A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO LABORATORY MEDICINE

some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – THYROID DISEASE IN PREGNANCY: DIAGNOSIS & MANAGEMENT

Korevaar TIM, Medici M, Visser TJ, Peeters RP. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. Nat Rev Endocrinol. 2017;13:610–22. Epub 2017 Aug 4. PMID: 28776582.

DOI: 10.1038/nrendo.2017.93. [Payment required]

ABSTRACT

Adequate thyroid hormone availability is important for an uncomplicated pregnancy and optimal fetal growth and development. Overt thyroid disease is associated with a wide range of adverse obstetric and child development outcomes. An increasing number of studies now indicate that milder forms of thyroid dysfunction are also associated with these adverse pregnancy outcomes.

The definitions of both overt and subclinical thyroid dysfunction have changed considerably over the past few years, as new data indicate that the commonly used fixed upper limits of 2.5 mU/l or 3.0 mU/l for thyroid-stimulating hormone (TSH) are too low to define an abnormal thyroid function. Furthermore, some studies now show that the reference ranges are not necessarily the best cut-off for identifying pregnancies at high risk of adverse outcomes.

In addition, data suggest that thyroid peroxidase autoantibody positivity and high or low concentrations of human chorionic gonadotropin seem to have a more prominent role in the interpretation of thyroid dysfunction than previously thought. Data on the effects of thyroid disease treatment are lacking, but some studies indicate that clinicians should be aware of the potential for overtreatment with levothyroxine.

Here, we put studies from the past decade on reference ranges for TSH, determinants of thyroid dysfunction, risks of adverse outcomes and options for treatment into perspective. In addition, we provide an overview of the current views on thyroid physiology during pregnancy and discuss strategies to identify high-risk individuals who might benefit from levothyroxine treatment.

READING 2 – SUBCLINICAL HYPOTHYROIDISM: WHEN TO CONSIDER TREATMENT

Donangelo I, Suh SY. Subclinical Hyperthyroidism: When to consider treatment. Am Fam Physician. 2017;95:710–6. Review. PubMed PMID: 28671443.

URL: http://www.aafp.org/afp/2017/0601/p710.html [Payment required]

ABSTRACT

Subclinical hyperthyroidism is defined by a low or undetectable serum thyroid-stimulating hormone level, with normal free thyroxine and total or free triiodothyronine levels. It can be caused by increased endogenous production of thyroid hormone (e.g., in Graves disease, toxic nodular goiter, or transient thyroiditis), by administration of thyroid hormone to treat malignant thyroid disease, or by unintentional excessive replacement therapy.

The prevalence of subclinical hyperthyroidism in the general population is about 1% to 2%; however, it may be higher in iodine-deficient areas. The rate of progression to overt hyperthyroidism is higher in persons with thyroid-stimulating hormone levels less than 0.1 mIU per L than in persons with low but detectable thyroid-stimulating hormone levels.

Subclinical hyperthyroidism is associated with an increased risk of atrial fibrillation and heart failure in older adults, increased

cardiovascular and all-cause mortality, and decreased bone mineral density and increased bone fracture risk in postmenopausal women. However, the effectiveness of treatment in preventing these conditions is unclear. A possible association between subclinical hyperthyroidism and quality-of-life parameters and cognition is controversial.
The U.S. Preventive Services Task Force found insufficient evidence to assess the balance of benefits and harms of screening for thyroid dysfunction in asymptomatic persons. The American Thyroid Association and the American Association of Clinical Endocrinologists recommend treating patients with thyroid-stimulating hormone levels less than 0.1 mIU per L if they are older than 65 years or have comorbidities such as heart disease or osteoporosis.

READING 3 – THYROTOXICOSIS: INVESTIGATION & MANAGEMENT

Gilbert J. Thyrotoxicosis — investigation and management. Clin Med (Lond). 2017;17:274–7. Review. PubMed PMID: 28572231.

DOI: 10.7861/clinmedicine.17-3-274.

ABSTRACT
Graves' disease (GD) and toxic nodular (TN) goitre account for most cases of thyrotoxicosis associated with hyperthyroidism. Hyperthyroidism is confirmed with measurement of a suppressed serum thyrotropin concentration (TSH) and elevated free thyroid hormones. The three therapeutic options are antithyroid drugs, radioactive iodine and surgery. Thionamides achieve long-term remission in 35% of cases. Many centres administer fixed doses of iodine-131; larger doses result in improved rates of cure at the cost of hypothyroidism. Surgery is usually considered for patients who have a large goitre, compressive symptoms or significant ophthalmopathy.

