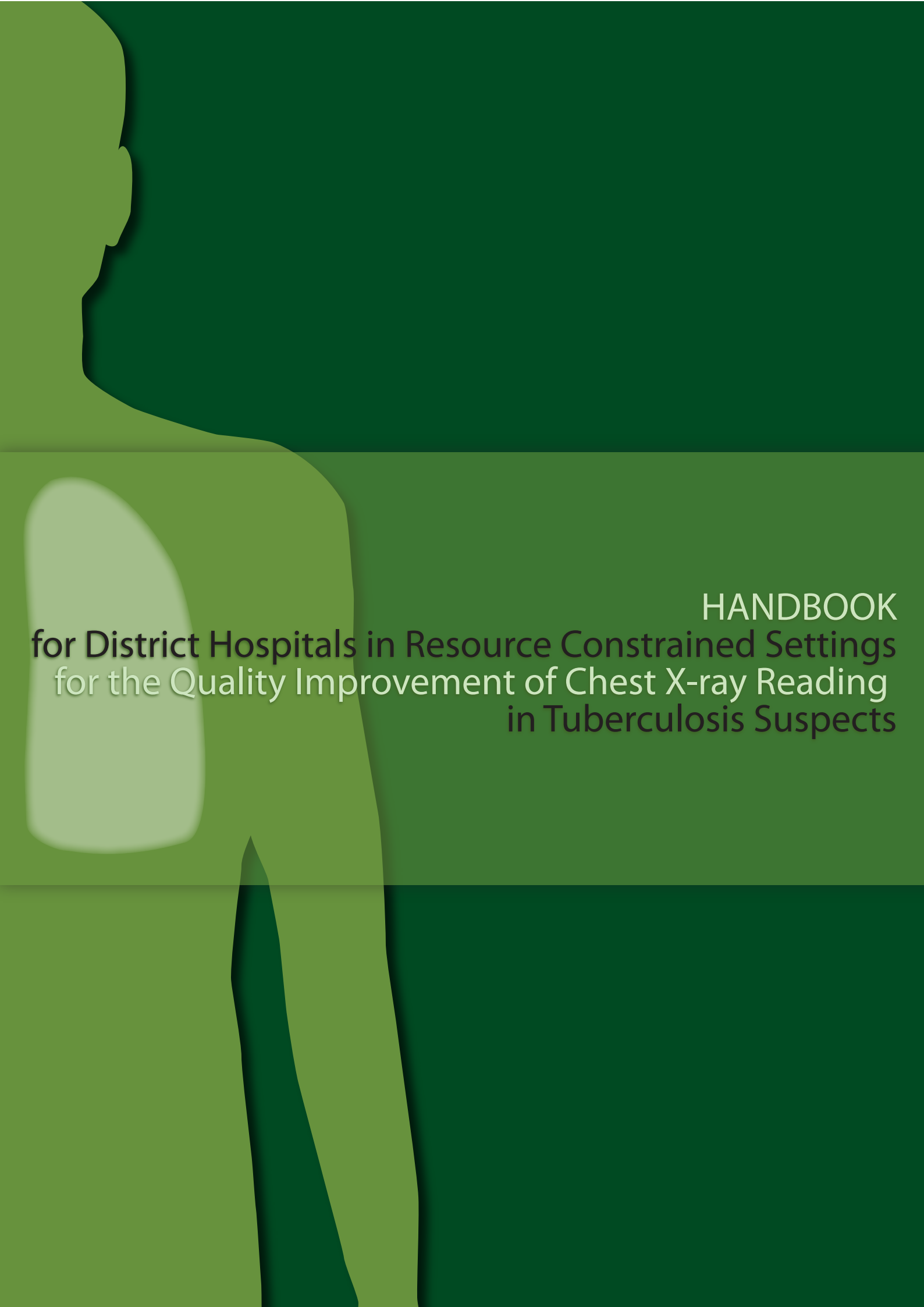

HANDBOOK
for District Hospitals in Resource Constrained Settings for the Quality Improvement of Chest X-ray Reading in Tuberculosis Suspects

Contents

This document is developed by the Tuberculosis Coalition for Technical Assistance (TBCTA).

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FROM THE AMERICAN PEOPLE

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August 2010

Abbreviations

AFB	Acid-fast Bacillus
AIDS	Acquired Immune Deficiency Syndrome
CHW	Community Health Worker
CXR	Chest X-ray
CD4	Cluster of Differentiation 4
DOTS	Directly Observed Treatment Short-course
EPTB	Extra pulmonary Tuberculosis
EQA	External Quality Assurance
HCW	Healthcare Worker
HIV	Human Immunodeficiency Virus
ISTC	International Standards for Tuberculosis Care
LTBI	Latent Tuberculosis Infection
NPV	Negative Predictive Value
NTM	Non-tuberculous Mycobacteria
PCR	Polymerase Chain Reaction
PPV	Positive Predictive Value
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
TBCTA	Tuberculosis Coalition for Technical Assistance
TPS	Tuberculosis Probability Score
WHO	World Health Organization

Glossary

Air Bronchograms	A radiographic shadow of an air-filled bronchus peripheral to the hilum and surrounded by airless lung (whether by virtue of absorption of air or replacement of air or both). The air is visible within the bronchus because the lung surrounding the bronchus is airless. Visualization of an air bronchogram usually implies the presence of an airspace filling process.
Atelectasis	Atelectasis is defined as the lack of gas exchange within alveoli, due to alveolar collapse or fluid consolidation. It may affect part or all of one lung. It is a condition where the alveoli are deflated, as distinct from pulmonary consolidation.
Bronchiectasis	Bronchiectasis is a disease state defined by localized, irreversible dilation of part of the bronchial tree. It is classified as an obstructive lung disease, along with emphysema, bronchitis and cystic fibrosis. Involved bronchi are dilated, inflamed, and easily collapsible, resulting in airflow obstruction and impaired clearance of secretions.
Dyspnea	Difficulty in breathing or shortness in breath.
Empyema	An empyema is a collection of pus within a naturally existing anatomical cavity, such as the lung pleura. It must be differentiated from an abscess, which is a collection of pus in a newly formed cavity.
Effusion	Effusion an abnormal collection of fluid in a body cavity or space.
Incidence	Incidence is a measurement of the number of new individuals who contract a disease during a particular period of time and is usually expressed as a percentage of the entire population per year.
Lymphadenopathy	Lymphadenopathy is a term meaning "disease of the lymph nodes." It is, however, almost synonymously used with "swollen/enlarged lymph nodes". It could be due to infection, auto-immune disease or malignancy.
Miliary TB	Miliary TB is a form of tuberculosis that is characterized by a wide dissemination into the human body and by the tiny size of the lesions (1–5mm). Its name comes from a distinctive pattern seen on a chest X-ray of many tiny spots distributed throughout the lung fields with the appearance similar to millet seeds—thus the term "miliary" tuberculosis. Miliary TB may infect any number of organs, including the lungs, liver and spleen.

Negative Predictive Value (NPV)	The proportion of patients with negative test results who are correctly diagnosed. The NPV can be calculated as the number of true-negatives divided by the number of true-negatives + the number of false-negatives.
Parenchymal Lesions	A localized pathological change in a functional tissue or cells of an organ or gland.
Positive Predictive Value	The proportion of patients with positive test results who are correctly diagnosed. The PPV can be calculated as the number of true-positives divided by the number of true-positives + the number of false-positives.
Post-primary TB	Occurs due to reactivation of infection or repeat exposure.
Prevalence	Prevalence is a measurement of all individuals affected by a disease within a particular period of time and expressed as the proportion of disease cases in a population at a given time point.
Primary Complex	The combination of a Ghon focus and a corresponding lymph node focus in primary tuberculosis; similar lesions are seen with other mycobacterial and fungal infections.
Primary TB	Tuberculosis caused by infection with tubercle bacilli and characterized by the formation of a primary complex in the lungs consisting of a small peripheral pulmonary focus and hilar or paratracheal lymph node involvement; it may cavitate and heal with scarring or progress.
Sensitivity	The proportion of true positives that are correctly identified by the test. The sensitivity can be calculated as the number of true-positives divided by the number of true-positives + the number of false-negatives.
Specificity	Specificity is the proportion of true negatives that are correctly identified by the test. The specificity can be calculated as the number of true-negatives divided by the number of true-negatives + the number of false-positives.
Tuberculomas	A non-neoplastic mass, usually in the lungs or brain, caused by a localized tuberculous infection.

Introduction

Aim

The Handbook for Quality Improvement of Chest X-ray Reading in Tuberculosis Suspects is written as guidance for chest X-ray reading in tuberculosis (TB) suspects. The main intention is to promote the rational use of chest X-rays in the diagnosis of TB. This handbook is published together with the *Handbook on Quality Assurance of Chest Radiography*, which focuses on the technical quality of the chest X-ray film[1]. The main scope of this handbook is to provide a useful tool for better diagnosing of smear-negative TB in adult TB suspects.

This document is intended for those health staff (medical officers, physicians and radiologists in hospitals) whose responsibility it is to read and to interpret chest X-rays from smear-negative TB suspects in order to establish the diagnosis of TB.

Rationale

Sputum smear negative TB is a difficult diagnostic category. Firstly, many symptoms that are very sensitive for TB have a very low specificity. Secondly, some smear-negative suspects have normal X-rays or X-rays with minimal abnormalities and indeed have TB. They can therefore be missed for treatment, sometimes with fatal outcomes. Thirdly, other smear-negative suspects do not have active TB but their symptoms mimic its clinical presentation, especially in the era of HIV. These patients may therefore be wrongfully treated for TB. Starting TB treatment on a TB suspect who does not have TB is undesirable because of the length of TB treatment (minimum six months) and the risk of developing toxic side-effects.

The global HIV epidemic has created an immense challenge in the diagnosis of tuberculosis. The high rates of sputum smear negative tuberculosis in HIV positive patients as well as the high mortality rates in TB-HIV co-infected patients call for more sensitive and more specific diagnostic tools. These tools should also be simple for use at non-specialized peripheral health centers.

Several guidelines for diagnosing TB have been published by The World Health Organization (WHO). They include clear algorithms for the management of TB suspects. TB suspects with a sputum smear that is negative for acid fast bacilli comprise the biggest diagnostic challenge. The WHO guidelines[2] *"Improving the diagnosis and treatment of smear-negative pulmonary and extra-pulmonary tuberculosis among adults and adolescents"* is a helpful tool in this group of patients. However, these guidelines do not give specific details on the characteristics of the chest X-ray in the diagnosis of sputum smear negative TB. In this handbook, we focus on characteristics of the chest X-ray in diagnosing sputum smear negative TB. We give a clear description and show some examples of typical radiographs. This should be useful in deciding whether or not a chest X-ray is suggestive for TB and even more importantly, whether to treat or not to treat.

In this handbook, we have tried to describe features of the chest X-ray which are indicative of TB and are useful in the process of diagnosing or excluding pulmonary TB. The handbook includes a TB Probability Scoring system, which includes a combination of diagnostic results, symptoms and characteristics of the chest X-ray. The TB Probability Scoring system provides a tool which allows the diagnosis of smear-negative TB patients. Although the scoring system has been based upon expert opinion and field experiences, it is important to realize that this system has not yet been validated in a thorough scientific manner. This will be done shortly both retrospectively and prospectively. Comments of the users of this scoring system would be most welcome.

