

# New Developments in the Management of Thyroid Disorders

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**T**he search for discovery of new methods and medications for management of thyroid disorders has continued during the last few years, in the third millennium. New developments have been made both in the management of incurable disorders such as metastatic medullary thyroid carcinoma, and in the domain of conditions where endocrinologists have had difficulty in proper management strategies, such as Graves' ophthalmopathy.

Thyroid cancer is increasing at a rate more rapid than that of any solid tumor, and many of the genetic mutations or chromosomal translocations that cause papillary, follicular, or modularly thyroid carcinoma have been identified, thus providing new insights into tumor pathogenesis, diagnosis and treatment. The development of a medication in the management of metastatic medullary carcinoma is promising. It has been shown that Vandetanib decreases tumor size in some and prevents the progression of disease in other patients with metastatic medullary carcinoma.<sup>1</sup> The disease control rate is 90% and this drug has demonstrated encouraging anti-tumor activity in patients with metastatic me-

dullary cancer. Promising results have also been reported for the use of fluoropyrimidine carbamate (capecitabine) in the treatment of medullary thyroid and radioiodine-resistant differentiated thyroid carcinomas.<sup>2,3</sup> This drug is converted to 5-fluoracil by thymidine phosphate inside targeted tissues.<sup>2</sup>

Clinical management of benign thyroid nodules has been a dilemma for endocrinologists. Although it has been recommended that nodules with negative FNA should not receive suppressive treatment, this approach is not acceptable for many patients who desire at least a decrease in the size of their thyroid nodules. Therefore, investigators have adapted modalities for reduction of nodule diameter, such as alcohol injection in the nodule, laser therapy<sup>4</sup> and recently percutaneous radiofrequency thermal ablation of thyroid nodules. The latter method induces stable thyroid nodule shrinkage and may prevent further increase in the size of the nodule. This method is also effective in reducing volume of large hyperfunctioning thyroid nodules.<sup>5</sup>

Management of thyroid-associated ophthalmopathy (TAO) may pose a serious challenge to the thyroidologist and ophthalmologist. High dose glucocorticoid therapy has been the mainstay of management of TAO. However, this treatment may not be effective

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in certain groups of patients. Recently Rituximab, a humanized chimeric anti-CD 20MAB, whose variable antigen binding region is derived from a mouse antibody, has been shown to positively affect the clinical course of TAO, independent of either thyroid function or circulating thyroid autoantibodies, including TRAb. The clinical activity score and severity of TAO decrease more significantly after treatment with rituximab, as compared to that of intravenous glucocorticoid therapy.<sup>6</sup>

Ease, effectiveness and low expense of radioiodine therapy has led to increasing reliance on radioiodine treatment for hyperthyroidism.<sup>7</sup> However, hypothyroidism occurs in 50-100% of patients treated with radioiodine. Variability in potency, uniformity and reproducibility of thyroxine preparations,<sup>8</sup> effects of over replacement of thyroxine in heart and bones,<sup>9</sup> and lack of patient compliance<sup>10</sup> may make the long-term precise

management of radioiodine-induced hypothyroidism problematic. In addition, a few reports of increased malignancy<sup>11</sup> and increased prevalence of non-communicable diseases<sup>12</sup> in radioiodine (RAI) treated hyperthyroid patients have also posed questions regarding the safety of RAI treatment for hyperthyroidism.

Recently, the potential molecular inhibition of TSH receptor has been studied. It has been shown that low molecular weight ligands that target the transmembrane region of TSH receptor might have therapeutic potential for the treatment of Graves' hyperthyroidism<sup>13</sup>. Another new development in the management of hyperthyroidism is the proposed method of continuous antithyroid therapy.<sup>14</sup> This method has been safe, less expensive and acceptable by the patients and causes less fluctuations in the concentration of serum TSH, when compared to RAI treated patients on maintenance doses of levothyroxine.

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