Screening for thyroid disease and iodine deficiency

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Summary
The high global prevalence of iodine deficiency and autoimmune thyroid disorders and the mental and physical consequences of these disorders creates a huge human and economic burden that can be prevented, in large part, by early detection and appropriate preventative or therapeutic measures. The availability of sophisticated, sensitive and accurate laboratory testing procedures provides an efficient and effective platform for the application of screening for these disorders.

Measurement of urine iodine concentration (UIC) in school children or pregnant women is the recommended indicator for screening populations for iodine deficiency. The severity of the iodine deficiency is classified according to the UIC.

Measurement of serum thyrotropin (TSH) as an indicator for population iodine deficiency is used only in neonates and is supplementary to UIC screening. Other indicators such as goitre rates, thyroid function and serum thyroglobulin levels are useful adjunctive but not frontline process indicators.

The human and economic benefits of screening for congenital hypothyroidism by measurement of heel-prick TSH have been well documented and justify its universal application. Using this measurement for monitoring population iodine intake is recommended by the World Health Organization but further validation is required before it can be universally recommended.

Subclinical thyroid dysfunction is readily detected by current highly sensitive serum TSH assays and its prevalence appears to increase with age, varies with iodine intake and ethnicity and may occur in up to 20% of older age people. Subclinical hyperthyroidism is the less common disorder and screening cannot be justified because of its low prevalence and minimal or insignificant clinical effects. The argument for screening for subclinical hypothyroidism in middle-aged and older women is stronger but lacks evidence of benefit from randomised controlled trials or cost benefit analyses of therapeutic intervention, so it cannot currently be recommended.

The publication of recent Clinical Practice Guidelines for management of thyroid disease in pregnancy from the American Endocrine Society and American Thyroid Association provide persuasive arguments for early detection and treatment of overt and subclinical hypothyroidism to prevent obstetric complications and potential neurocognitive disorders in the offspring. Given the indisputable benefits of therapy, the sooner thyroid dysfunction is detected, before or as early as possible in gestation, the more likely there will be a better outcome. Because of the limitations of targeted case detection in women at risk of subclinical hypothyroidism, there has been a gradual shift in opinion to universal TSH screening of all women as soon as practicable in pregnancy. While a positive association exists between the presence of anti-thyroid antibodies and increased pregnancy loss, universal screening of all pregnant women for underlying autoimmune thyroid disease is difficult to justify until there is evidence of beneficial outcomes from randomised controlled trials. Vigorous and liberal targeted case detection remains the recommended strategy to address this problem.

INTRODUCTION
Screening is an important concept in public health medicine, especially as an integral component of disease detection, and is the application of a diagnostic procedure in a population, or population subset, to detect asymptomatic disease. In the case of non-communicable diseases, the purpose of screening is to discover asymptomatic, affected individuals so that they can receive appropriate treatment. Case detection in everyday medical practice overlaps with screening but there are subtle distinctions as case detection procedures are applied, in large part, to individuals in a selective ‘sick or at risk population’ usually attending for medical care, whereas screening is usually applied to the theoretically asymptomatic, well population. In many situations these distinctions may be semantic as the distinction between screening and case detection is often blurred. The prerequisites before screening for disease is undertaken are well documented.

Screening for thyroid dysfunction is an attractive and much debated proposition in clinical medicine because of the high, global prevalence of iodine deficiency and autoimmune thyroid disorders affecting people of all ages. The availability of effective therapies, coupled with sophisticated sensitive and accurate screening testing procedures, provides the platform for a discussion of the applicability of screening for iodine deficiency and thyroid disorders at certain life stages and in specific ethnic and geographic populations.

LABORATORY METHODS FOR SCREENING
Urine iodine concentration
Iodine is an essential component of the thyroid hormones that are crucial for regulation of metabolism and human physical
and neurological development. Insufficient iodine intake leads to decreased thyroid function resulting in multiple physical and mental disorders, collectively known as iodine deficiency disorders (IDD). The expression of these disorders is dependent upon the severity and timing of the iodine deficiency. As it is generally assumed that 90% of recent iodine intake subsequently appears in the urine of an iodine sufficient person within the next few days, the urinary iodine concentration (UIC) is an excellent proxy marker for current iodine intake.