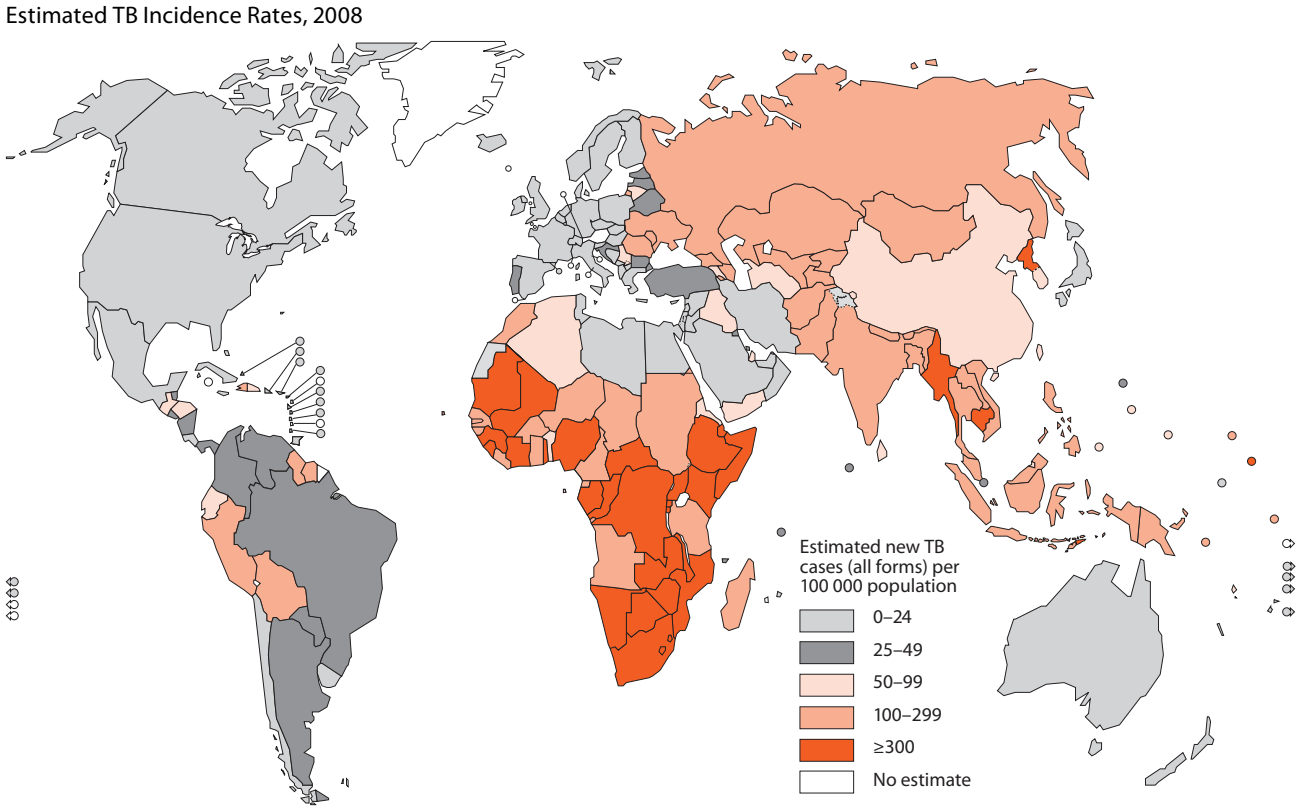
1 Handbook for District Hospitals in Resource Constrained Settings on Quality assurance of Chest Radiography: for better TB control and health system strengthening. 2008, http://www.tbcta.org//Uploaded_files/Zelf/XRayHandbook1225440283.PDF

2 http://www.who.int/tb/publications/2006/tbhiv_recommendations.pdf

Background on Tuberculosis

Tuberculosis worldwide

In 2008, 9.4 million new tuberculosis (TB) cases and 1.8 million deaths from TB were estimated to have occurred worldwide. Of all TB cases, 4.1 million were smear-positive of which approximately 1.4 million were dually infected with HIV. The highest rates for both TB and TB/HIV occurred in sub-Saharan Africa [WHO].



Source: WHO Report 2009 - Global TB Control

Diagnosis of Tuberculosis

Early and accurate tuberculosis diagnosis is needed to improve treatment outcomes for individual patients and to reduce transmission. The new Global Plan to stop TB, 2006-2015, states that all TB cases should have access to the TB diagnostic and treatment services. In many low income countries, mycobacterial culture facilities are not readily available. Culture is the current gold standard for detecting TB as it is more sensitive and specific than AFB sputum microscopy and more specific than chest X-ray. In many low income countries, the tools to diagnose TB are limited to sputum smear microscopy and chest X-ray. Although sputum smear microscopy is highly specific (almost 98%), its sensitivity is low: on average it cannot detect more than 50-60% of the symptomatic culture positive TB cases. Therefore, many pulmonary TB cases may not be recognized as such and may not be adequately treated for TB.

TB and HIV

Tuberculosis is the leading cause of mortality in people living with HIV/AIDS worldwide. TB can spread rapidly and recur frequently among people with HIV/AIDS. The probability of progression from latent infection to active disease is higher in people living with HIV/AIDS compared to HIV-seronegative patients. The largest challenge in diagnosing TB in AIDS patients is the atypical presentation of TB. In many cases, classical signs and symptoms are absent. Chest X-rays may show no abnormalities or present as TB in children. Sputum smear-negative pulmonary TB as well as extra-pulmonary TB occur more frequently among HIV infected persons, especially in cases with advanced HIV disease.

Chest X-ray and TB Diagnosis

The screening tools for the diagnosis of TB include symptom screening, sputum microbiology (sputum smear and culture) and chest X-ray. If sputum smears are negative, chest radiography is important to diagnose sputum smear negative TB. The chest X-ray, therefore, becomes even more important in the era of HIV. Chest radiography is also a tool which in some settings can be applied for active screening of TB suspects.

The major difficulty of using chest X-ray in the diagnosis of sputum smear negative TB is the non-specific nature of their symptoms and the large variety of other diseases which could be the cause of these symptoms. Therefore, an adequate diagnosis of TB is important.

Unfortunately, many HIV positive TB suspects present with a normal or minimal abnormal chest radiograph and TB treatment is often delayed in these patients, if TB is diagnosed at all. A negative sputum smear is not always sputum smear negative TB.

The scope of this handbook is to describe the features of the chest X-ray which are most relevant for the diagnosis of TB. The pre-eminent position of *Mycobacterium tuberculosis* as the major pathogen must be emphasized in these circumstances. However, other causes of sputum smear negative disease should be considered. They can be divided into false negative sputum smear results or other medical conditions such as asthma, emphysema, silicosis, lung carcinomas or other non-tuberculosis infectious lung diseases. The probability of having these medical conditions depends on the individual patient characteristics e.g. age, smoking habits, occupational history as well as the prevalence of the specific illness and/or pathogen in a given country or region.

TB Diagnosis in Sputum Smear Negative TB Suspects

TB case detection will be done in two phases which are complementary and successive. Both phases are based on the use of bacteriology and sputum smear examination.

The first phase is carried out according to public health criteria and should be applied in all health facilities, it begins with an identification and sputum smear examination of TB suspect cases. It is not necessary for physicians to perform this procedure. It can be done by nurses, lab technicians and trained community health workers (CHWs). This phase is an absolute priority.

The second phase is a diagnostic follow-up of suspects with negative sputum smear results but with persistent respiratory symptoms. This phase either eliminates or confirms TB or other respiratory pathology by means of a differential diagnostic process that is supported by culture, radiography and other auxiliary examinations, in addition to observation and clinical follow-up.

The International Standards for Tuberculosis Care[3] recommendations include one standard which refers to the diagnosis of sputum smear negative tuberculosis among adults:

> **Standard 5**
> The diagnosis of sputum smear negative pulmonary tuberculosis should be based on the following criteria: 1) at least two negative sputum smears (including at least one early morning specimen); 2) chest radiographic findings consistent with tuberculosis; and 3) lack of response to a trial of broad spectrum antimicrobial agents. (Since the fluoroquinolones are active against *M.tuberculosis complex* and, thus, may cause transient improvement in persons with tuberculosis, they should be avoided). For such patients, sputum cultures should be obtained. In persons who are seriously ill or have known or suspected HIV infection, the diagnostic evaluation should be expedited and if clinical evidence strongly suggests tuberculosis, a course of anti-tuberculosis treatment should be initiated.

In countries where culture of sputum samples is readily available, sputum smear negative cases can be classified as either definite tuberculosis cases (culture positive for *M.tuberculosis complex*) or otherwise sputum smear negative tuberculosis cases (culture-negative or unavailable)[2].

Pathogenesis of Tuberculosis

After the inhalation of *Mycobacterium tuberculosis* into the lung, the bacilli typically reach the most oxygenated segments of the lung (middle and lower regions). The local inflammatory response which may follow this inhalation is referred to as a primary or Ghon focus.

Primary Tuberculosis

Mycobacteria can spread via lymphatics to regional lymph nodes. This can result in hilar and mediastinal lymph node enlargement. The combination of the primary focus and the enlarged lymph node is called the primary complex. The bacteria can also spread throughout the body via lymphatics and the blood stream. In most cases, the developing immune reaction results in the control of the infection and within 3-8 weeks leads to a positive reaction on a tuberculin skin test. The newly infected individual usually does not have any symptoms and will likely not seek medical attention. The lymph node enlargement may be visible on a chest X-ray. If the body's immune response prevents the infection from advancing to active disease with further spreading, a calcification of the Ghon focus and/or of the regional lymph node may be visible on the X-ray, usually years after the initial infection. When the initial infection is not controlled by the body's immune system, it can progress to active primary tuberculosis with uncontrolled growth of the bacteria and the patient will likely now develop signs and symptoms.

3 International Standards for Tuberculosis Care, Edition 2, 2009

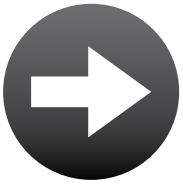
Post-Primary Tuberculosis

If the primary infection is controlled by the body's immune system, the healed lesions often contain viable *Mycobacterium tuberculosis*. In this state, the bacteria can survive for many years in the body without causing any illness - this condition is called Latent Tuberculosis Infection (LTBI). One third of the world's population is latently infected with TB. These surviving bacteria may progress to active disease anytime during a latently infected individual's lifetime. This is called reactivation and leads to post-primary tuberculosis. Of the patients who reactivate, 80% do so within the first two years after infection with TB. HIV positive patients with LTBI have a high risk of developing active TB (10% risk per year) compared to non-immune compromised persons with LTBI (10% risk over their entire lifetime). HIV-infected persons with LTBI who take anti-retroviral medications are less likely to develop active TB; however, their lifetime risk for active TB still remains higher than for HIV-negative persons. The radiographic findings of active TB after reactivation (post–primary tuberculosis) depend on the age and the immune status of the patient.

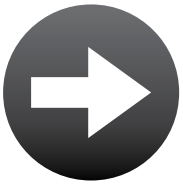
Among immune-competent individuals who develop active TB, the majority of cases (approximately 80%) have active TB localized in the lungs (Pulmonary TB). Extra-pulmonary TB (approximately 20 %) is the result of the initial spreading of bacteria through the body and may affect lymph nodes, bones, meninges, urogenital system and others. It may develop directly after the spread of bacteria (especially meningitis, miliary TB) or after a latency. Among HIV infected individuals with advanced immune-suppression, typically 50-70% of the cases have active TB localized in the lungs.

How to Read a Normal Chest X-Ray

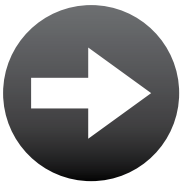
Before starting to read an X-ray it is important to evaluate the quality of the X ray.
The following issues need to be checked in order to be able to evaluate the X-ray properly[4]:



Exposure: thoracic vertebrae and vessels visible behind the heart



Proper positioning: symmetrical location of claviculae and scapulae



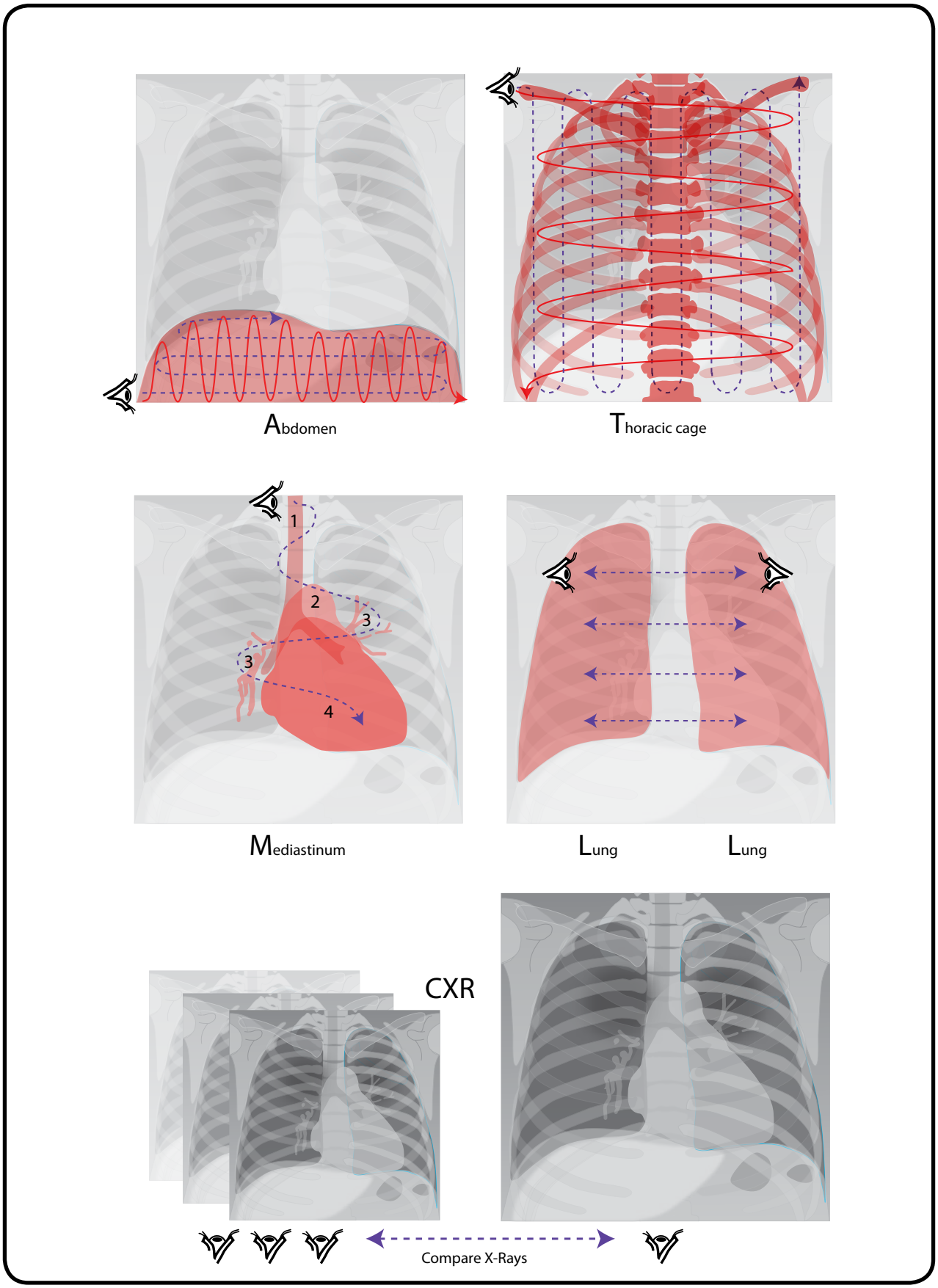
Inspiratory effort: posterior 10th rib visible above the diaphragm

Furthermore, reading X-rays needs a good understanding of normal anatomy and an orderly search pattern, in order to maximize accuracy.

