Thyroid Disorders and Pregnancy Part 1

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Over the past decade there has been a rapid expansion in our knowledge regarding thyroid function and thyroid diseases in pregnancy. These advances include development of guidelines for the optimal management of pregnant women on thyroxine replacement therapy; research studies detailing the adverse effects of iodine deficiency on the mother and the developing foetus; the negative impact of mild or even subclinical hypothyroidism on the pregnancy and the foetus; and a better understanding of detection and management of autoimmune thyroid disease during pregnancy and the postpartum period. In hindsight, it is clear that many of these problems have been overlooked or managed poorly in the past. Unfortunately, not enough attention is being paid to prevention and management of thyroid disorders in pregnancy and the postpartum period and we should be asking Obstetricians, GPs and Endocrinologists to pay more attention to preventing and treating these disorders. In the first of two articles I will deal with disorders that result in underactivity (hypothyroidism) of the thyroid during pregnancy and in the second article I will deal with disorders causing overactivity (hyperthyroidism) and also benign and malignant tumours of the thyroid that may occur coincidentally in pregnant women.

Pregnancy and the Thyroid Gland

A normal pregnancy, even in a woman without thyroid disease, poses a major challenge to the thyroid gland to dramatically increase thyroid hormone production by at least 50% above the prepregnant output. This must all happen within the first few months of the pregnancy. If the maternal thyroid gland is unable to meet the requirements for increased thyroid hormone production early in pregnancy, either because of iodine deficiency in the diet, or because of underlying thyroid disease, then the pregnancy will be at risk of early miscarriage, premature labour and foetal loss. Even if the baby survives it may suffer irreversible brain damage from

thyroxine deficiency leading to learning difficulties, lower IQ, hearing impairment and other neurological problems. All of this comes about because it is thyroid hormone (thyroxine) from the mother that supplies all of the developing baby's needs during the first two thirds of the pregnancy. It is only in the last trimester that the baby's thyroid gland is sufficiently mature to produce enough thyroid hormone to look after its own requirements. We need to remember that the thyroid gland of the developing foetus remains totally dependent upon the mother for an adequate supply of iodine to make its own thyroid hormone during the latter part of gestation. This dependence on the mother for iodine will continue while the baby is being breast-fed.

Iodine and Thyroid Physiology

Iodine is essential for the synthesis of the thyroid hormones (thyroxine-T4 and triiodothyronine-T3) by the thyroid gland. Iodine is absorbed into the body from iodine containing foods such as iodised salt, milk and other dairy products, sea foods and eggs. The growing child requires around 100 µg per day and a healthy adult around 150 µg per day. But during pregnancy the iodine intake needs to be stepped up to at least 250 µg per day. This increased intake should be maintained while the woman is breast-feeding, as the infant's thyroid gland needs around 100 micrograms per day. Failure to maintain an adequate iodine intake throughout the pregnancy will result in the mother's thyroid gland enlarging and struggling to produce enough thyroxine to maintain the pregnancy and meet the needs of the foetus. If the iodine deficiency is severe enough to compromise thyroid function, the foetus may be spontaneously aborted, or the woman may go into premature labour endangering the survival of the foetus. Miscarriage rates and premature deliveries are greatly increased in iodine deficient women. The children who survive are at risk of suffering irreversible brain damage.

Recent research studies in pregnant women in NSW, Victoria and Tasmania have shown around half of the pregnant women living in these states are mild to moderately iodine deficient. On average, we have calculated the daily iodine intake to be around 130 micrograms per day, which is about half of what the WHO and other expert groups recommend for pregnant women to maintain normal thyroid function. If a woman has sufficient iodine stored in her thyroid gland she may get

through the pregnancy without any adverse effect on her thyroid function, the pregnancy or on foetal brain development. However, it is not worth taking that risk. We strongly recommend that every woman takes an iodine supplement before getting pregnant or as soon as she confirms her pregnancy. The only exception to this recommendation would be women who are certain that their daily iodine intake is sufficient for pregnancy and women with active Graves' disease or a past history of hyperthyroidism. Women in these circumstances should seek expert advice from an Endocrinologist regarding their iodine intake. Combining the iodine supplement with folic acid makes good clinical sense. The WHO recommends a supplement of 250 micrograms per day that will provide all the iodine a woman needs on a daily basis. Taking more than 250 micrograms will not provide any more benefit to the pregnant woman or her foetus. Taking more than 500 micrograms of iodine per day is considered excessive and while this excessive quantity is unlikely to cause any harm it certainly will not do any good and therefore should be avoided. If women follow these recommendations there is no need to perform routine urinary iodine excretion testing during pregnancy. However, some women may want to know what their urinary iodine excretion level is before commencing a supplement.