Analytical methods for measurement of urinary iodine have conventionally been based on the manual spectrophotometric measurement of the Sandell-Kolthoff reduction reaction. Currently, routine clinical laboratories generally employ one of several, automated or microtitre plate methods, with the ‘gold standard’ being inductively coupled plasma mass spectrometry (ICPMS). Participation of laboratories in an accredited quality assurance program is essential. The methods for collection of urine vary from a ‘spot urine’ sample to 24 hour collections and expression of results from μg/L to μg/g creatinine. While 24 hour urine collections remain the reference standard, they are notoriously unreliable and difficult to obtain from healthy volunteers so that casual ‘spot’ samples are preferred for population screening and results are expressed as μg/L. Expression of the UIC as μg/g creatinine allows for variations in urine output, but has the disadvantage in populations where there are large inter-individual variations in creatinine excretion. Day to day variations in UIC preclude the use of the UIC as a diagnostic tool of iodine nutritional status in an individual. Several methods have been proffered to correct for the day-to-day (i.e., within-person) variation in population survey data. One method is to collect a second set of data from a subset of the survey population to calculate a correction factor which is then applied to the main survey population distribution.

The World Health Organization (WHO) / United Nations Children’s Fund (UNICEF) / International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommended method for population screening for iodine deficiency is measurement of UIC in spot urine samples collected from school-aged children (6–12 years) and the population iodine nutritional status is determined by the median UIC (Table 1). A median UIC of <100 μg/L represents iodine deficiency in children and adults, but a median UIC of <150 μg/L indicates iodine deficiency in pregnant women. The higher value in pregnant women corresponds to the significantly increased recommended daily intake (RDI) of 250 μg, compared with an RDI of 150 μg for non-pregnant adults.

Table 1 Recommendations for iodine intake and related urinary iodine concentration

<table>
<thead>
<tr>
<th>WHO recommendation</th>
<th>Recommended Iodine intake (μg/day)</th>
<th>UIC for adequate iodine intake (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 0–5 years</td>
<td>90</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Children 6–12 years</td>
<td>120</td>
<td>100–199</td>
</tr>
<tr>
<td>Adolescents and adults</td>
<td>150</td>
<td>100–199</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>250</td>
<td>150–249</td>
</tr>
<tr>
<td>Lactation</td>
<td>250</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

UIC, urinary iodine concentration; WHO, World Health Organization.

Adapted from Andersson et al. Serum thyrotropin (TSH) and free thyroxine (FT4)

Measurement of serum TSH by highly sensitive, third generation, immunometric assays is the single best test of thyroid function, being able to distinguish both hyperthyroid and hypothyroid patients from normal euthyroid subjects. The functional sensitivity of 0.01 mIU/L is particularly useful in permitting quantitation of the normal low serum TSH concentrations in early pregnancy and for optimising thyroxine dosages in patients taking replacement therapy. Population TSH values are skewed, necessitating log-transformation of values to determine reference ranges from the 95% confidence intervals of the population being studied. With these sensitive, precise assays the upper limit of the euthyroid reference range has decreased from around 5.0 to 10.0 mIU/L, measured in first generation TSH assays, to currently 3.6 mIU/L, but these ranges are subject to influences such as diurnal variation, age, iodine nutritional status, presence of co-existing thyroid antibodies, pregnancy, and the assay platform. Controversy continues about the upper limit of the normal reference range for TSH in an iodine sufficient population. The authoritative US National Academy of Clinical Biochemistry (NACB) guidelines state that ‘greater than 95% of healthy euthyroid subjects have a serum TSH concentration between 0.4 and 2.5 mIU/L’. Gestational specific reference ranges are required to evaluate TSH levels in pregnant patients.

Currently there is considerable uncertainty about the validity of many different assay methods for measuring FT4 concentrations during pregnancy and most clinical laboratories erroneously use non-pregnant reference ranges provided by the assay manufacturer. Thus there is no place for FT4 measurements as an individual screening tool in pregnant women. Measurement of FT4 should only be performed as an adjunct to the serum TSH determination.

Thyroglobulin

Thyroglobulin (Tg) is produced by thyroid epithelial cells and is stored in the follicular lumen. Thyroid hormone biosynthesis requires iodide incorporation into the Tg molecule. Small quantities of Tg are released into the circulation after thyroid stimulation and can be used as a marker of thyroid activity. The serum Tg concentration reflects the mass of differentiated thyroid tissue, the degree of stimulation by TSH and any physical damage or inflammation of the thyroid gland causing release of thyroid hormones and Tg. In essence, it is a non-specific marker of thyroid activity.