4 Handbook for District Hospitals in Resource Constrained Settings on Quality Assurance of Chest Radiography: For Better TB Control and Health System Strengthening - TBCTA, 2008

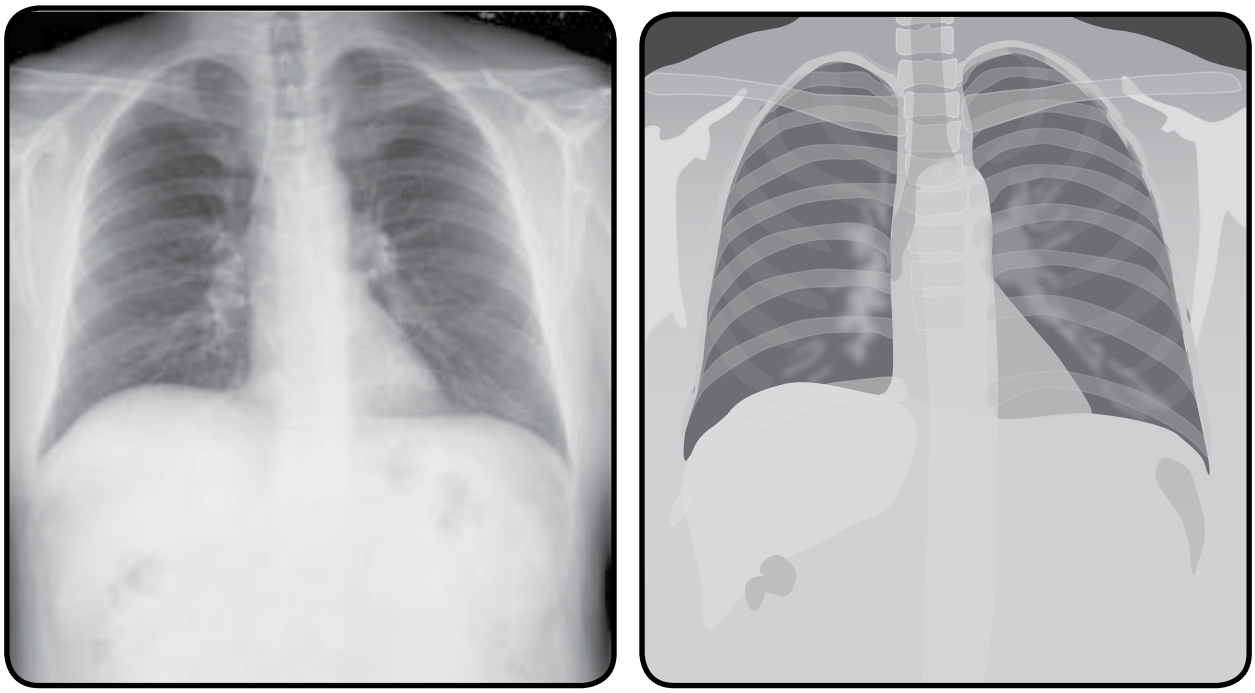
An example[5] of such a search pattern can be: start in the upper abdomen (A), look at the thoracic cage and spine (T), then the mediastinal structures (M) and lastly the lung (L). Look at each lung individually and then compare right and left lung (L) (ATMLL). In case you have a previous chest X-ray: compare the new and old one. This can be helpful in detecting new disease and changes in pre-existing disease.

Figure 1: Drawing of Chest X-ray with Indications How to Read According to ATMLL



5 Goodman L.R., Felson's Principles of Chest Roentgenology, 2nd edition. 1999

Figure 2: Normal Chest X-ray



A lateral view might give some additive information, especially on the localization of segmental lesions and the existence of lymphadenopathy. This is a common presentation in children and HIV positive patients. In case of an atypical pattern the clinician should consider other possible diagnoses as well. Among adults, the clinical presentation, together with age and immune status of the patient will play an important role in decision making.

Roentgenology

Primary TB

Typical Characteristics Among HIV negative patients and HIV positive patients with CD4 > 200 mm^3

1. Parenchymal lesions: homogeneous airspace consolidations, preferentially in the lower lobes. Air bronchograms may be seen. Anterior segment involvement can occur. Cavitation is unusual but can occur.
2. Nodular lesions: miliary pattern can occur.
3. Pleural effusions: 30-40% of primary TB cases, usually unilateral, same side as primary infection. 5% of TB cases present with pleural fluid as the only manifestation, especially in adolescents and young adults.
4. Central structures: unilateral hilar and/or mediastinal lymph node enlargement are common.

Typical Characteristics Among HIV Infected Patients:

1. Parenchymal lesions: Upper and lower lobes affected equally, homogeneous opacities. Cavities are rare.
2. Nodular lesions: a miliary pattern can occur in progressive primary tuberculosis in HIV infected patients regardless of CD4 count.
3. Pleural effusions: effusion common in HIV infected with > 200 cells. Not common in patients with low CD4 cell count (< 200 cells).
4. Central structures: lymphadenopathy is particularly common in patients with low CD4 cell count (< 200 cells).
5. Other: often normal radiography in patients with low CD4 cell count (< 200 cells).

Table 2: Roentgenology in Primary Tuberculosis

Primary TB	Parenchymal Lesions	Nodular Lesions	Pleural effusions	Central structures	Other
HIV negative patients and HIV positive patients with CD4 > 200 mm^3	Lower lobes, homogeneous opacities. Cavities can occur in progressive disease	Miliary pattern can occur in progressive disease	Common in HIV-negative adolescents and young adults, and in HIV positive CD> 200 at all ages	Unilateral lymph node enlargement is common	
HIV infected CD4 < 200 mm^3	Multilobular lower lung zones. Cavities are rare	Miliary pattern can occur	Effusion not common	Lymphadenopathy is particularly common	Normal radiograph

Post-Primary TB

Typical Characteristics Among HIV negative patients and HIV positive patients with CD4 > 200 mm^3

1. Parenchymal lesions: heterogeneous consolidations situated in the apico-posterior segments of the upper lobes and the superior segments of the lower lobes, often associated with cavities. These cavities can contain a small level of fluid.
2. Involvement of anterior segment without the apico-posterior segment makes post-primary TB very unlikely.

3. Nodular lesions: nodules may be a sign of bronchogenic spread, typically 5-10 mm diameter, involving the lower lung zones. Miliary pattern.
4. Pleural effusions: up to 20% of cases present with unilateral pleural fluid. The effusion is more likely to be associated with parenchymal abnormalities.
5. Central structures: lymph node enlargement are uncommon (5% of cases). Hilar elevation, mediastinal shift and tracheal retraction can be caused by fibrosis and atelectasis.
6. Other: tuberculoma, 1-5 mm diameter smooth and sharply defined, usually found in the upper lobes.

Typical Characteristics Among HIV Infected Patients:

1. Parenchymal lesions: opacities occur in the upper lobes, cavities occur less in patients with low CD4 cell counts.
2. Nodular lesions: miliary pattern is uncommon in patients with CD4 count < 200 cells
3. Pleural effusions: common in patients with CD4 count > 200 cells, uncommon in patients with low CD4 counts.
4. Central structures: hilar and paratracheal lymph node enlargement is more common in patients with low CD4 cell counts.
5. Other: normal radiograph (10-20% of persons with severe immunosuppression).

Table 3: Roentgenology in Post-Primary Tuberculosis

Primary TB	Parenchymal Lesions	Nodular Lesions	Pleural effusions	Central structures	Other
HIV negative patients and HIV positive patients with CD4 > 200 mm³	Heterogeneous opacities in the upper lobes. Cavities are observed	Nodules 5-10 mm, due to bronchogenic spread. Miliary pattern more present lower lung zones	Pleural effusions in 20% of cases	Hilar elevation, mediastinal shift and tracheal retraction possible and caused by fibrosis and atelectasis	Fibrotic lesions are common in the upper lobes
HIV + CD4 < 200 mm³	Multilobular opacities in the lower lung zones. Cavities uncommon	Not common	Pleural effusion uncommon	Hilar and paratracheal lymph node enlargement common	Normal radiograph

Other X-ray Abnormalities

A chest X-ray at the end of treatment could be utilized as a reference record to prevent some patients with prior (but no longer active) TB undergoing unnecessary retreatment for TB in the future. Persisting cavitary lesions or a destroyed lung after treatment may also result in various non-TB opportunistic infections. An aspergilloma may form which can cause recurrent and sometimes fatal haemoptysis. Non-tuberculous mycobacteria (NTM) are nowadays more and more isolated and recognized as true the pathogens in chronic pulmonary diseases and may cause severe disease resembling TB. These pathogens are AFB positive micro organisms and only with species identification testing with molecular methods e.g. PCR and culturing is it possible to distinguish them from *Mycobacterium tuberculosis*.

Calcified pleural abnormalities due to tuberculosis empyema may cause relapse tuberculosis due to persistent viable bacteria in this region. Tuberculous empyema may also cause a trapped lung with restrictive pulmonary function loss presenting with dyspnea on exertion. Bronchiectasis, especially in the lower lung regions, may cause recurrent lower respiratory tract infections due to colonisation with common pathogens as *H.influenza, S.aureus* or even *Pseudomonas aeruginosa*.

Examples of Tuberculosis Roentgenology

1 Parenchymal Lesions
1.1 Child with Primary Complex and Lymphadenopathy
1.2 Heterogenous Consolidation in Both Upper Lobes
1.3 Heterogenous Consolidation in Left Upper Lobe with Cavity with Fluid Level
1.4 Apical Pleural Thickening and Heterogenous Consolidation Right Upper Lobe
1.5 Atelectasis Right Lung due to Tuberculosis Consolidations in Upper Lobe and Lower Lobe with Tracheal and Cardial Shift

2. Nodular Lesions
2.1 Diffusely Spread Miliary Pattern
2.2 Tuberculoma in Left Upper Lobe

3. Pleural Abnormalities
3.1 Left-Sided Pleural Fluid

4. Central Structures
4.1 Mediastinal and Hilar Lymph Node Enlargement
4.2 Mediastinal Lymph Node Enlargement

5. Other
5.1 Fibrotic Lesions Left Upper Lobe

6. Healed Tuberculosis
6.1 Atelectasis
6.1.1 Start Treatment
6.1.2 End Treatment

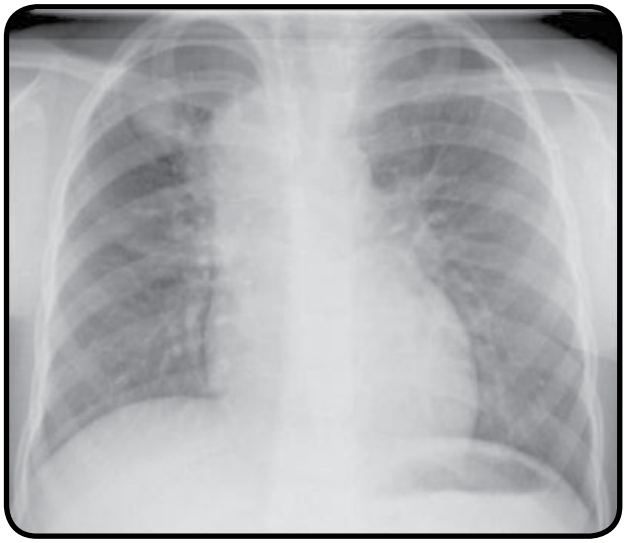
6.2 Destroyed Lung with Non-tuberculous Mycobacterial Infection (NTM)

