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## Editorial

### **COMMON FALLACIES IN THE MANAGEMENT OF GRAVES' DISEASE**

**D Khoo**

Graves' Disease is common in Singapore affecting some 1.28% of the population. A number of fallacies about the management of this condition continue to be perpetuated causing patients unnecessary anxiety, confusion and resulting in sub-optimal management. One common misconception is that patients with hyperthyroidism should not conceive while on anti-thyroid drugs. It is not the anti-thyroid drugs, but rather uncontrolled thyrotoxicosis, particularly in the second half of gestation, which is associated with maternal and foetal morbidity<sup>(1)</sup>. All 3 anti-thyroid drugs currently in use in Singapore – Carbimazole, Methimazole and Propylthiouracil, are generally safe for pregnancy. While patients who are severely thyrotoxic should be advised to delay pregnancy till euthyroidism is achieved, the results are generally favourable if conception occurs after the disease has been adequately controlled. The dose of anti-thyroid drugs should, however, be kept as low as possible throughout pregnancy with the guiding principle that enough be given to maintain the free T4 levels at the high end of the normal range. For those planning pregnancy, Propylthiouracil remains the drug of choice<sup>(1)</sup> since Carbimazole and Methimazole have been associated with aplasia cutis. However the risk of aplasia cutis is extremely low and patients who conceive while on Carbimazole or Methimazole should be reassured.

Unfounded fears regarding carcinogenesis and teratogenicity following radioiodine continue to persist. A recent population-based study reported in the Lancet showed no increased risk of carcinogenesis<sup>(2)</sup>. Incidence of cancers of the pancreas, bronchus, trachea, bladder, and lymphatic and haemopoietic systems was lowered following radioiodine therapy. There were, however, small but significant increases in incidence and mortality for cancers of the small bowel and thyroid. Overall cancer risk was lowered. While many doctors continue to advise women in their child-bearing years against radioiodine, the dose of radiation to the ovaries following the procedure are lower than those resulting from procedures such as barium enemas, urography or even barium meals<sup>(3)</sup>. Even in the worst-case scenario, it has been estimated that the rate of spontaneous anomalies would rise from 800 to 803 among 100,000 women given 10mCi of radioiodine prior to conception<sup>(3)</sup>. The only adverse effects of this treatment are occasional worsening of Graves' ophthalmopathy and rarely, radiation thyroiditis. The risk of hypothyroidism is approximately 50% at 1 year, 5% per year thereafter up to 5 years and then 1% a year<sup>(4)</sup>. However post-radiation hypothyroidism is far simpler to treat than hyperthyroidism.

Block and replace regimens for Graves' disease in which combinations of high-dose anti-thyroid drugs and L-thyroxine are used became popular in Singapore in the early 1990s. Initial reports suggested that remission rates were superior with these regimens compared to decremental doses of these drugs although many subsequent studies have since contradicted this. Commencing in 1996, we conducted a prospective trial in which 130 patients were randomised to receive either a block and replace regimen of Carbimazole 30 mg a day combined with L-thyroxine or a titration regimen using maintenance doses of Carbimazole 10 mg a day. Patients were treated for 12 months and then followed up for a further 12 months. The relapse rates in the 2 groups were 57.2% and 46.8% respectively. On this basis, we no longer recommend the block and replace regimen except in rare cases that respond poorly to the decremental regimen.

Finally, the role of smoking in Graves' disease is often not recognised. Smoking increases the risk of Graves' disease and is particularly deleterious in Graves' ophthalmopathy<sup>(5)</sup>. Such patients should therefore be strongly advised to give up smoking.

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