Measurement of serum Tg has become a valuable monitoring tool in the management of thyroid cancer patients who have been treated by total thyroidectomy and ablative radioactive iodine therapy, to assess if there is any residual functioning, normal or metastatic thyroid tissue. Therefore, it is used as a tumour marker. Until recently it was generally considered that the serum Tg concentration had little or no diagnostic value in screening for thyroid dysfunction; however, Zimmermann and colleagues have proposed that Tg measured in a dried blood spot is a good marker of iodine deficiency in children. Further studies are required to confirm the value of the serum Tg level in screening for iodine deficiency.

Thyroid autoantibodies

Autoimmune thyroid disease is a common disorder and causes tissue damage by both humoral and cell-mediated immune
mechanisms. Thyroid directed autoantibodies bind to thyroid peroxidase (TPO) or thyroglobulin (Tg) autoantigens within the cell or to cell surface TSH receptors. TPO antibodies (TPOAb) reflect the cell mediated inflammation characteristic of Hashimoto’s thyroiditis, hence TPOAb is the best marker of autoimmune thyroiditis, and the presence of these antibodies in the circulation precedes any abnormality in thyroid function. Tg antibody (TgAb) also reflects thyroiditis, but is a less specific marker and lacks specificity in screening for autoimmune thyroid disease. TgAb alone in the absence of TPOAb is not significantly associated with thyroid disease. TSH receptor antibodies (TRAb) are characteristic of Graves’ disease, but may also be blocking antibodies causing hypothyroidism, as well as the more common stimulating antibodies that cause hyperthyroidism. While measurement of TRAb is a useful diagnostic test to confirm or follow the progress of Graves’ disease it is of no value as a screening tool.

PREVALENCE OF THYROID DISORDERS

Iodine deficiency

The first comprehensive global review of nutritional iodine deficiency was conducted by the WHO in 1960. Data provided at that time by member countries were most likely unreliable but did suggest that iodine deficiency, as measured by goitre prevalence, was widespread, affecting up to half the world’s population. In 1993 using more reliable data, the WHO estimated a global goitre prevalence of 12%, affecting 655 million people in 110 countries. Unfortunately, these surveys of goitre rates, obtained by visualising and/or palpating thyroid glands, were fraught with error and completely overlooked the much more serious underlying disorder of brain damage in the newborn resulting from iodine deficiency in the mother. In addition to documenting goitre rates, other methods employed for screening populations for iodine deficiency have included UIC and serum TSH concentrations. Each of these methods has limitations. Measurement of TSH as an indicator for iodine deficiency is used only for neonates. Since 2001, measurement of (UIC) has been the recommended indicator for monitoring iodine status. The severity of iodine deficiency in a population is classified according to the UIC (Table 1).

Iodine deficiency has re-emerged in Australia. Well recognised as a cause of endemic goitre in the first half of the last century, particularly in Tasmania, and in communities living along the Great Dividing Range in eastern Australia, iodine deficiency disappeared in the 1960s because of abundant quantities of iodine in the diet from milk and other dairy products leaking from iodophore sanitisers used in the dairy industry. Substitution by non-iodine containing sanitisers in the dairy industry in the 1990s, coupled with decreasing iodised salt intake, has seen iodine intakes decline by more than half resulting in Australia being classified as a mildly iodine deficient country. The Australian National Iodine Nutrition Survey (NINS) conducted in school age children in 2003–2004 reported a national median UIC of 98 μg/L, but with significant differences among the states. Since then there have been several studies reporting UIC in pregnant women in NSW, Victoria and Tasmania, with each one confirming mild to moderate iodine deficiency.

Functional thyroid disorders

Thyroid dysfunction appears to increase with age, varies with iodine intake and ethnicity and may occur in up to 20% of older age people. Population based studies of TSH and thyroid antibodies provide valuable insights into the prevalence and incidence of thyroid disorders. There are major differences in published reports, most likely reflecting screening criteria, methodology employed, ethnic and geographic influences and nutritional iodine status. The Whickham epidemiology study conducted in the UK originally in 1977 and reported the prevalence of thyroid disorders in an adult population and has been the standard against which other epidemiological studies have been compared. Major constraints of this study were the use of insensitive, first generation TSH assays and lack of information of iodine intake in the population. The Colorado study in the USA reported a prevalence of 9.5% raised serum TSH and 2.2% decreased serum TSH in a self-selected, well population. These data included patients taking thyroxine medication. In the NHANES III study reported in 2002, the prevalence of hypothyroidism in the US population was 4.6%.