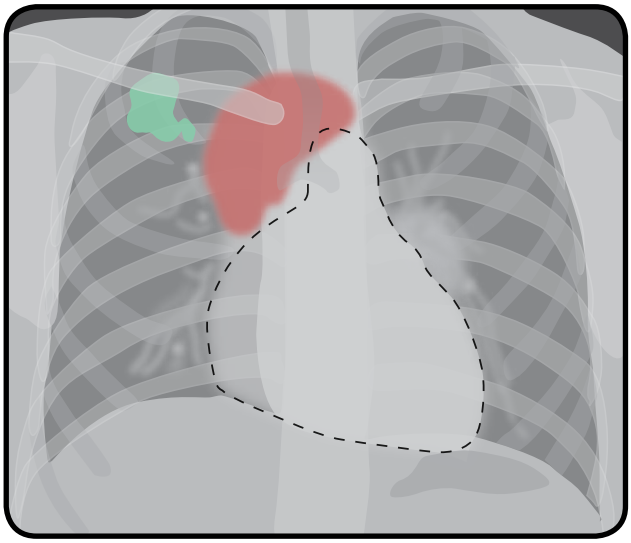
6.3 Calcified Pleura
6.3.1 Posterior Anterior View
6.3.2 Lateral View

6.4 Trapped Lung Due to Tuberculous Empyema
6.4.1 During Treatment
6.4.2 End of Treatment
6.4.3 Spontaneous Recovery

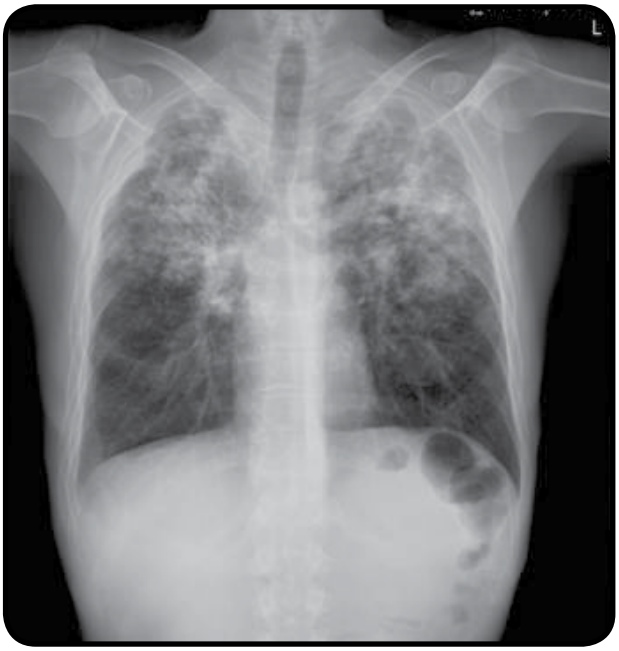
1 Parenchymal Lesions

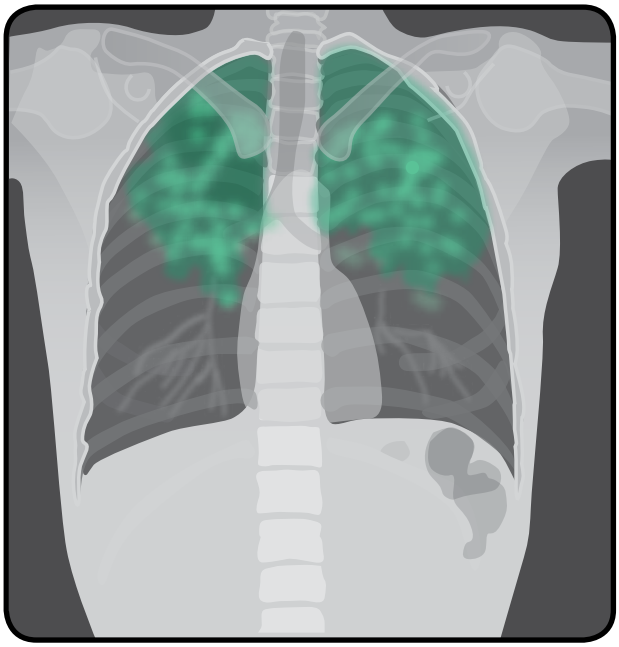
1.1 Parenchymal Lesions: Child with Primary Complex (Primary Focus & Lymphadenopathy)



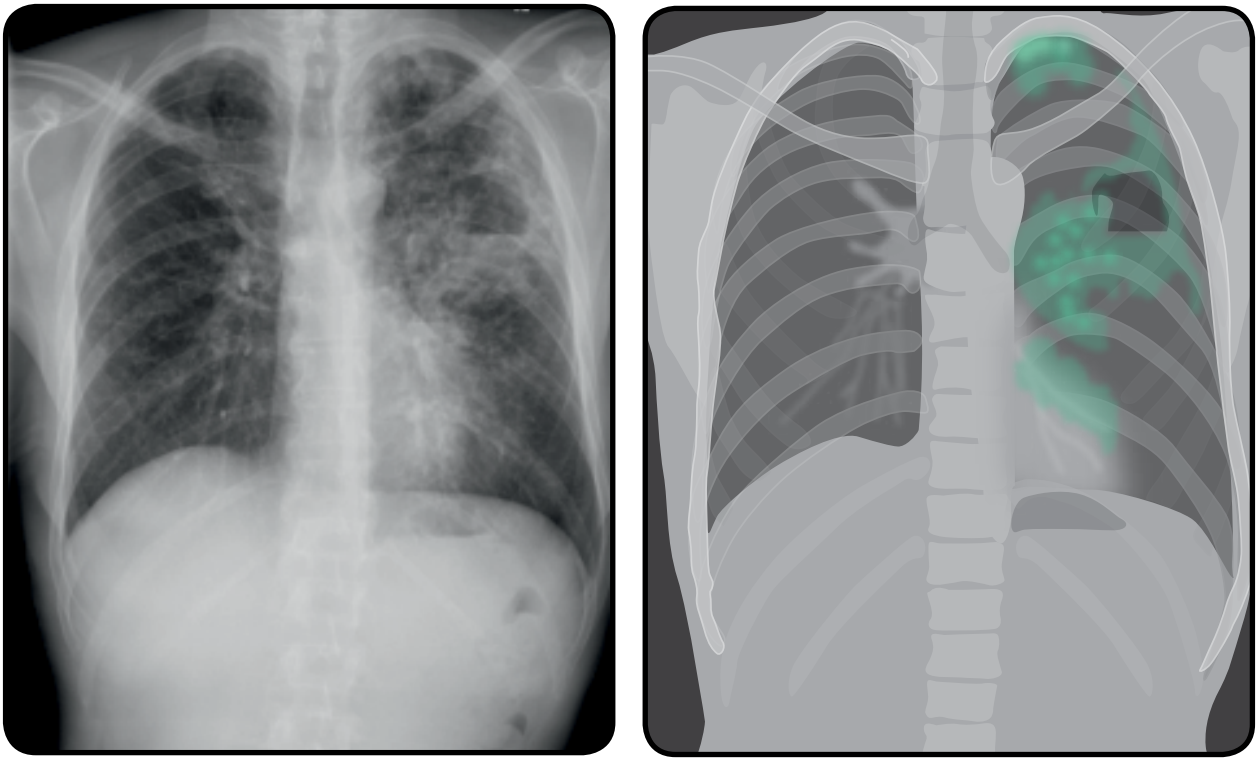


1.2 Parenchymal Lesions: Heterogenous Consolidation in Both Upper Lobes

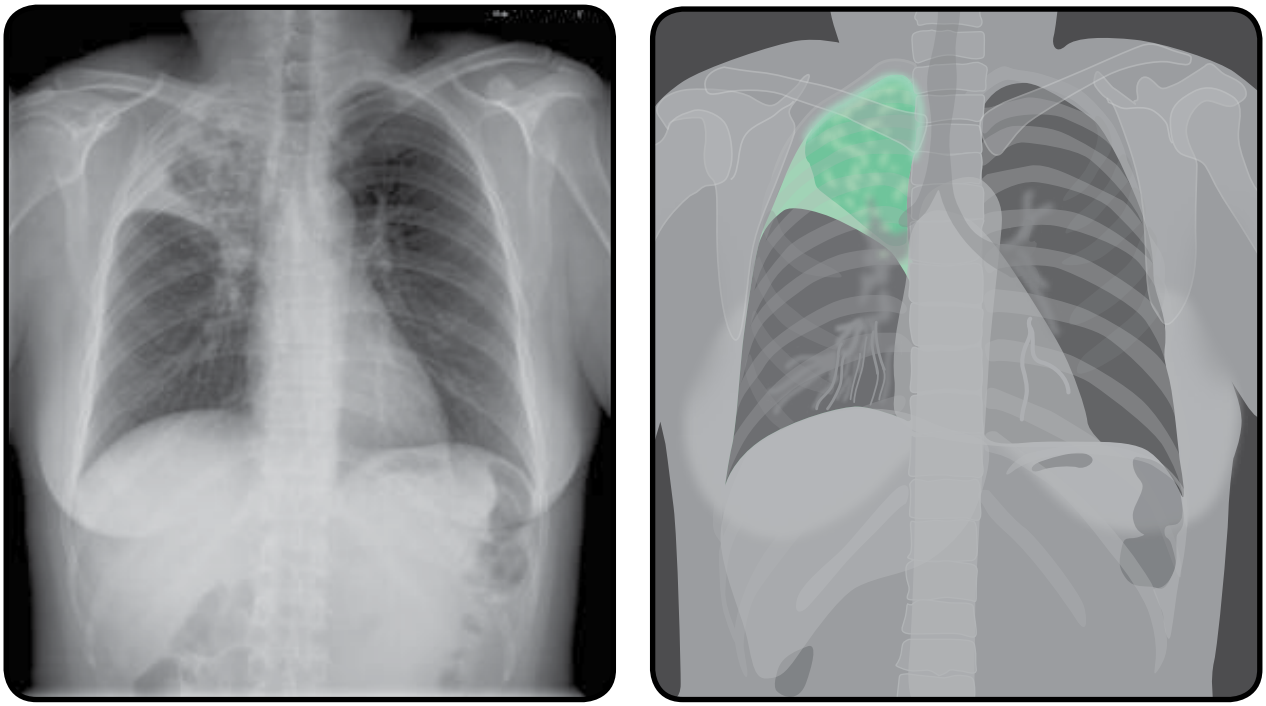




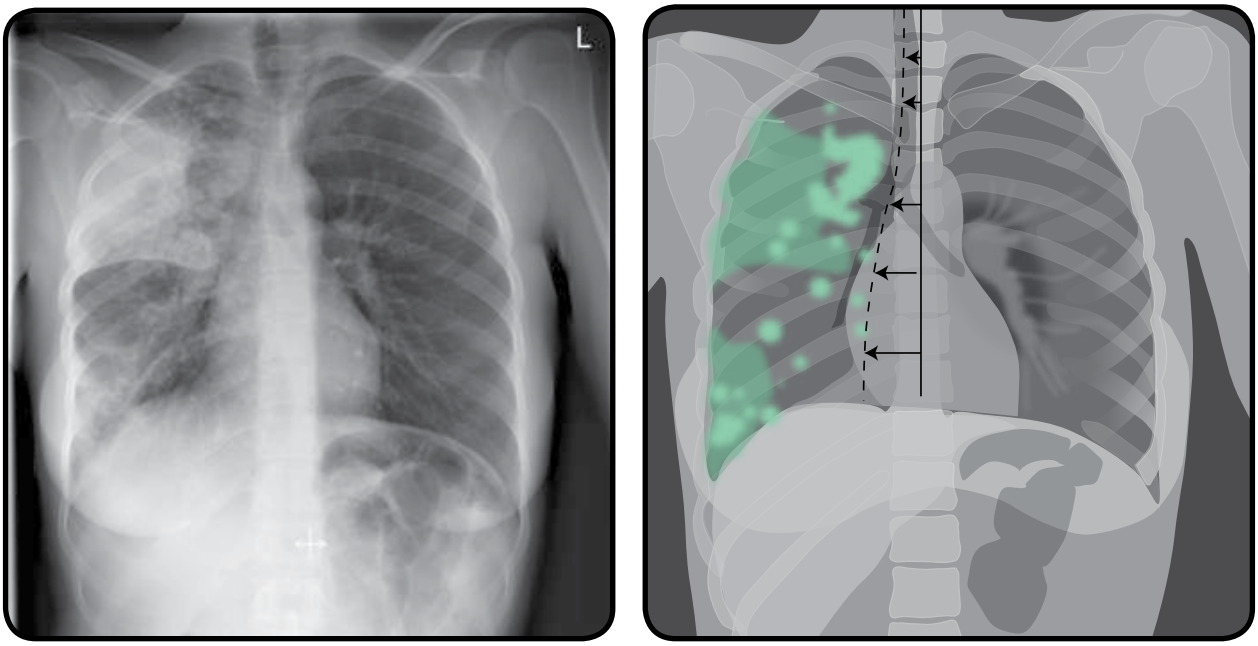
1.3 Parenchymal Lesions: Heterogenous Consolidation in Left Upper Lobe with Cavity with Fluid Level



