



European Respiratory
Society

ERS Vienna 2009 Congress
September 12–16, 2009

**PG12 – EU FP7/TB PAN-NET: Update in
tuberculosis: advances in the management of drug
resistant and multi-drug resistant tuberculosis
cases**

Thank you for viewing this document.

We would like to remind you that this material is the property of the author. It is provided to you by the ERS for your personal use only, as submitted by the author.

© 2009 by the author

Saturday, September 12, 2009
09:30–13:00
Room Lehár 3-4

Common causes of treatment mismanagement

*Dr Jean-Pierre Zellweger
Cabinet Medical
Rue de Locarno 1
1700 Fribourg, Switzerland
zellwegerjp@swissonline.ch*

Aims

Although the cause, the development, the treatment and the surveillance of tuberculosis are well defined, not all cases of tuberculosis respond to treatment as expected. There is frequent delay in the diagnosis, difficulties in interpretation of symptoms and radiological abnormalities, uncertainties and changes in the drug treatment, and problems in follow-up. Some of the obstacles are due to the fact that the patients do not have access to quality care and receive therefore attention below the expected standards of care.

This presentation will focus on the most common obstacles to rapid diagnosis and appropriate treatment. At the end, the attendants should be aware of the common pitfalls in the management of tuberculosis in practice and should be able to foresee them.

Summary

Tuberculosis (TB) is an infectious disease caused by mycobacteria of the *M.tb complex*, usually located in the lungs, slowly progressing to severe forms, but in most cases curable by a treatment combining several specific antituberculous antibiotics.

Although the cause, the development, the treatment and the surveillance are well defined^{1, 2}, not all cases of TB respond to treatment as expected. There is frequent delay in the diagnosis, difficulties in interpretation of symptoms and radiological abnormalities, uncertainties and changes in the drug treatment, and problems in follow-up. Furthermore, the patients may have other simultaneous diseases and drug treatment, creating interactions and obstacles to the normal treatment schedule. This explains that the cure rate, far from 100%, lies between 50% in some countries and 90% at best³.

The main obstacles to a straightforward diagnosis and management of TB will be addressed

Pitfalls in diagnosis

Interpretation of symptoms

Patients with TB are detected at variable stages of progression of the disease. Patients detected by routine screening (for instance contacts of source cases of TB or migrants submitted to active screening at the border) are frequently in an earlier stage of the disease and have less symptoms than patients who seek care for advanced forms of the disease^{4, 5}. Furthermore, some categories of patients have less complaints or seek help later than others. Undocumented foreign-born migrants in the US have a significantly higher frequency of cough and hemoptysis and a longer durations of symptoms than US-born persons⁶, but the extension of the radiological lesions and the proportion of smear-positive cases at diagnosis was not different between the groups. A long duration of symptoms before diagnosis is associated with a higher rate of transmission to contacts⁷.

Symptoms of TB are not specific and may be found or mentioned in many other respiratory diseases. Only weight loss and night sweats seem to be more common in TB than in other respiratory infections⁸.

Interpretation of X-ray

Most patients with pulmonary TB have abnormal X-rays. In countries where radiological equipments are readily available, performing a chest X-ray belongs to the assessment of a patient with respiratory symptoms suspect of TB. The technical requirements for the performance of X-rays and the rules for interpretation have been well codified⁹. The lesions are frequently typical, but may be unusual or absent. Among HIV-infected patients with documented TB (positive culture for *M.tbc*), up to 22%

may have a normal chest X-ray and even non-HIV infected patients may have normal chest X-rays in up to 5% of cases ¹⁰. The majority of patients with TB but a normal chest X-ray have few or no symptoms. Elderly patients are less likely to have the « typical » upper lobe infiltrates usually seen in young adults ¹¹. It is therefore important to obtain sputum (usually induced sputum or by bronchoalveolar lavage) in cases suspect of TB but with normal chest images.

Chest X-rays are not only suggestive of the presence of active TB but they also can demonstrate lesions of ancient, untreated TB which correlate with the risk of future reactivation and are an indication for preventive treatment ¹².

The persistence of a cavitation on the chest X-ray at 2 months after the beginning of treatment is predictive of failure or relapse and the persistence at the end of treatment is predictive of relapse ¹³.

History and origin of the patients

The origin of the patient with suspect symptoms or radiological signs is of great importance. African-born immigrants in UK have 100 times and Indian-born 70 times the TB rate of local population (UK report 2008). Travel to a high-incidence country ^{14, 15} and receiving a visitor from a country with a high prevalence also play a role ¹⁶.

Several factors increase the probability of TB and the delay in seeking health care. Among them are nonwhite race, language different from the local language, concern about costs, fear of immigration authorities and lower level of education. Migrants, particularly undocumented migrants, tend to combine several of these factors and are therefore *a priori* more likely to have TB than the local residents. Therefore, due attention should be paid to any suspect symptom or radiological abnormality in foreign-born migrants, particularly if they are undocumented. Low-threshold health facilities have been shown to contribute to the early detection of TB ¹⁷ and should be available for this group of high-risk patients.

Quinolones, even used as single drugs, may temporarily improve the symptoms and radiological appearance of TB. Treatment with quinolones of patients with pulmonary infiltrates and respiratory symptoms due to an undetected TB may mask the real cause of the disease, as TB and may expose the patients to the development of quinolone resistance.

Interpretation of laboratory tests

Routine blood tests play no role in practice for the diagnosis of tuberculosis. The recent disponibility of Interferon-Gamma Release Assays (IGRAs) has changed the place of laboratory tests in supporting the diagnosis of tuberculosis but a positive IGRA result cannot be interpreted as a proof of TB ¹⁸.

Serological tests have no convincing role in the diagnosis of TB, due to their poor accuracy in both pulmonary ¹⁹ and extrapulmonary TB ²⁰.

Collecting a sputum specimen

Obtaining a sputum sample for bacteriological confirmation of a radiological or clinical suspicion may not be easy. Children and ladies do not spit ! Performing a bronchoscopy is invasive and may not be easy to perform depending on the local conditions and equipment. Induced sputum, although slightly less efficient, is inexpensive, non invasive, easy to perform even with a minimal equipment and increases the yield compared with spontaneous sputum to a level comparable with bronchoalveolar lavage ^{21, 22}. The benefit of induced sputum is particularly evident in cases with limited radiological involvement and few symptoms ²³. Some experts use just an inhalation of two puffs of a beta-mimetic bronchodilator to obtain bronchial secretions, avoiding the need for any technical equipment apart from a hand-held metered-dose inhaler. In children, nasopharyngeal aspiration also has a high yield ²⁴.

Obtaining and interpreting the bacteriology

A large proportion of cases, even pulmonary, are not confirmed by a bacteriological examination, be it because no sputum sample has been sent to the laboratory or because there was no growth of mycobacteria. The consequence is that some 30 to 40% of cases of TB are started under drug treatment without confirmation of the disease, the rate being higher in extrapulmonary TB and in

