management of hyperthyroidism and key research findings that have guided clinical approaches over the last 2 decades. Literature review highlighted some niche areas that have predominantly been the focus of research. These include, evaluation of diagnostic criteria, interpretation of laboratory results and prognostic implications of subclinical thyroid disease.

## **Diagnostics**

Thorough clinical assessment of patients continues to be indispensable with serum TSH level being the standard screening test for suspected hyperthyroidism. A combination of normal free T3 and free T4 in association with depressed TSH levels is not uncommon. Further, it is increasingly being

acknowledged that free hormone levels are highly susceptible to changes in binding protein levels induced by drugs, pregnancy or other severe illnesses. The artefactual alteration in free hormone levels is a major impediment in proper treatment of hyperthyroidism in general practice. (TFT Guidelines Development Group, 2006)

The high prevalence of subclinical thyroid dysfunction particularly in association with Grave's disease is largely acknowledged. However, a clear consensus on the desirability of intervening in subclinical thyroid dysfunction is yet to emerge. (Rugge, Balshem, Sehgal, 2011) Nonetheless, it is now recommended that persisting subclinical hyperthyroidism should at a minimum prompt referral for expert evaluation.

Another study investigating management trends over the last 10 years revealed the dominance of thyrotrophin and free thyroxine as the most common tests employed for in vitro diagnosis of Graves' disease. (Escobar-Jiménez et al 2000) There was a concomitant declining trend in the use of total thyroxine, total triiodothyronine, and thyroglobulin in comparison with the surveys conducted 10 years back. Among immune markers used for diagnostic purposes, the use of thyrotrophin receptor antibodies was found most prevalent. The slow but steady increase in use of antithyroperoxidase antibodies was also noticeable.

### **Genetic basis of autoimmune hyperthyroidism.**

Genome-wide association studies over the years have benefited from access to larger disease cohorts, evolution of high throughput genotyping technologies and better documentation of genome scale variations. This has

helped clearly delineate the auto immune pathways in Grave's disease, e. g., identification of novel AITD risk genes. With confirmation of AITD susceptibility loci, a number of pathophysiological mechanisms have now been attributed to their immunological origins. Investigation of new risk genes and the correlation of implicated variants with specific gene regions are identified priorities for future research. (Hadj-Kacem et al., 2009) (Manji et al., 2006)

## **Treatment**

Much of the treatment modalities have remained the same with some regional variations in treatment approaches coming to light. Notwithstanding the preferences, antithyroid drugs continue to be the pre eminent primary therapeutic option for Grave's disease. There is a noticeable tendency to resort to surgical treatment only in case of large sized goiter or in cases of recurrent hyperthyroidism with antithyroid pre treatment. Radioiodine therapy has been preferred in cases of recurring hyperthyroidism presenting after antithyroid treatment or goitre surgery. In the shorter term, first line <sup>131</sup>I therapy is associated with fewer relapses in comparison to antithyroid drugs. The need for outcomes research in this subject is compelling and establishment and maintenance of case directories is a fundamental requirement to ascertain investigate long term treatment outcomes in hyperthyroidism. (Elston & Conaglen, 2005)

## **Progression**

Basal TSH level has a strong prognostic value particularly with respect to recurring hyperthyroidism with a reported efficacy approaching 75%.

However, false positives and false negative should be considered in interpreting TSH levels. (TFT Guidelines Development Group, 2006) It is widely noted that hyperthyroidism associated with presence of thyroid nodules is more likely to progress to frank hyperthyroidism than hyperthyroidism associated with Grave's disease. Evidence supports the case for more conservative treatment in patients with subclinical hyperthyroidism due to Grave's disease, while more definitive treatment like Radioactive Iodine and surgery may be desirable early in the course in hyperthyroidism associated with one or more nodules. (Elston & Conaglen, 2005)

### **Patient monitoring**

The need to monitor patients for other effects of hyperthyroidism has also been emphasized. e. g., bone mineral density scanning in postmenopausal women and in cases with family history of osteoporosis. Ambulatory ECG monitoring to rule out dysarrhythmias in symptomatic patients, and CT scan of neck to rule out tracheal or oesophageal obstruction.

Patients with subclinical hyperthyroidism that cannot be explained by other illness or drug therapy should have repeat thyroid functioning with a frequency initially determined by the clinical findings. Untreated subclinical hyperthyroidism should be followed up by repeat thyroid function test every 6 to 12 months. (TFT Guidelines Development Group, 2006)

### **Thyroid Eye Disease**

Last decade has witnessed significant advances in understanding the pathophysiology of Grave's ophthalmopathy. A preliminary study has

suggested a potential remedy for inducing remission in cases of Grave's diseases associated with low TSH-receptor antibody levels. (El Fassi et al. 2007) This prospective study of monoclonal CD20 antibody, Rituximab, also revealed improvement in signs of Ophthalmopathy in these patients. However, its utility is limited by both cost and toxicity. Alongside some candidate drugs have been identified with potential for availability in near future. Despite earlier view that surgery (thyroidectomy) may protect against future development of Thyroid Eye Disease, there is no confirming evidence to support this assertion.