1.4 Parenchymal Lesions: Apical Pleural Thickening and Heterogeneous Consolidation Right Upper Lobe

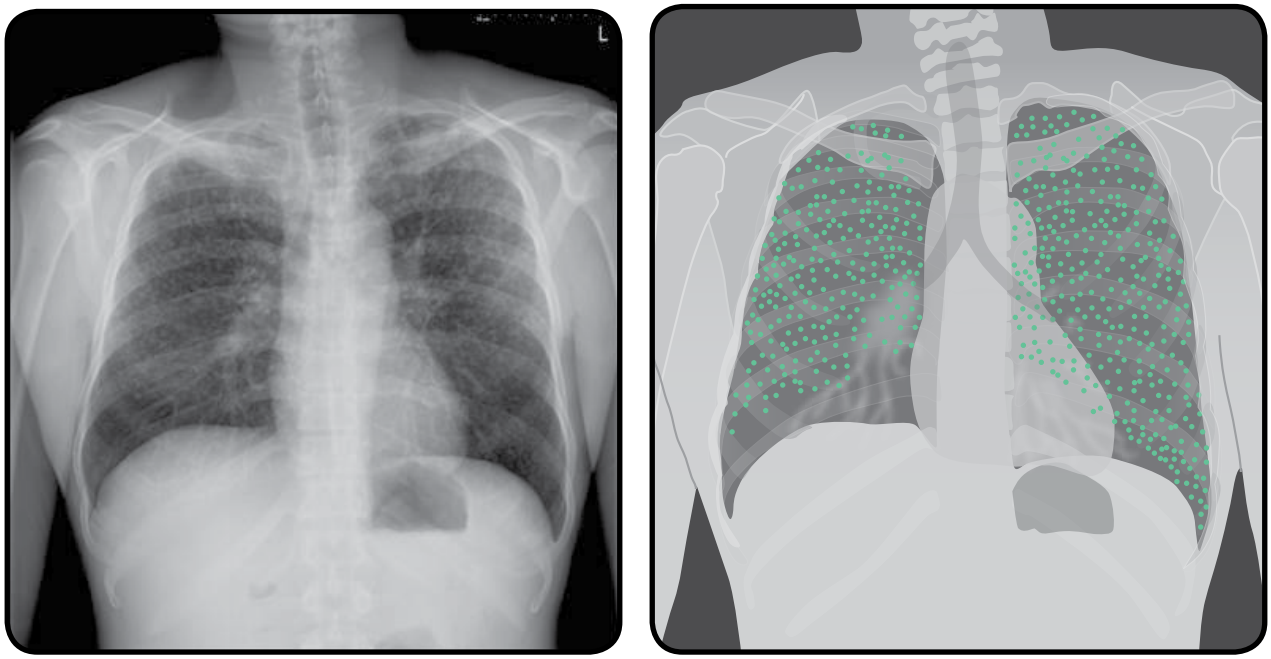


1.5 Parenchymal Lesions: Atelectasis Right Lung due to Tuberculosis Consolidations in Upper Lobe and Lower Lobe with Tracheal and Cardial Shift.

