

Tuberculosis diagnostics

General:

Tuberculosis is an underestimated infectious disorder. Factors triggering an infection are: malnutrition, stress, high age, long term therapy with corticoids, diabetes mellitus, alcoholism, stomach resection, measles, whooping cough, silicosis, lymphomata, leukosis, AIDS. As opportunistic infectious microorganisms, "atypical" mycobacteria (Avium complex) play a role in immunosuppressed patients. Atypical or ubiquitous mycobacteria occur in large quantities in tap water.

Classification of mycobacteria:

1. Mycobacteria of the tuberculosis complex: *M. tuberculosis*, *M. africanum*, *M. bovis*;
2. Atypical mycobacteria (MOTT: mycobacteria other than tubercle bacilli, ubiquitous mycobacteria): *M. avium/intracellulare* (MAI complex), *chelonae*, *fortuitum*, *gordoniae*, *haemophilus*, *kansasii*, *malmoense*, *marinum*, *simiae*, *szulgai*, *scrofulaceum*, *ulcerans*, *xenopi*;

Disease forms:

Primary tuberculosis: first contact with *M. tuberculosis*, primary complex (mostly in lungs) after 5-6 weeks, symptoms mostly silent, subfebrile temperatures, cough, night sweat, appetite loss, erythema nodosum. Complication: primary cavern, "open" TB, pleuritis exsudativa, miliary TB.

Hilar lymph node TB: in the context of the primary TB swelling of the hilar lymph nodes. Complication: atelectasis, middle lobe syndrome.

Pleuritis exsudativa: the most frequent manifestation of primary TB, at the beginning often "wet" pleuritis, sometimes pleuritis sicca, pain when breathing, pleural pains. Tuberculosis is the most frequent cause of a pleural effusion in younger patients < 30 years (cultural microorganism determination in the exsudate is successful only in 20% of the cases!!).

Minimal lesions: in a part of the cases the primary complex is spread hematogenically into organs. Temporarily without symptoms. Reactivation, can lead to post-primary TB of organs.

Miliar TB: hematogenic generalization in the following organs: lungs, meninges, liver, spleen, kidneys, adrenal glands, chorioidea of the eyes.

Post-primary TB: frequently observed by endogenous reinfection of formerly infected organ (lungs 90%, kidneys, bones) with living tubercle bacilli. Late forms manifest as urogenital tuberculosis (microorganism determination in urine possible), tuberculosis of bones, intestinal tuberculosis (microorganism determination in stool possible), age tuberculosis and tuberculosis arthritis.

Primary infiltrate and cavernous lung TB: reactivation of a center in the lungs, uncharacteristic clinical symptoms. Necrosis to a primary cavern can result in "open" TB (tubercle bacilli in sputum).

Tuberculosis in HIV: frequently as skin TB, clinical symptoms atypical, few centers, often extrapulmonary, hardly any granuloma histologically detectable, very often association with meningitis, fast reactivation of TB (in approx. 40% of cases) up to multi organ failure and ARDS at final stage, MDR-resistance not rare (Multi-Drug-Resistance). Opportunistic secondary infections with MAI (*M. avium*/intracellulare complex) are problematic. Also secondary infections with *M. kansasii*, pneumocystis carinii, cytomegaly, cryptosporidia, cryptococcae and complications by Kaposi sarcoma and malignant lymphomata. Screening of TB in HIV infection every 3 months advisable.

Atypical mycobacteria: lung disease similar to tuberculosis, weak immune system and non-specific chronic lung disorders are predisposition, high temperature, general lymphadenitis in infection with MAI complex (*M. avium*/intracellulare), skin infections (*M. marinum*), *M. scrofulaceum*/ *M. intracellulare* are found as microorganisms in cervical lymphadenitis in children. Atypical mycobacteria are also detectable in HIV infection (see above). Microorganism determination from sputum, urine, blood and stool.

The following tests are available:

- **Cultural determination**

Indication: suspicion of TB, persisting therapy-resistant pneumonia, hemoptysis, clarification pleural effusion.

Material: sputum on three subsequent days, gastric juices (request special vial), urine (best is concentrated morning urine), pleural aspirate, pus, tracheal secretion, effusion or abscess aspirate, bronchial lavage, CSF, larynx swab;

Identification in blood: 5 ml heparin or citrate blood (susp. of miliary TB), menstrual blood

Further examinations: blood differential (leucocytosis), ESR, CRP, organ specific parameters, Eli-Spot (if available).

TAT: up to 8 weeks*

Method: MGITT; microscopic examination for acid-resistant rod-shaped bacillae (Kinyoun staining), cultivation on Loewenstein-Jensen-/Stonebrink-special nutrient mediums, bacterial determination with MGITT methods as well as TB complex determination, differentiation of atypical mycobacteria by sequencing (PCR, 16 S rRNA).

- **Mycobacterium tuberculosis DNA**

General:

Highly recommended test !

Material: EDTA blood, sputum, BAL, tracheal secretion, gastric juice, aspirate, CSF, urine, biopsy

TAT: 7-10 days*

Method: PCR

Units: qualitative

Ref. range: negative

- **Quantiferon Test Gold (QFT)**

General:

Quantiferon Test Gold detects the release of interferon-gamma in fresh heparinized whole blood from sensitized persons when it is incubated with mixtures of synthetic peptides representing two proteins present in *M. tuberculosis*: early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10). These antigens show higher specificity than tests using purified protein derivatives as the tuberculosis antigen. In direct comparisons, the sensitivity of QFT-G was statistically similar to that of the tuberculin skin test (TST) for detecting infection in persons with untreated culture-confirmed tuberculosis. The test detects *M. tuberculosis*, *bovis*, *caprae* or *africanum*. *M. bovis*-BGC will not interfere. In case of an acute infection a positive test can be expected after 2-8 weeks.

Indication: Persons at increased risk for latent *Mycobacterium tuberculosis* infection (e.g., recent immigrants, injection-drug users, and residents and employees of prisons and jails), persons at low risk for latent *M. tuberculosis* infection but whose future activity might place them at increased risk (e.g., healthcare workers and military personnel), persons who are not considered to have an increased probability of *M. tuberculosis* infection but who require testing for other reasons.

Material: 3 x 1 ml whole blood for 3 x Quantiferon Gold vials as "Single Patient Pack".

TAT: 7-12 days*

Method: ELISA for IFN-gamma

- **Gastric juice for MTB**

Indication: Suspicion of MTB

TAT: 7-10 days*

Method: PCR

Ref.- range: negative

For complete list of laboratory test offered at Freiburg Medical Laboratory, please visit
<http://www.fml-dubai.com/parameter-listings/>