Table 2 Trimester specific reference ranges for serum TSH mIU/L

<table>
<thead>
<tr>
<th>Reference</th>
<th>First</th>
<th>Second</th>
<th>Third</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haddow et al.</td>
<td>0.94 (0.08–2.73)</td>
<td>1.29 (0.39–2.70)</td>
<td>No data</td>
</tr>
<tr>
<td>Panesar et al.</td>
<td>0.80 (0.03–2.30)</td>
<td>1.10 (0.03–3.10)</td>
<td>1.30 (0.13–3.50)</td>
</tr>
<tr>
<td>Stricker et al.</td>
<td>1.04 (0.09–2.83)</td>
<td>1.02 (0.20–2.79)</td>
<td>1.14 (0.31–2.90)</td>
</tr>
<tr>
<td>Bocos-Terraz et al.</td>
<td>0.92 (0.03–2.65)</td>
<td>1.12 (0.12–2.64)</td>
<td>1.29 (0.23–3.56)</td>
</tr>
<tr>
<td>Gilbert et al.</td>
<td>0.74 (0.02–2.15)</td>
<td>No data</td>
<td>No data</td>
</tr>
</tbody>
</table>

5th to 95th centiles: Haddow et al., Panesar et al.
2.5–97.5th centiles: Stricker et al., Bocos-Terraz et al.
deficient environment. In the WA study of 1045 participants, disease in the older population in NSW living in a mildly iodine limited to Western Australia (WA) and New South Wales (NSW). The findings show a 14% overall prevalence of thyroid studies have now been conducted in Australia but have been limited to Western Australia (WA) and New South Wales (NSW). The findings show a 14% overall prevalence of thyroid disease in the older population in NSW living in a mildly iodine deficient environment. In the WA study of 1045 participants, positive TPOAbs and TgAbs were present in 18% and 9%, respectively, and serum TSH was raised in 9% of the population. It is usually stated that patients with subclinical hypothyroidism progress to overt hypothyroidism at an annual rate of 2.5–5.0%. In a follow-up study of an older cohort in NSW, in those documented as suffering from subclinical hypothyroidism, the progression to overt hypothyroidism over 5 years was 17.9%. Hypothyroidism and pregnancy

Pregnancy provides a unique challenge to the synthesis and secretion of thyroid hormones unlike any other stage of adult life. The maternal thyroid must respond rapidly within the first trimester to increase thyroid hormone production rate by up to 50% to maintain a normal plasma FT4 level and to ensure the transport of T4 across the placenta to the fetus. Consequently, serum TSH levels undergo dynamic changes from soon after conception until very late in pregnancy. The serum TSH during the first trimester is lower than in the non-pregnant state and is inversely related to the hCG mediated direct stimulation of the thyroid in the first half of pregnancy. As hCG stimulation declines during the later stages of pregnancy the serum TSH level rises. These dynamic changes in serum TSH levels mandate the need for clinical laboratories to develop and implement pregnancy specific TSH reference ranges. If trimester specific reference ranges are not available in a laboratory, the following reference ranges are recommended by the American Thyroid Association: first trimester, 0.1–2.5 mIU/L; second trimester 0.2–3.0 mIU/L; third trimester, 0.3–3.0 mIU/L. Autoimmune thyroid disease is common in women of reproductive age. Thyroid antibodies are found in 10–20%, but are not necessarily associated with discernible abnormalities in thyroid function. An optimal outcome for any pregnancy requires maintenance of normal thyroid function throughout the pregnancy. Pregnancy complications associated with disturbed thyroid function include increased rates of miscarriage, gestational hypertension, pre-eclampsia, placental abruption and pre-term delivery. Furthermore, if there is an inadequate transfer of T4 from the maternal circulation, the fetal brain will not develop optimally, suffering a spectrum of neurological disorders from mild loss of intelligence through to the severe brain damage manifested by neurological cretinism. In addition to a cause and effect relationship between lack of thyroid hormone and adverse pregnancy outcome, there appears to be a positive association between the presence of thyroid autoantibodies in the maternal circulation and pregnancy loss, even where thyroid function is normal as judged by serum TSH and FT4 levels. It is not unexpected that there are now many advocates for screening women of reproductive age for thyroid dysfunction, either preconception or as soon as possible after pregnancy has been confirmed. The potential benefits of screening in these women depend on being able to prevent the adverse consequences of the thyroid disorder on the obstetric and fetal outcomes. Van den Boogard and colleagues have recently conducted a systematic review and meta-analysis of the literature to examine the proposition that clinical and/or subclinical hypothyroidism is associated with adverse pregnancy outcomes. They concluded that ‘there is clear evidence for a relationship between the presence of thyroid antibodies or subclinical hypothyroidism on several pregnancy outcome parameters’. In women with subclinical hypothyroidism, compared with those with normal thyroid function, there is an increased risk of pre-eclampsia and increased risk of perinatal mortality. Meta-analysis of studies with women having positive thyroid auto-antibodies showed an increased risk of unexplained subfertility, increased and recurrent miscarriages, preterm birth and post-partum thyroid disease. The damaging effects of overt maternal hypothyroidism are well accepted as demonstrated by diminished IQ in the offspring of untreated hypothyroid mothers. The adverse effects of subclinical hypothyroidism on neurocognitive development of the progeny, while likely, are less certain and remain the subject of intensive investigation. Despite this lack of evidence that early therapeutic intervention in women suffering from subclinical hypothyroidism will improve neurocognitive performance in their progeny, the improved obstetric outcome from intervention mounts an overwhelming case for screening all pregnant women for subclinical or overt hypothyroidism. Those not supporting universal screening advocate targeted screening of women considered to be at high risk of developing hypo- thyroidism during pregnancy and the post-partum period. However this strategy has been questioned by several studies that have demonstrated that a high percentage of patients will be missed if screening is not universal.