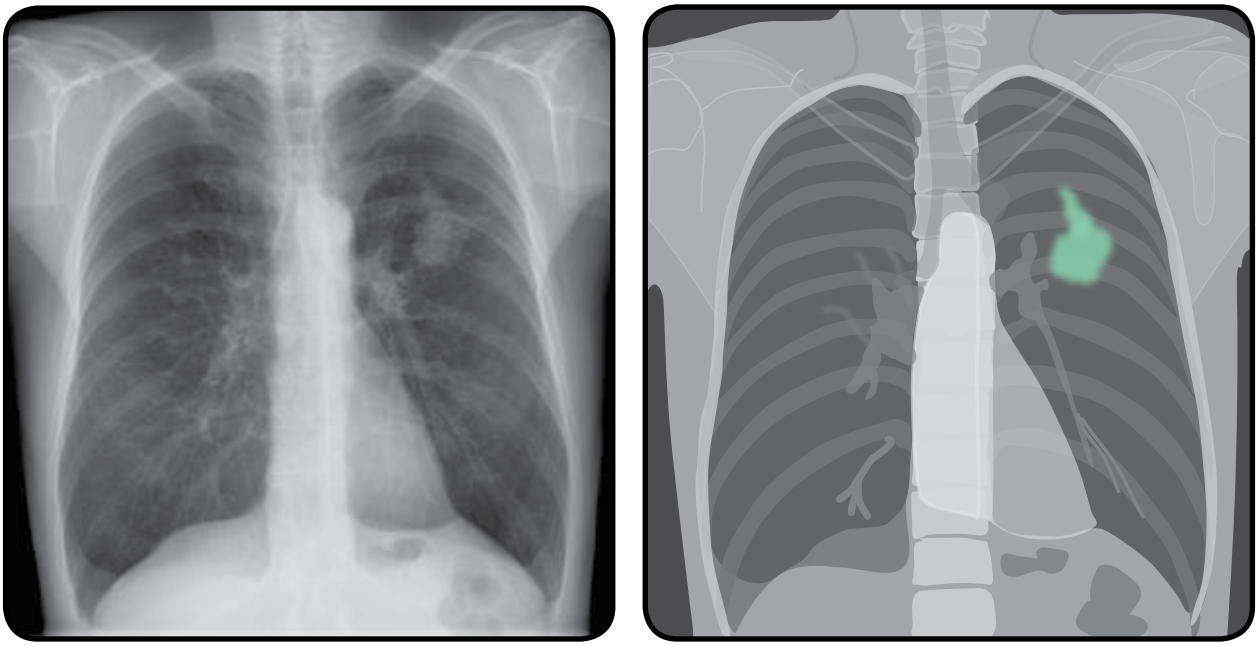


2 Nodular Lesions

2.1 Nodular Lesions: Diffusely Spread Miliary Pattern

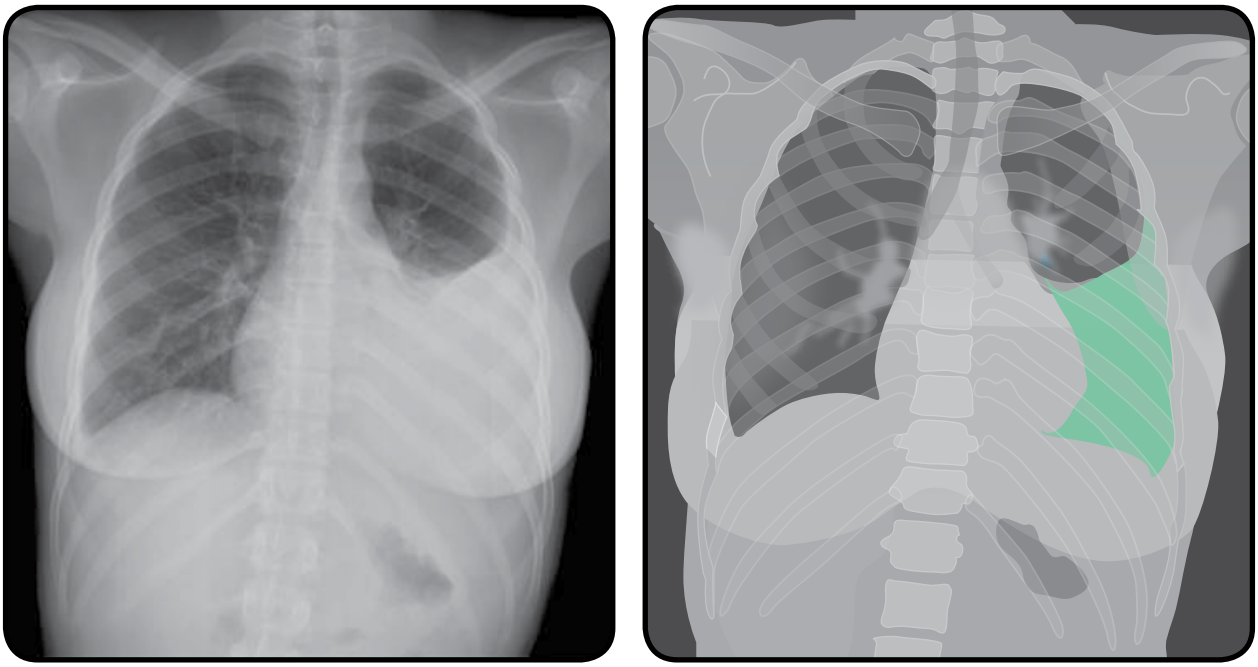


2.2 Nodular Lesions: Tuberculoma in Left Upper Lobe



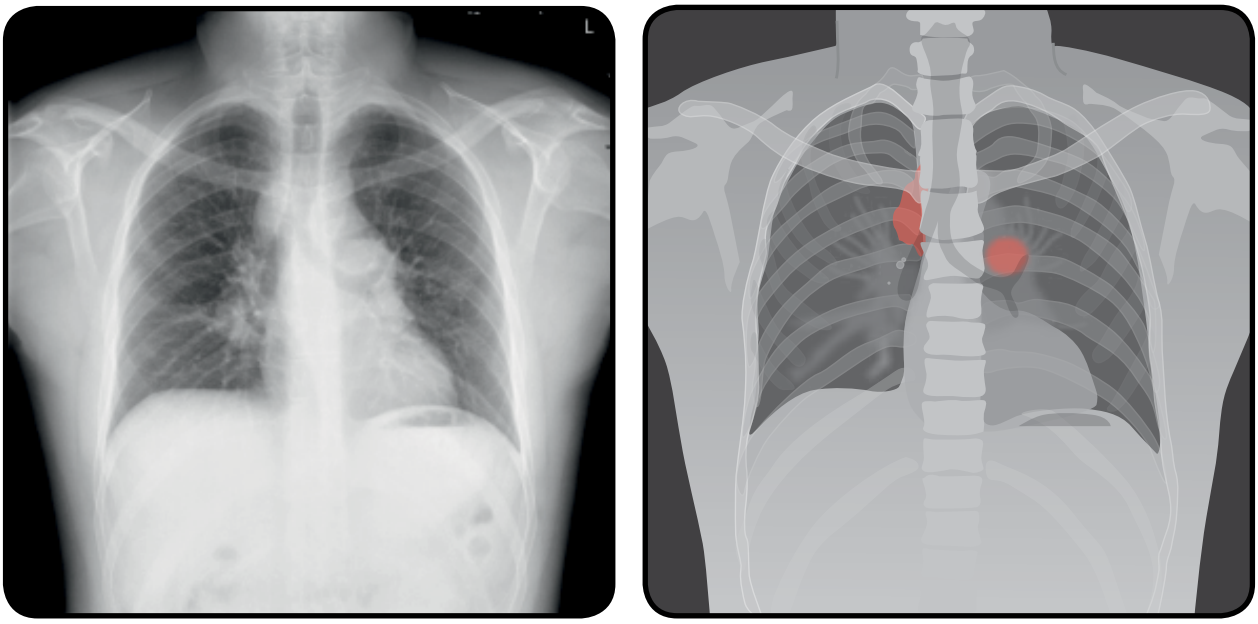
3 Pleural Abnormalities

3.1 Pleural Abnormalities: Left Sided Pleural Fluid

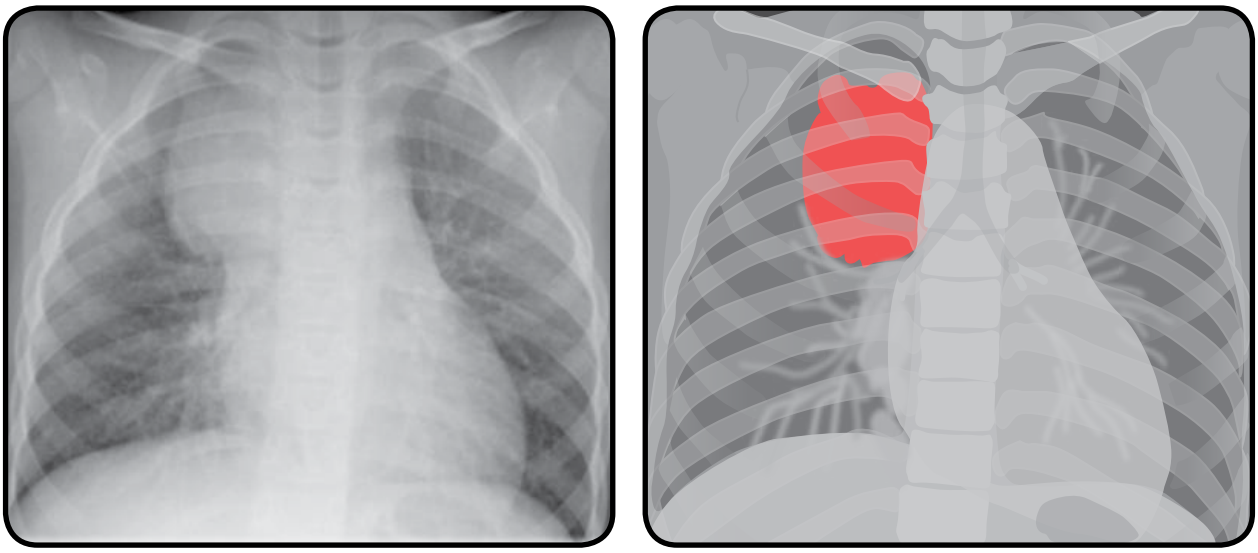


4 Central Structures

4.1 Central Structures Abnormalities: Mediastinal and Hilar Lymph Node Enlargement

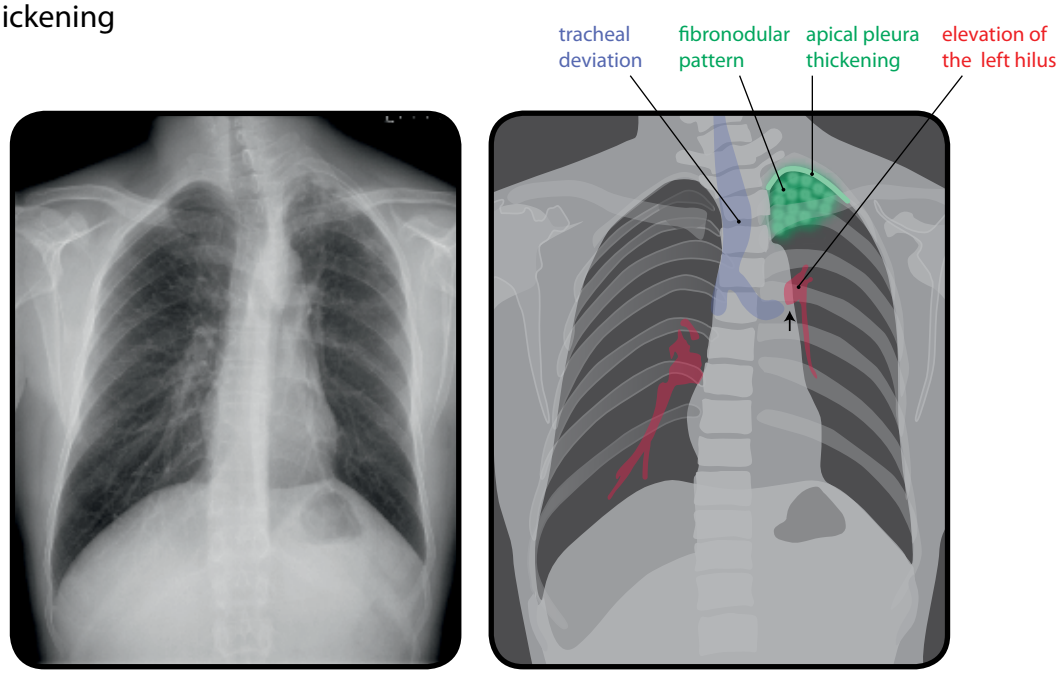


4.2 Central Structures Abnormalities: Mediastinal Lymph Node Enlargement



5 Other Abnormalities

5.1 Other: Fibronodular Pattern Left Upper Lobe with Tracheal Deviation, Elevation of the Left Hilus and Apical Pleural Thickening



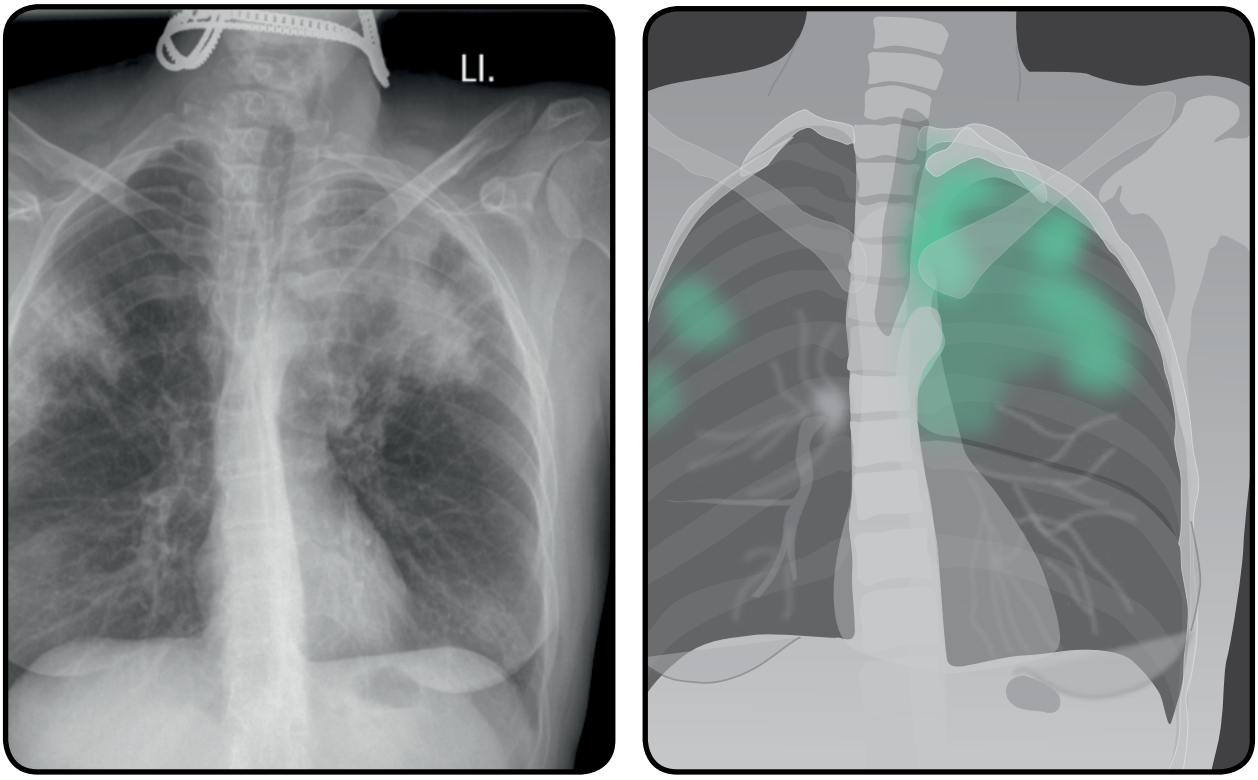
6 Healed Tuberculosis

Patients may also suffer from symptoms consistent with TB, when treated and healed from TB that they experienced in the past. Contrary to sputum smear-positive TB where we monitor the end of treatment with a sputum smear examination, for smear-negative TB end-monitoring usually doesn't take place. A smear-negative case of TB is reported as cured when the treatment is completed.

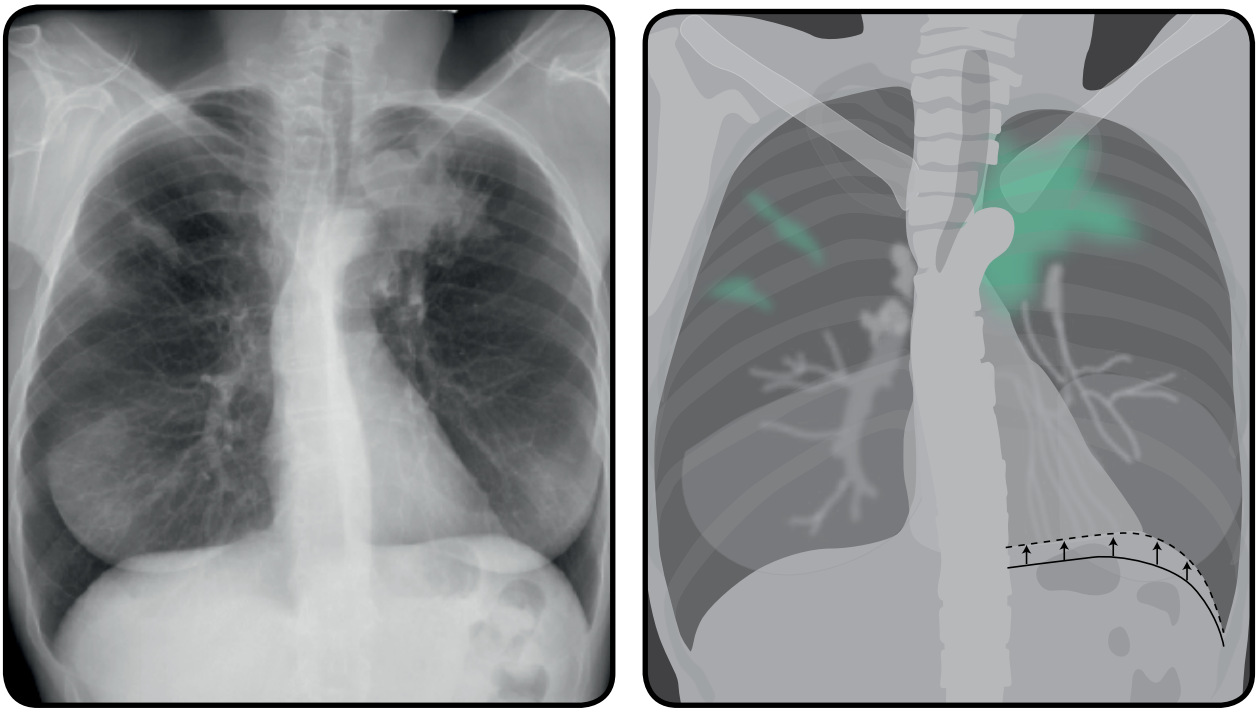
Cure/Completion is based on a full course of treatment. The clinical condition is another factor to be considered but is not included in the regular Recording & Reporting system. However, when a full course of treatment is completed, the chest X-ray may still show abnormalities. As mentioned earlier, a chest X-ray at the end of treatment could be utilized as a reference record to prevent some patients with prior but no longer active TB, from unnecessary retreatment for TB in the future. Persisting lesions or a destroyed lung after treatment may also result in various non-TB opportunistic infections. This chapter describes images, when patients are actually healed from TB.