READING 4 – PREVALENCE OF LATENT TUBERCULOSIS

Hung WT, Lee SS, Sy CL, Wu KS, Chen JK, Tsai HC, Chen YS. Prevalence of latent tuberculosis infection in BCG-vaccinated healthcare workers by using an interferon-gamma release assay and the tuberculin skin test in an intermediate tuberculosis burden country. J Microbiol Immunol Infect. 2015;48:147–52. Epub 2013 Sep 23. PubMed PMID: 24071516.

DOI: 10.1016/j.jmii.2013.07.008 [Payment required]

ABSTRACT
BACKGROUND: The risk of healthcare workers (HCWs) acquiring tuberculosis (TB) infection is high. We determined the prevalence of latent TB infection (LTBI) in HCWs with a high Bacille Calmette-Guérin (BCG) vaccine coverage in an intermediate TB burden country by using an interferon-gamma release assay [QuantiFERON-TB Gold (QFT-G)] and by using the tuberculin skin test (TST). Risk factors associated with a positive test were determined.
METHODS: This prospective cross-sectional study enrolled HCWs from a medical center in Taiwan. Participants were grouped into workers without exposure (Group 1) and workers who self-reported a history of TB exposure (Group 2). All participants completed a questionnaire to collect demographic information and risk factors for acquiring TB. The QFT-G test and the TST were administered and risk factors for a positive test were analyzed.
RESULTS: We recruited 193 HCWs [149 (77.2%) female workers] with a mean age of 35.6 years. All were BCG-vaccinated. The prevalence of LTBI was 88.8% (based on the TST) and 14.5% (based on the QFT-G test). There was no difference between HCWs with and without known exposure to TB. Agreement between the tests was poor (i.e., the kappa value was less than 0.05). Multivariable logistic regression showed that only the QFT-G test was associated with age (35 years or greater) (adjusted OR, 2.53; p = 0.03).
CONCLUSION: By using the QFT-G test or TST, this study found a similar prevalence of LTBI in HCWs with and without known exposure to TB. This suggests that in intermediate TB burden countries exposure to TB may occur within

the hospital and within the community. Compared to the TST, the QFT-G test was correlated better with age, which is a known risk factor for latent TB infection.

READING 5 – LATENT TUBERCULOSIS — DIAGNOSIS & MANAGEMENT

Turetz ML, Ma KC. Diagnosis and management of latent tuberculosis. Curr Opin Infect Dis. 2016;29:205-11. Review. PubMed PMID: 26836374.

DOI: 10.1097/QCO.0000000000000253. [Payment required]

ABSTRACT

PURPOSE OF REVIEW: Latent tuberculosis infection (LTBI) may affect over two billion individuals and serves as a potential reservoir for future active tuberculosis. The identification and treatment of LTBI in those at highest risk for progression is an essential part of tuberculosis control.
RECENT FINDINGS: Interferon-γ release assays are increasingly used for targeted testing and diagnosis of latent disease. The performance of these immunodiagnostic tests has been studied in various groups and may be better than the tuberculin skin test in certain populations. Ongoing research is focused on new biomarkers that may diagnose LTBI or predict progression to active tuberculosis. Isoniazid preventive treatment is effective at reducing risk of active disease, but length of treatment and potential side-effects limit patient acceptance and compliance. Rifamycin-based regimens are increasingly studied as a shorter and perhaps less toxic alternative for preventive therapy.
SUMMARY: Identification of those with LTBI is important as it allows treatment of those at highest risk of progression to active disease and thus decreases the overall burden of tuberculosis. The development of new immunodiagnostics may further improve identification of those at risk and alternative medication regimens may increase compliance with and efficacy of preventive therapy.

READING 6 – DIAGNOSIS OF LATENT TUBERCULOSIS — TUBERCULIN TEST VS GAMMA INTERFERON RELEASE

Ferreira TF, Matsuoka Pda F, Santos AM, Caldas Ade J. Diagnosis of latent Mycobacterium tuberculosis infection: tuberculin test versus interferon-gamma release. Rev Soc Bras Med Trop. 2015;48:724–30. PubMed PMID: 26676497.

