Belgian Guidelines 2019 on the Diagnosis and Management of Latent Tuberculosis Infection

- https://www.fares.be/fr/ltbi-guidelines-belgium/
- https://tuberculose.vrgt.be/nieuws/

Some highlights for Occupational Medicine

In low-incidence countries like Belgium, tuberculosis (TB) is concentrated in recent contacts of infectious TB cases and in vulnerable groups such as those with low socio-economic status, homeless persons, newly-arrived migrants from high-incidence countries, people living with human immunodeficiency virus, people with drugs or alcohol dependency, prisoners, older adults and children, particularly those below 5 years of age.

In low-incidence countries, efforts must be made to identify asymptomatic carriers, i.e. those that are at greatest risk of reactivation and subsequent progression to symptomatic and contagious TB.
The lifetime risk of TB reactivation for a person with documented latent tuberculosis infection (LTBI) is estimated to be 5-15 %, with the majority developing TB disease within the first five years after primary infection.

Systematic testing and treatment of LTBI are strongly recommended in:
- household contacts or close contacts of pulmonary TB cases, especially those contacts less than five years of age;
- people living with Human Immunodeficiency Virus (HIV) at high risk of developing active TB;
- patients initiating immunosuppressive therapy, including but not limited to anti-tumour necrosis factor (anti-TNF) treatment, anti-CD52, anti-CD20, patients preparing for organ transplantation...;
- patients undergoing dialysis.

Testing and treatment of LTBI should be considered for:
- prisoners;
- high-risk immigrants from high-burden countries, i.e. asylum seekers aged less than 5 years and pregnant women;
- patients presenting with silicosis (to be assessed on individual basis);
- patients with fibrotic lesions;
- people traveling to/living in high-prevalence countries;
- health care workers and other professionals in contact with person from high risk groups.

Tuberculin skin test (TST) and interferon gamma release assay (IGRA) have characteristics that need to be considered when choosing the specific test for specific populations, including - but not limited to - technical feasibility, cost, and availability. The results of TST and IGRA should be interpreted in the context of the pertinent clinical data (including age, Bacillus Calmette Guérin (BCG) vaccination status, contact with active TB, immunodepression and other risk factors...).

TST is recommended in cases of continuous exposure to *Mycobacterium tuberculosis*, for instance in the context of occupational exposure in health care workers, personnel of detention centres or asylum seekers centres.
Ideally, at baseline (e.g., at hiring), 2 TST should be done with a 1 to 2-week window period to allow boosting. The result of the second test is the one to be taken into consideration.

The TST result must be measured and recorded in millimeters. Although larger indurations are more likely to be the result of a TB infection, the TST results should be interpreted using risk-stratification cut-offs, considering TB prevalence, BCG vaccination status, immunological status, medical history, screening context and age. In a person at high risk of developing TB (e.g. people living with HIV or other immunocompromised host), a smaller diameter of induration should be considered as positive. A table gives the general criteria for the interpretation of a TST in adults.

TST can be repeated over time if the test remains negative. If the initial TST is positive, or if the TST becomes positive at a certain moment, it is not useful to continue the periodic testing. If a risk event occurs (contact with infectious case, developing a condition that increases the risk of TB), the person needs to be evaluated clinically and

radiologically and instructed/informed on the need for another evaluation if signs and symptoms appear.

IGRA has shown to have too many reversions/conversions and is not recommended for periodic testing.
If the initial testing was done by IGRA nevertheless, the test should not be repeated periodically. IGRA should only be repeated if a risk event occurs.
An IGRA will be useful in situations where the TST could show a false positive result because of earlier BCG vaccination.

The following individuals should preferably be tested by IGRA :
- vaccinated with BCG in the course of the previous 12 months;
- having received repeated BCG-vaccinations;
- BCG administered when older than 1 year of age.

Interpretation of the IGRA should be through positive, negative and borderline laboratory results.

The double testing (TST first, followed by IGRA if TST is negative) will be useful
- to increase sensitivity for persons with immunodepression, such as HIV-infected individuals, dialysis patients and individuals undergoing immunosuppressive therapies;
- to increase specificity for persons who have been exposed to non-tuberculous mycobacteria or have received a BCG vaccination.
IGRA should be done within 72 hours to avoid false positivity of the IGRA, or both tests can be done simultaneously.

The use of both a TST and an IGRA in LTBI screening is limited to specific situations and often leads to discordant results. Treatment for LTBI should be considered if the risk to develop TB is high (e.g., immunodepression, recent contact...).

Assessing the probability of LTBI requires a combination of epidemiological, historical, medical and diagnostic findings that should be taken into account when interpreting test results. The test results interpretation has to deal with possibilities of false positive results, false negative results, conversions, reversions , booster effects (TST) and amplifications (IGRA after TST).

TB testing activities should be conducted among high risk groups, with the intent to treat if LTBI is detected.

The standard recommended LTBI regimen in Belgium is Isoniazid (INH) daily during 6 months. If compliance is a concern, daily Rifampicin (RMP) and INH during 3 months or daily RMP during 4 months are alternatives. When a person is known to be exposed to an infectious person with an INH-resistant strain or is intolerant to INH, a course of treatment using RMP is recommended. Currently available regimens for the treatment of LTBI have an efficacy ranging from 60 % to 90 %.

After the LTBI treatment has ended, patients should be counselled to contact their treating physician if possible symptoms of active TB develop, such as coughing, hemoptysis, fever, night sweats and unexplained weight loss.
A new (latent) infection can always occur; previous exposure does not protect against re-infection. Regardless of whether the patient completes treatment for LTBI , serial or repeat chest radiographs are not required unless the patient develops signs or symptoms suggestive of TB disease.

Some 2019 guidelines focuse on the diagnosis and management of LTBI in some specific situations :
- pregnancy and lactation
- persons living with HIV
- presence of fibrotic lesions on chest X-ray
- travelers and/or expatriates
- ageing persons
- children
- professionals with high risk of exposure to tuberculosis

For workers, the 2019 guidelines give reference to the 2014 Superior Health Council policy advisory report that provides recommendations regarding the prevention of TB in health care facilities. This document detailed the legal requirements, risk assessment for individual health care workers, the outlines of a prevention plan, the use of TST, IGRA , chest X-ray and BCG vaccination. However, the document is equally valuable and applicable for other categories of workers with a high risk of exposure to pulmonary TB, such as prison wardens, personnel in contact with asylum seekers.

There are multiple steps in the care process from initial identification of people with LTBI who could potentially benefit from therapy, until treatment completion. Patients can, and do, drop-out or are lost at each of these steps. Interventions that aim to reduce losses at the early steps of the latent tuberculosis “cascade of care” should enhance the impact of diagnosis and treatment of infection in public and occupational health.