6.1 Developing Atelectasis During Treatment

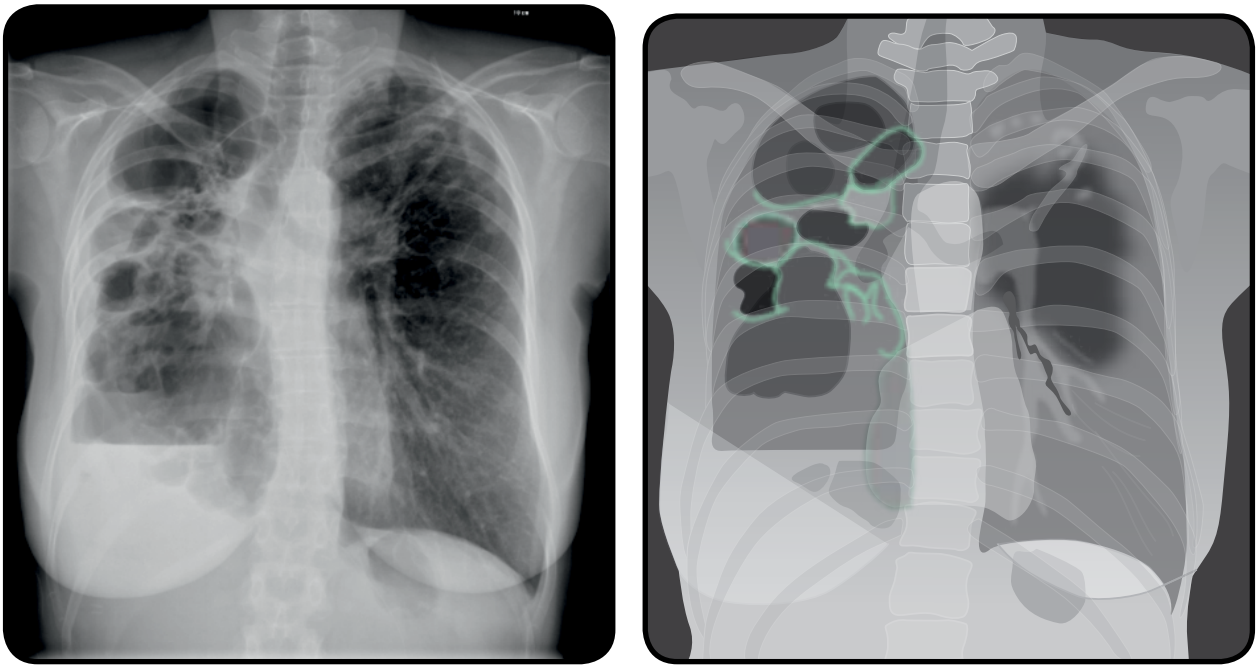
6.1.1 Start of Tuberculosis Treatment: Consolidations in Left and Right Upper Lobe



6.1.2 End of Tuberculosis Treatment: Atelectasis Left Upper Lobe with Retraction of Left Hilus and Diaphragm

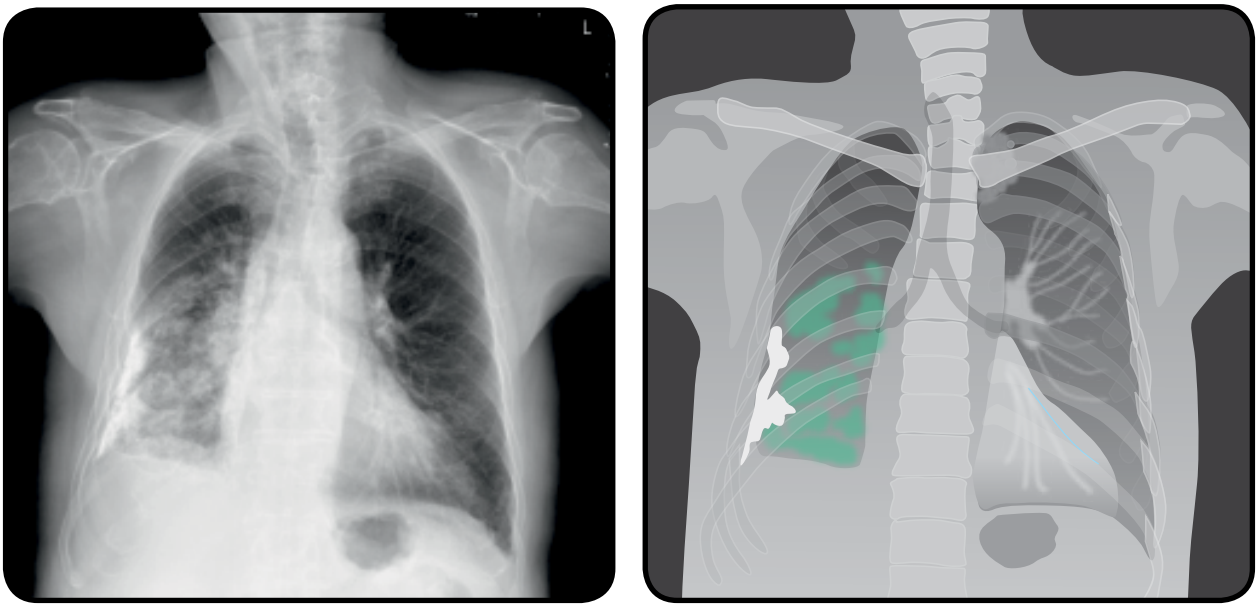


6.2 Destroyed Right Lung After Treatment with Current New Lesions in Left Upper Lobe

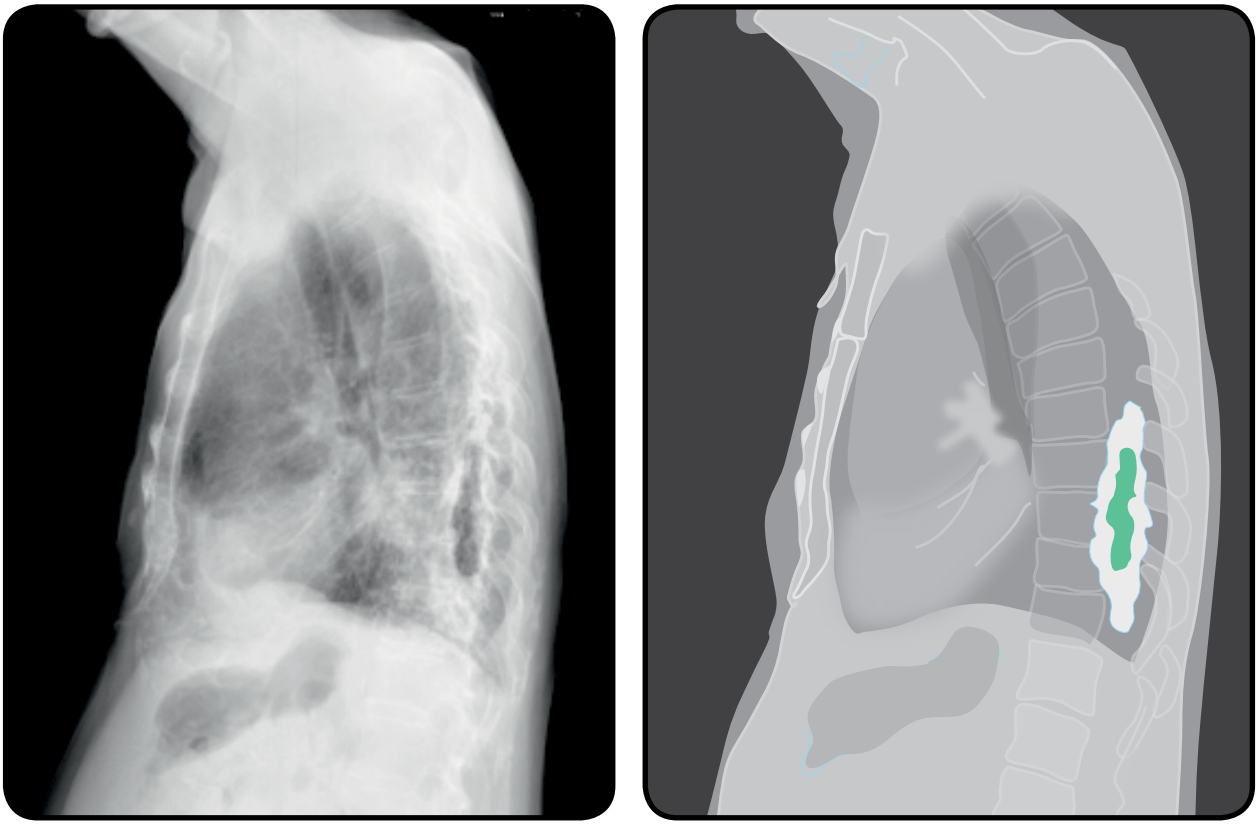


6.3 Calcified Pleura after Pleural Tuberculous Empyema with Consolidation in Right Lower Lobe due to the Reactivation of TB

6.3.1 (Posterior–Anterior view)