DOI: 10.1590/0037-8682-0258-2015. [Free full text]

ABSTRACT

INTRODUCTION: The treatment of individuals with active tuberculosis (TB) and the identification and treatment of latent tuberculosis infection (LTBI) contacts are the two most important strategies for the control of TB. The objective of this study was compare the performance of tuberculin skin testing (TST) with QuantiFERON-TB Gold In TUBE(r) in the diagnosis of LTBI in contacts of patients with active TB.
METHODS: Cross-sectional analytical study with 60 contacts of patients with active pulmonary TB. A blood sample of each contact was taken for interferon-gamma release assay (IGRA) and subsequently performed the TST. A receiver operating characteristic curve was generated to assess the cutoff points and the sensitivity, predictive values, and accuracy were calculated. The agreement between IGRA and TST results was evaluated by Kappa coefficient.
RESULTS: Here, 67.9% sensitivity, 84.4% specificity, 79.1% PPV, 75% NPV, and 76.7% accuracy were observed for the 5mm cutoff point. The prevalence of LTBI determined by TST and IGRA was 40% and 46.7%, respectively.
CONCLUSIONS: Both QuantiFERON-TB Gold In TUBE(r) and TST showed good performance in LTBI diagnosis. The creation of specific diagnostic methods is necessary for the diagnosis of LTBI with higher sensitivity and specificity, preferably with low cost and not require a return visit for reading because with early treatment of latent forms can prevent active TB.

READING 7 – TUBERCULOSIS TESTING — WHICH PATIENTS, WHICH TESTS

Elliott C, Hall J. Tuberculosis testing: Which patients, which test? J Fam Pract. 2015;64:553–65. PubMed PMID: 26546956.

Erratum in J Fam Pract. 2015;64:762.

URL: http://www.mdedge.com/jfponline/article/102196/infectiousdiseases/tuberculosis-testing-which-patients-which-test [Free full text]

ABSTRACT

The most appropriate test to identify latent TB depends on the patient's risk for developing active TB and other factors. This review provides practical guidance on who to test, how, and when.

PRACTICE RECOMMENDATIONS

- Test for latent tuberculosis (TB) infection by using a tuberculin skin test (TST) or interferon gamma release assay (IGRA) in all patients at risk for developing active TB. B
- Consider patient characteristics such as age, previous vaccination with bacille Calmette-Guérin (BCG), and whether the patient will need serial testing to decide whether TST or IGRA is most appropriate for a specific patient. C
- Don't use TST or IGRA to make or exclude a diagnosis of active TB; use cultures instead. B
- STRENGTH OF RECOMMENDATION (SOR)

  A Good-quality patient-oriented evidence

  B Inconsistent or limited-quality patient-oriented evidence

  C Consensus, usual practice, opinion, disease-oriented evidence, case series

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READING 8 – PREVENTIVE TREATMENT FOR TUBERCULOSIS IN SPECIAL HIGH-RISK POPULATIONS

Diel R, Lampenius N, Nienhaus A. Cost effectiveness of preventive treatment for tuberculosis in special high-risk populations. Pharmacoeconomics. 2015;33:783–809. PubMed PMID: 25774015.

DOI: 10.1007/s40273-015-0267-x. [Payment required]

ABSTRACT

OBJECTIVE: In view of the goal of eliminating tuberculosis (TB) by 2050, economic evaluations of interventions against the development of TB are increasingly requested. Little research has been published on the incremental cost effectiveness of preventative therapy (PT) in groups at high risk for progression from latent TB infection (LTBI) with Mycobacterium TB (MTB) to active disease. A systematic review of studies with a primary focus on model-driving inputs and methodological differences was conducted.

METHODS: A search of MEDLINE, the Cochrane Library and EMBASE to July 2014 was undertaken, and reference lists of eligible articles and relevant reviews were examined. RESULTS: A total of 876 citations were retrieved, with a total of 24 studies being eligible for inclusion, addressing six high-risk groups other than contact persons. Results varied considerably between studies and countries, and also over time. Although the selected studies generally demonstrated cost effectiveness for PT in HIV-infected subjects and healthcare workers (HCWs), the outcome of these analyses can be questioned in light of recent epidemiologic data. For immigrants from high TB-burden countries, patients with end-stage renal disease, and the immunosuppressed, now defined as further vulnerable groups, no consistent recommendation can be taken from the literature with respect to cost effectiveness of screening and treating LTBI. When the concept of a fixed willingness-to-pay (WTP) threshold as a prerequisite for final categorization was used, the sums ranged between 'no specification' and US$100,000 per quality-adjusted life-year.