NEONATAL SCREENING FOR SPORADIC CONGENITAL HYPOTHYROIDISM

Congenital hypothyroidism (CH) is the most frequent congenital endocrine disorder. The incidence (birth prevalence) of CH varies from country to country, but in most iodine replete populations it is usually between 1 in 3000 and 1 in 4000. Systematic neonatal screening programs for detecting CH in newborn babies have been in use for almost four decades and have been adopted by most developed countries without question, and for that matter many developing countries as well. The symptoms and signs of congenital hypothyroidism are often subtle and may not be recognised until the infant is several months old and by then irreversible brain damage has occurred. Early diagnosis and thyroxine replacement prevents overt intellectual disability; however, subtle neurological disorders have been reported in a minority of children treated after early detection by a CH screening program. Nonetheless neonatal TSH screening is a proven, cost-effective method that should be available to every newborn.

NEONATAL TSH SCREENING FOR POPULATIONIODINE DEFICIENCY

Iodine and thyroid hormone transport across the placenta to the fetus is essential to maintain normal fetal thyroid function. The
developing human brain may be damaged when maternal thyroid hormone supply is compromised. To meet the challenge of pregnancy the recommended maternal iodine intake must be increased from 150 μg to 250 μg per day. Maternal iodine nutrition and disturbed thyroid function can negatively influence neonatal TSH secretion. Multiple studies have shown an inverse relationship between neonatal TSH concentration >5 mIU/L and maternal urinary iodine concentration. The data relating serum TSH level in the newborn with maternal iodine intake was considered convincing enough for the WHO to advocate neonatal TSH screening to monitor population iodine intake was considered convincing enough for the WHO to advocate neonatal TSH screening to monitor population iodine deficiency. The published criterion for iodine sufficiency is that there should be <3% frequency of neonatal TSH levels >5 mIU/L in the newborn population. In a recent analysis of all published data on neonatal TSH screening for monitoring population iodine deficiency, Li and Eastman concluded that there are many technical issues, including the time of sampling after birth, that remain unresolved with the use of neonatal TSH screening as a tool for monitoring population iodine nutritional status and that data should be interpreted with caution until these issues have been resolved.

DISCUSSION AND RECOMMENDATIONS

The growing interest and intense scrutiny of population screening data for thyroid disorders in recent years has provided a large body of literature from which we can derive some evidence based recommendations for specific screening programs. First, with respect to iodine deficiency, population screening by measurement of UIC in spot urine samples is the simplest and best way of defining population iodine nutrition. The survey and laboratory methodologies are provided in detail by the WHO/UNICEF/ICCIDD manual. The median UIC is used to define the population status with a value of 100 μg/L defining the cut-off point for both children and adults and 150 μg/L being the cut-off point for pregnant women.

Supplementary testing procedures or process indicators include serum TSH and Tg levels and blood-spot TSH in neonates, but these measures should remain as supplementary and not frontline screening. If an estimation of thyroid volume is required, as an outcome indicator, this can be done by ultrasound measurement and reference to international standards. Measurement of UIC to test an individual’s iodine status is not recommended because of day to day variation in iodine excretion.

