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Position Statement from the New Zealand Microbiology Network regarding the use of the QuantiFERON Gold In-Tube (QFN) assay to screen for tuberculosis infection among healthcare workers, students, travellers, and other occupational groups in New Zealand

This position statement from the New Zealand Microbiology Network (NZMN) contains information for relevant stakeholders including respiratory physicians, infectious diseases physicians, public health, occupational health, and universities (student health services). It refers to QuantiFERON Gold test (QFN) as it is the only interferon-gamma release assay (IGRA) currently in use in New Zealand.

Introduction

The New Zealand Microbiology Network (NZMN) core membership comprises clinical microbiologists representing laboratories interested in and supporting public health microbiology testing in New Zealand, representatives of the Ministry of Health, and representatives of the Institute of Environmental Science and Research Limited (ESR).

The vision of the NZMN is to build national capability, optimise technical methods and collaborative processes in public health microbiology across New Zealand.

Issue

The NZMN is concerned that the groups of people who are required to have QFN testing appears to have widened and that requiring a person to have a test on the basis of what they are studying at university rather than on the basis of what their risk factors for tuberculosis are leads to false positive test results and associated issues of cost, worry and additional laboratory testing.

Recommendations

The NZMN makes the following recommendations.

1. *Screening for latent tuberculosis infection (LTBI) for healthcare workers (HCW), students, and others (police, prison workers, etc.)*

    a. Testing should only be performed on higher exposure-risk persons as established by history taking or questionnaire (Appendix 1).

    b. The choice of test depends on Bacille Calmette-Guerin (BCG) history and test type availability:

        i. Where there is no history of BCG testing – either a tuberculin skin test (TST) or QFN may be used
        ii. Where there is a past history of BCG – QFN is preferred.

    c. It is recommended that numerical results of Antigen-Nil be reported for non-indeterminate results with a grey zone comment to be determined by each laboratory. The range of 0.35 to 0.75 is one suggested range for occupational health screening.

These recommendations are not consistent with the *Guidelines for Tuberculosis Control in New Zealand 2010*, (these guidelines are currently under review) and a further recommendation (to the Ministry of Health) is that these guidelines are updated with a reassessment of the use of IGRAs/QFN to include recent literature highlighting issues with their performance.

Rationale

1. The positive predictive value (PPV) of any test is reduced in a low prevalence setting; thus the PPV of the QFN test is lower among those with low risk for LTBI.
2. The reproducibility of the QFN test is now recognised to be poor, particularly around the cutoff, due to both intra-sample and inter-sample variability. Many authors recommend a grey zone for reporting low risk screening for occupational health to reduce false conversion and reversions (see below). [1]
3. The published studies on HCW screening demonstrate both conversions and reversions that appear to be related to the reproducibility of the QFN test and unrelated to exposure risk to tuberculosis. [2-6]
4. There are potential unintended consequences of screening low risk populations where the PPV of LTBI is low and so the PPV is also low. These include, for example, repeating QFN or TST testing, undertaking chest X-rays, and initiation of anti-tuberculosis treatment, which may result in harm to the person being tested as well as being a resource burden.

Appendix one: establishing risk for LTBI

The questionnaire must include information on the following.

- Place of birth, place of residence, and history of any extended travel to a country with a high prevalence of tuberculosis.
- History of any previous tuberculosis infection.
- Results of any previous TST or IGRA results.
- History of known exposure to tuberculosis from known active case, family or workplace.
- Information about previous occupations.
- Information about any clinical conditions that increase the risk of developing active tuberculosis disease.

***Higher risk includes persons who fulfil at least one of the following*.**

1. Known contact of case with pulmonary tuberculosis disease.
2. Foreign-born persons from geographic regions with a high incidence of tuberculosis disease (see Appendix 2).
3. Persons who have travelled or resided in countries with a high incidence of tuberculosis disease within the last five years.
4. HCWs who have previously or currently cared for patients who are at high risk (respiratory and dialysis wards); have worked in high risk areas of the microbiology laboratory (respiratory and mycobacteria benches); or have had prolonged travel to, or resided in countries with a high incidence of tuberculosis disease, particularly within the last five years.

5. Persons at increased risk of occupational exposure to bovine tuberculosis.
6. HCWs or students who have worked in any kind of healthcare setting in countries with an incidence of > 10 case of tuberculosis per 100,000 population per annum (appendix two).

Appendix two: country risk profiles

A list of countries and their incidence rates can be found at:
http://www.who.int/tb/publications/global_report/en/

Incidence is measured in cases per 100 000 population.

Low incidence: countries with fewer than 10 / 100 000
Intermediate incidence: countries with 10 – 40 / 100 000
High incidence: countries with > 40 / 100 000

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