CONCLUSIONS: To date, incremental cost-effectiveness analyses on PT in groups at high risk for TB progression, other than contacts, are surprisingly scarce. The variation found between studies likely reflects variations in the major epidemiologic factors, particularly in the estimates on the accuracy of the tuberculin skin test (TST) and interferon-gamma release assays (IGRA) as screening methods used before considering PT. Further research, including explicit evaluation of local epidemiological conditions, test accuracy, and methodology of WTP thresholds, is needed.

READING 9 – MONITORING RESPONSE TO TREATMENT FOR TUBERCULOSIS

Clifford V, He Y, Zufferey C, Connell T, Curtis N. Interferon gamma release assays for monitoring the response to treatment for tuberculosis: A systematic review. Tuberculosis (Edinb). 2015;95:639–50. Review. PubMed PMID: 26515270.

DOI: 10.1016/j.tube.2015.07.002. [Free full text]

ABSTRACT

INTRODUCTION: The ability to monitor the response to therapy for tuberculosis (TB) and confirm adequate treatment would be a major advance. The utility of interferon gamma assays (IGRA) for this purpose remains uncertain.

METHODS: A systematic search of all studies investigating commercial IGRA to monitor anti-tuberculous treatment was done. Studies were included if they included an IGRA before the start of, and at least once during, treatment for active or latent TB.

RESULTS: We identified 30 studies, of which 24 used QuantiFERON-TB (QFT), three used T-SPOT.TB and three used both QFT and T-SPOT.TB. Most studies were done in low TB incidence countries. No uniform pattern was seen in IGRA conversion and reversion rates at the end of treatment for active or latent TB. In most studies, the majority of IGRA results remained positive at the end of treatment. In many studies, the quantitative levels of IFN-γ decreased during treatment, particularly in active TB. There was significant heterogeneity in the included studies.

CONCLUSION: While quantitative IGRA responses generally fall during treatment for TB, the large degree of variation in results between participants in each study means that IGRAs are unlikely to be useful for monitoring anti-tuberculous treatment in clinical practice for any individual patient.

READING 10 – PREDICTING DEVELOPMENT OF ACTIVE TUBERCULOSIS DURING FOLLOW-UP

Altet N, Dominguez J, Souza-Galvão ML, Jiménez-Fuentes MÁ, Milà C, Solsona J, et al. Predicting the development of tuberculosis with the tuberculin skin test and QuantiFERON testing. Ann Am Thorac Soc. 2015;12:680–8. PubMed PMID: 25699406.

DOI: 10.1513/AnnalsATS.201408-394OC. [Payment required]

ABSTRACT

RATIONALE: The identification of patients with latent tuberculosis infection, who are at higher risk to develop active disease, is an important component of disease control.

OBJECTIVES: We aim to compare the usefulness of the QuantiFERON-TB Gold in-tube assay and the tuberculin skin test to predict the development of active tuberculosis during follow-up, using positive and negative predictive values, positive likelihood ratios, and stratified level of risk. METHODS: The study included contacts of tuberculosis cases diagnosed between 2007 and 2009. All contacts included were from the first circle of exposure. Tuberculin skin test and QuantiFERON test were performed and a chest radiograph was obtained during the contact's study.

MEASUREMENTS AND MAIN RESULTS: A total of 1,335 contacts were followed up for 4 years: a smear-positive index case was identified for 937 contacts, of whom 15 developed active tuberculosis and had initially presented with positive tuberculin skin test/QuantiFERON results, a normal chest radiograph, and no symptoms. The positive predictive value was 4% for QuantiFERON and 2% for the tuberculin skin test (when ≥5 mm). The probability of developing active disease was 2.36 times higher with a positive QuantiFERON, and 1.3 times higher with a positive tuberculin skin test. The positive predictive value was 17%, and the positive likelihood ratio was 7.53 for untreated contacts with a positive QuantiFERON. Stratifying according to initial QuantiFERON results showed a 6.36 times higher risk of developing active tuberculosis for patients with a QuantiFERON result greater than or equal to 10 IU/ml. Among bacillus Calmette-Guérin-vaccinated patients, a tuberculin skin test induration greater than or equal to 15 mm correlated better with a positive QuantiFERON.
CONCLUSIONS: QuantiFERON results were more accurate than tuberculin skin test results in predicting tuberculosis. Although all contacts with QuantiFERON-positive results are at risk of developing tuberculosis, those with a tuberculin skin test induration greater than or equal to 15 mm and QuantiFERON greater than or equal to 10 IU/ml are at highest risk. This has important implications in the clinical management of tuberculosis contacts.