Autoimmune Thyroid Disease and Hypothyroidism in Pregnancy

Autoimmune thyroid disease (AITD) is characterised by the presence of destructive circulating thyroid autoantibodies, especially anti-thyroid peroxidase antibodies (anti-TPOAb) and anti-thyroglobulin antibodies (anti-Tg) that usually indicate the presence of underlying lymphocytic thyroiditis (inflammation of the thyroid) also known as Hashimoto's disease. The other thyroid antibodies that can be present in the blood are the stimulating thyroid receptor antibodies (TRAB) that cause Graves' disease and hyperthyroidism and that disorder will be discussed in the second article in this series.

We do not know how common (prevalent) AITD is in Australian women of child-bearing age. We do not have any good studies. We think it may affect between 5% and 10% of women. While most of these women will not show any evidence of disturbed thyroid function and not have any symptoms or signs of thyroid disease before conceiving, they are at risk of developing mild hypothyroidism early in

pregnancy because their thyroid glands are damaged and cannot meet the challenge of increasing thyroxine production by at least 50% that is required to sustain a normal pregnancy.

Management of Hypothyroidism Due to Autoimmune Thyroid Disease

Autoimmune Thyroid Disease Hypothyroidism and Subclinical Hypothyroidism

A raised serum TSH and decreased serum Free Thyroxine (FT4) in the blood, accompanied by the presence of positive thyroid antibody levels, is diagnostic of primary hypothyroidism caused by autoimmune thyroid disease. When the serum TSH level is mildly raised and FT4 normal we call this subclinical hypothyroidism. Regardless of whether the disorder is clinical or subclinical in pregnant women or who are trying to become pregnant, it is imperative that they be treated with Thyroxine to prevent miscarriage or damage to the foetus. If hypothyroidism has been diagnosed before pregnancy the woman should ensure she is getting enough thyroxine to keep the serum TSH within the low normal range (TSH less than 2.0mIU/L). The daily dose of Thyroxine will need to be increased by a minimum of 25% as soon as the pregnancy has been confirmed and thyroid function tests monitored every 4 to 6 weeks to adjust the Thyroxine dosage. It is my experience that most women will require an increase in Thyroxine dosage of around 50% of the preconception dosage, but some patients may need up to a 100% increase in dosage. It is my recommendation that women taking Thyroxine who are trying to get pregnant should increase their daily dosage by 25% before they try to conceive. After delivery most hypothyroid women need a decrease in the thyroxine dosage they received during pregnancy. While breastfeeding these women will need to ensure an adequate intake of iodine to pass onto their breastfed infants.

Autoimmune Thyroid Disease and Normal Thyroid Function

We are still uncertain how to manage women who have positive thyroid autoantibodies (particularly high levels of anti-TPOAb) but have normal levels of TSH and FreeT4 in the blood. We know that these women have a threefold increased risk of miscarriage and premature labour. Some experts are now recommending that all

of these women be treated with Thyroxine during pregnancy while others remain cautious. There is some evidence that treatment with Thyroxine may prevent obstetrical complications, but we need more evidence from clinical trials before we treat all thyroid antibody positive women. While we are waiting for this evidence I strongly recommend that pregnant women who are thyroid antibody positive be monitored with TSH and FreeT4 tests at 6 weekly intervals throughout pregnancy. This ensures that those who will develop overt hypothyroidism or subclinical hypothyroidism will be picked up and treated. For thyroid antibody positive women who have a history of miscarriage, some experts believe Thyroxine treatment should be commenced as soon as pregnancy is confirmed.

Screening for Thyroid Disorders

The authoritative American Endocrine Society has recently stated that the question of universal screening of pregnant women for thyroid disease remains unsettled. While some experts consider screening desirable, Medicare will not pay rebates for this form of screening in Australia. Therefore, we should be educating women at risk and developing guidelines for diagnosing thyroid disease in women who are trying to get pregnant or who are pregnant. Those at risk of developing thyroid disease are women with; a previous history of miscarriage or premature labour, past history of thyroid disease or known to have a positive thyroid antibody test , goitre, family history of thyroid disease, other autoimmune disorders (for example coeliac disease or Type 1 diabetes). If there is any suspicion of thyroid disease then I would recommend testing with serum TSH, FreeT4 and thyroid antibodies and then performing a thyroid ultrasound if autoimmune disease is likely to be present.

Acknowledgement: For this article I have drawn heavily on the American Endocrine Society's 2007 Clinical Guidelines: Management of Thyroid Dysfunction during Pregnancy and the Postpartum.