The relatively low frequency of subclinical hyperthyroidism and lack of evidence for benefit from treatment in adult populations does not justify the expense of population screening for thyroid disorders characterised by mild overactivity. However, because of the potentially serious consequences of undiagnosed hyperthyroidism in the elderly, clinicians should adopt a high level of vigilance and apply a vigorous case-finding approach in older patients by measuring serum TSH whenever there is the possibility of occult hyperthyroidism. There are strong advocates of screening for hyperthyroidism by serum TSH measurement in neonates, pregnant women and females of mature age. The benefits of screening for congenital hyperthyroidism have been well documented and screening should be universally adopted for all neonates regardless of ethnic or geographical influences, not only for the inestimable benefits for the affected individuals, but also for the significantly decreased burden of disease and costs of long-term care. By contrast, it is difficult to justify population TSH screening for hyperthyroidism in mature age men and women with no evidence of benefit from randomised controlled trials or cost benefit analyses of therapeutic interventions. Our prospective Australian population-based study confirmed a relatively low progression of one in six persons progressing from subclinical to overt hypothyroidism over 5 years. If these data are more widely applicable, then a targeted case finding approach is the preferred option and medical practitioners should be made aware of the risk factors to detect hypothyroidism in the most vulnerable.

Authoritative professional organisations, such as the American Thyroid Association and the American Endocrine Society, have produced guidelines for the diagnosis and management of thyroid disease during pregnancy and the post-partum period. These guidelines provide persuasive arguments for early detection of overt and subclinical hypothyroidism and the urgent prescription of thyroxine replacement therapy to prevent obstetric complications and potential adverse neurocognitive disorders in the progeny of these women. Given the indisputable benefits of therapy, the sooner thyroid dysfunction is detected before, or as early as possible in gestation, the more likely there will be a better outcome. The unresolved question has been ‘do we screen all pregnant women or alternatively perform intensive case-detection testing in women at high risk of thyroid dysfunction?’ Implicit in this question is when before or during pregnancy screening should take place. The American Thyroid Association guidelines, while recognising the continuing controversy, state that ‘there is insufficient evidence to recommend for or against universal TSH screening at the first trimester visit’. Similarly, the 2011 American Endocrine Society guidelines state that ‘universal screening of healthy women for thyroid dysfunction by serum TSH measurement before pregnancy is not recommended, but care-givers should identify women at high risk and test thyroid function’. Further, the latter guidelines state that ‘the committee could not reach agreement with regard to screening recommendations for all newly pregnant women; some members recommended screening of all pregnant women for serum TSH abnormalities by the 9th week or at the time of their first visit, whereas others recommended aggressive case detection’. The crucial issue at the centre of this debate is the lack of evidence from appropriately conducted, randomised controlled trials of a benefit in neurocognitive function in the offspring of pregnant women suffering from subclinical hypothyroidism who have been detected and treated with thyroxine early in the first trimester of pregnancy. As there is ongoing, intensive investigation of this question, an answer should be forthcoming in the near future. This author is a member of the American Endocrine Society Guidelines Committee and believes there is sufficient evidence for universal screening and therapeutic intervention as early as possible in the first trimester of pregnancy.

In a recent large study Negro and colleagues concluded that rates of pregnancy-related adverse events were reduced by nearly 40% after detection and treatment of subclinical hypothyroidism. In numerical terms one can calculate that approximately 40 low-risk women would require screening and intervention to prevent a single adverse event. If universal screening of pregnant women was introduced into Australia, assuming 300,000 pregnancies per annum, this would translate into significant benefit to 7500 pregnancies annually. Given that we accept neonatal screening provides benefit to 1 in 4000 newborns, one can argue for the introduction of screening all pregnant women in this country as soon as a pregnancy is...
confirmed. An economic cost-benefit analysis is urgently required to test this proposition.

A positive association exists between the presence of anti-thyroid antibodies and increased pregnancy loss and, if identified, affected women should be screened for serum TSH abnormalities before pregnancy, as well as during the first and second trimesters of pregnancy. Universal screening for anti-thyroid antibodies, and institution of thyroxine treatment early in pregnancy, cannot be recommended at this time. The question of screening for thyroid autoantibodies in conjunction with serum TSH estimations remains under consideration, but if more evidence emerges from randomised controlled trials to confirm a significant decrease in adverse obstetric events after detection and treatment with thyroxine medication, even in euthyroid women, it is likely that antibody screening will be added to TSH testing. In the interim, vigorous targeted case detection is recommended with associated measurement of serum TSH level in pregnant women at risk.

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References