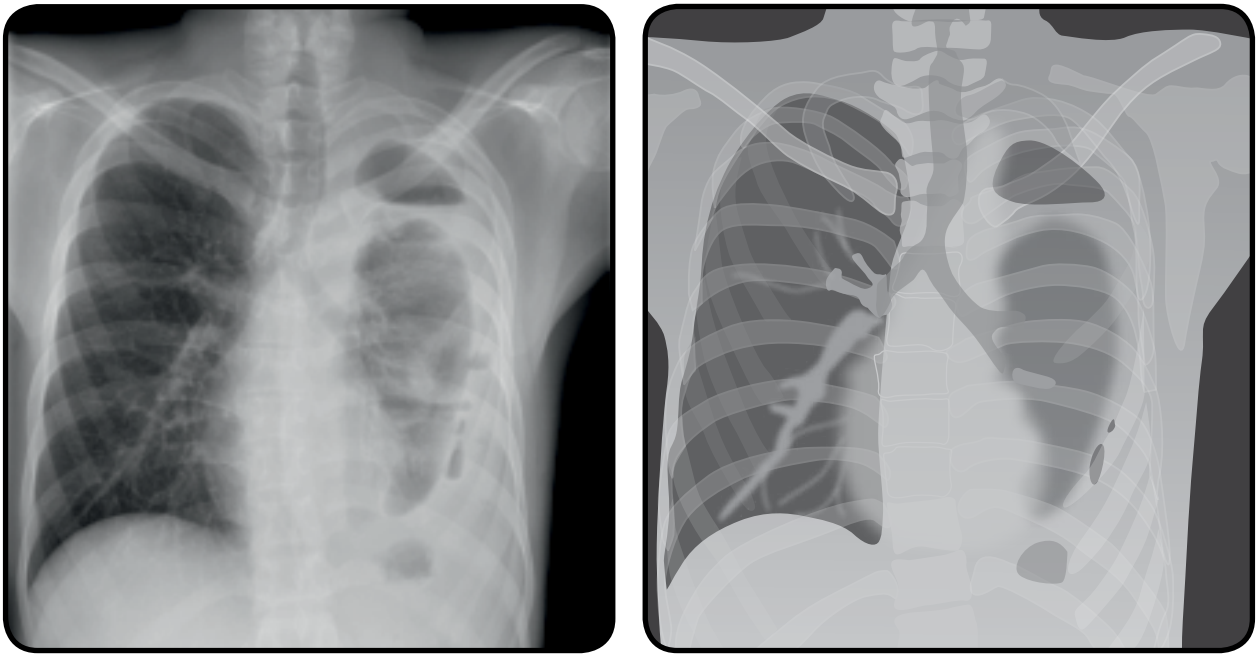


6.3.2 Lateral View Calcified Pleura

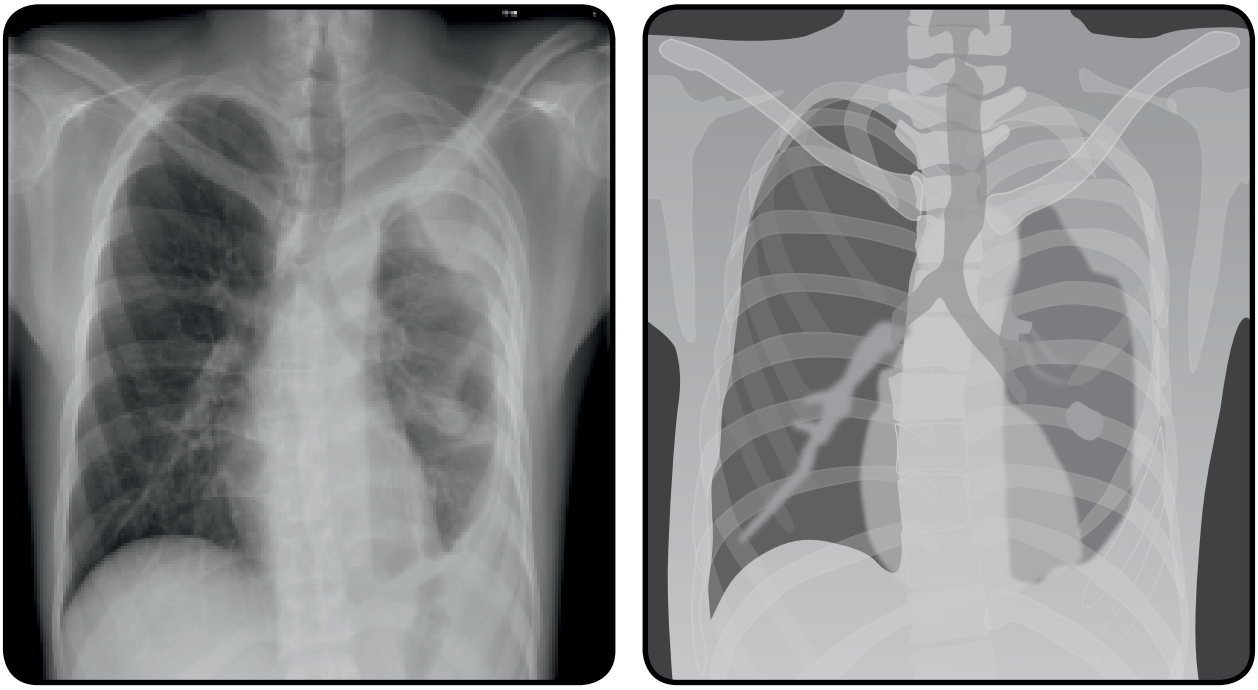


6.4 Trapped Left Lung due to Tuberculous Empyema

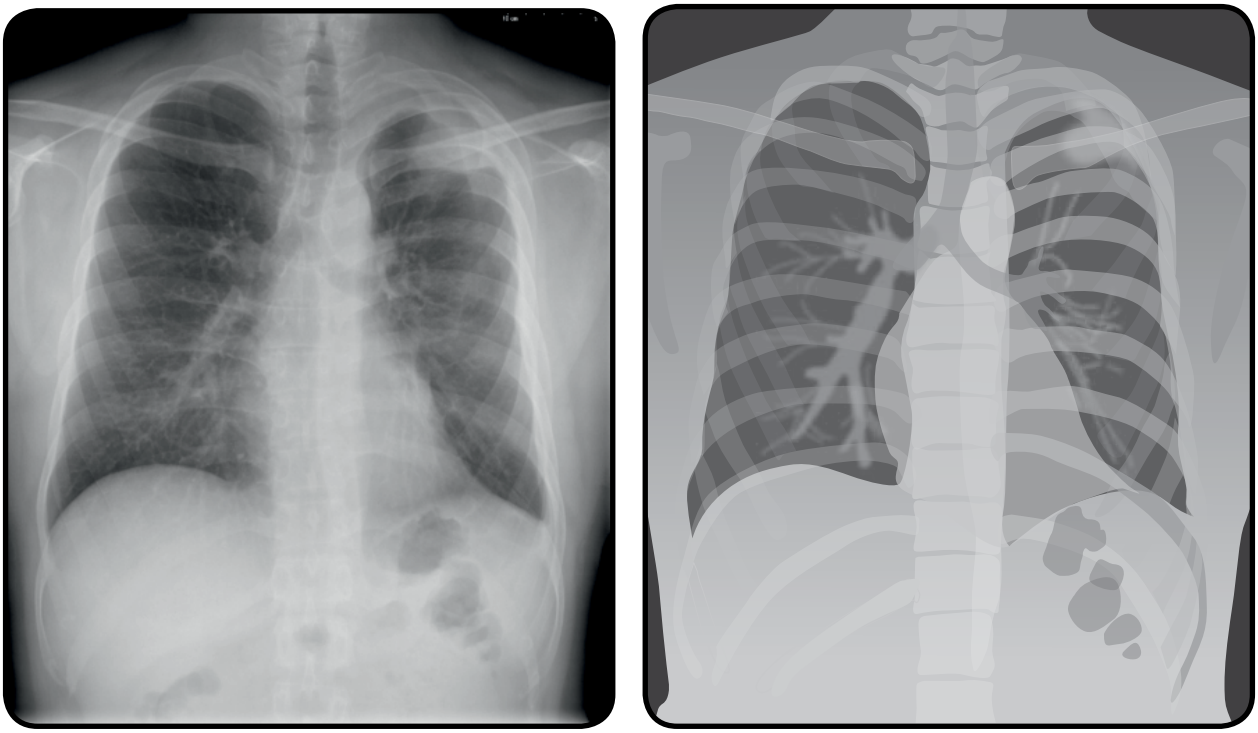
6.4.1 During Treatment



6.4.2 End of Treatment



6.4.3 Spontaneous Recovery and Normalization of Lung Capacity Two Years after Treatment



Predicting Tuberculosis

In the pathogenesis of tuberculosis, 4 steps can be identified: exposure, infection, disease and death[6,7]. If we leave out the last one, death, for the three remaining steps determinants can be identified. Determinants include: the number of incident cases, duration of infectiousness and number of case-contact interaction (for exposure); host immune response, age, sex, socioeconomic circumstances (for transition from exposure to infection); and HIV co-infection, genetic factors, environmental factors and other medical conditions (for transition from infection to disease). For a detailed and complete overview refer to the monograph on *Epidemiological Basis of TB Control*[8].

Predictability is the degree to which a correct prediction or forecast of a system's state can be made either qualitatively or quantitatively. The **positive predictive value** (PPV) or post-test probability of disease is the proportion of patients with positive test results who are correctly diagnosed. It is the most important measure of a diagnostic method as it reflects the probability that a positive test reflects the underlying condition being tested for. Note that the PPV is not intrinsic to the test—it depends also on the prevalence of the condition. PPV is directly proportional to the prevalence of the disease or condition. In other words the importance of any risk factor in public health is determined by both the strength of the association and the prevalence of the risk factor in the population.

Sensitivity and specificity are statistical measures of the performance of a binary classification test. **Sensitivity** measures the proportion of actual positives which are correctly identified as such (e.g. the percentage of sick people who are identified as having the condition). **Specificity** measures the proportion of negatives which are correctly identified (e.g. the percentage of healthy people who are identified as not having the condition). A theoretical, optimal prediction can achieve 100% sensitivity (i.e. predict all people from the sick group as sick) and 100% specificity (i.e. predict anyone from the healthy group as not being sick), but this is highly unlikely to occur.

Tuberculosis

Some symptoms and chest X-ray characteristics are sensitive and/or specific to TB. Yet, it is difficult to assign them a positive or negative predictive value. These predictive values depend largely on the prevalence of TB, the prevalence of HIV and NTM in a given population (i.e. TB suspects with symptoms of cough attending a chest clinic) or the subgroup in which the chest X-ray is used (i.e. HIV positive and/or sputum smear negative TB suspects). The predictive values also depend on the prevalence of other (pulmonary) diseases which present with similar symptoms or signs on chest X-rays. The prevalence of HIV is of particular importance, since HIV seropositive TB suspects with a low CD4 cell count (<200) present differently from HIV negative TB suspects.

As the presence or absence of such variables influences the predictive factors, it is important that they are taken into consideration when establishing the diagnosis of sputum smear negative TB. As such they are reflected in the TB Probability Score (TBS) that we introduce as a tool to help health staff improve the specificity of the diagnosis of sputum smear negative TB. In this chapter, an overview of demographics, symptoms and other diagnostic characteristics that are often seen in tuberculosis patients are described.

Patient Symptoms

Cough for at least two to three weeks is the most important symptom for TB disease it is the main characteristic on which a patient enters the screening process. Cough may not be a presenting symptom of TB in patients with HIV/AIDS, but if an HIV positive patient presents with cough, the patient will

6 American Thoracic Society, Centers for Disease Control. Diagnostic standards and classification of tuberculosis and other myco bacterial diseases (14th edition). Am Rev Respir Dis 1981;123:343-58.

7 Rieder HL. Opportunity for Exposure and Risk of Infection: The Fuel for the Tuberculosis Pandemic. (Editorial). Infection 1995;23:1-4.

8 Rieder HL. Epidemiologic Basis of Tuberculosis Control. International Union Against Tuberculosis and Lung Disease. First reprint, April 2003.

become a "TB suspect". The presence of symptoms - or a combination of them - such as fever, weight loss, night sweats and haemoptysis are associated with TB and increase the positive predictive value.

Other Risk Factors

To be in close contact with someone who has infectious TB is another important factor which increases the risk of having TB. In general, you must spend an extended period of time with someone with untreated, active TB to become infected yourself. You're more likely to catch the disease from an infectious family member, roommate, cell mate, friend or close (health) co-worker. Particularly at risk, are people who live/work in prisons or other congregate settings because the risk of the disease is higher due to overcrowding, poor ventilation and crowded/unsanitary conditions. Demographic factors which are related to TB include living in a country with a high TB incidence and working in the mining industry.

Having a disease which suppresses immunity, such as HIV/AIDS, diabetes, end-stage kidney disease, certain cancers or the lung disease silicosis, can reduce your body's ability to protect itself. Your risk of having TB is also higher if you take corticosteroids, certain arthritis medications, chemotherapy drugs or other drugs which suppress the immune system. Long-term drug or alcohol use also weakens the immune system and makes you more vulnerable to TB.

Tuberculosis Probability Score (TPS)

The Tuberculosis Probability Score has yet to be validated in a clinical trial, it is based on several observations in the literature[9], signs and radiological features[10] and expert clinical opinion. It is meant to help in determining whether or not it is probable, possible or unlikely that a patient has TB. Of course culturing *M.tuberculosis complex* remains the gold standard for the definite diagnosis of TB. It may be a helpful tool in decision making in daily practice in TB suspects coughing at least 2-3 weeks with AFB negative sputum. For positive signs and symptoms there is a certain score. The highest scores give an immediate indication to start anti-tuberculosis treatment. Patients with the other scores will need further follow-up.

Table 3: TB probability Scoring: Diagnostic Evaluation Among AFB Smear-Negative Patients with > 3 weeks cough.

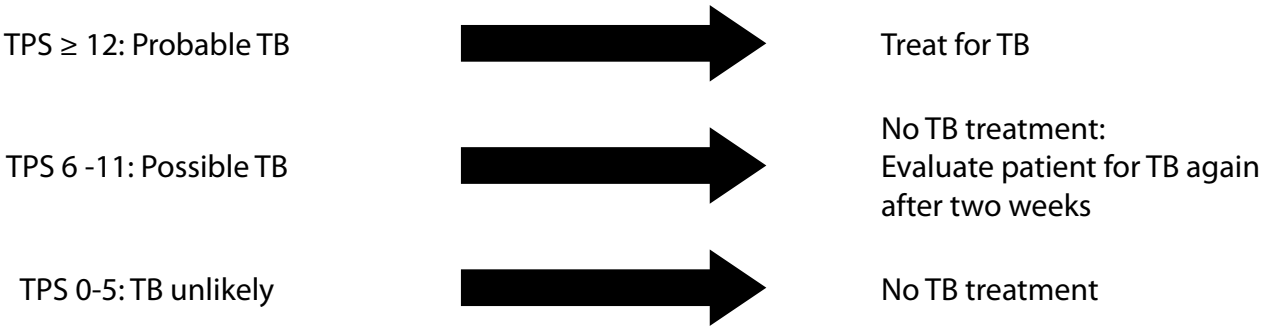
Tuberculosis Probability Score	2	5
Patient Symptoms:		
Fever > 4 weeks	+	
Lymph Node Enlargement	+	
Night Sweats	+	
Weight Loss > 5 kg / BMI < 18 kg/m²	+	
Other Risk Factors:		
Household/Close Contact TB Patient		+
HIV Positive		+
CD4 Cell Count	≥200	<200
Diabetes Mellitus	+	
Alcohol/Drug Abuse	+	
Chest X-ray:		
Parenchymal Lesions		
Consolidation	+	
Cavity Upper Lobe		+
Atelectasis *	+	
Nodular Lesions		
Miliary Pattern		+
Nodules 4-10 mm	+	
Tuberculoma	+	
Pleural Abnormalities		
Unilateral Pleural Fluid	+	
Central Structures		
Mediastinal or Hilar Lymph Nodes	+	
Other		
Primary Complex**		+
Fibrotic Lesions	+	

*Atelectasis = volume loss by fibrotic scarring, endobronchial obstruction or compression by enlarged lymph nodes.
**Primary complex = Ghon's focus and ipsilateral hilar lymphadenopathy (typical of primary tuberculosis in a child).

9 *A Simple Screening Tool for Active Tuberculosis in HIV-infected Adults Receiving Antiretroviral Treatment in Uganda*. Were, W. et al. The International Journal of Tuberculosis and Lung Disease, Volume 13, Number 1, January 2009 , pp. 47-53(7)
Identifying Pulmonary Tuberculosis in Patients With Negative Sputum Smear Results. Alka M. Kanaya, David V. Glidden, and Henry F. Chambers. CHEST August 2001 Vol. 120 No. 2 349-355
Evaluation of clinical parameters to predict Mycobacterium tuberculosis in inpatients, Juan P. Wisnivesky, Arch Intern Med 2000; 160;2471-2476

10 *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians*. Daley, Gotway, Jasmer.

Definitions: Tuberculosis Probability Score



The global DOTS strategy implies that diagnosis is based on sputum smear microscopy and restricts chest X-ray only for the diagnosis of "smear-negative TB cases". When establishing the diagnosis of smear-negative TB, the clinical officer often completely relies on the chest X-ray result, while the radiologist usually has no information about the characteristics of the patient (such as e.g. HIV status, or past TB history) which could help him/her to interpret the chest X-ray. This Tuberculosis Probability Score (TPS) merges information and could (ideally) be made together during clinical conferences to optimize a final result.

The purpose of the TPS is really to help the clinical officer responsible for starting TB treatment, in the absence of a culture result, decide whether a patient can be put on TB treatment right away or otherwise. The introduction of this TPS system, starting only those patients with a score "Possible TB" directly on treatment and starting a course of broad spectrum antibiotics on those suspects with a score "Possible TB" intends to improve the diagnostic performance of smear-negative TB.

Taking the different characteristics of the patient and the examination results into account, the clinical officer can score each smear–negative TB suspect. As the expected specificity of having TB with a TPS > 12 is higher than with a TPS <12, the latter group needs follow-up or can be sent home. As mentioned earlier, the diagnosis of "smear-negative TB" is, without a culture result, never certain; there will always be some patients with a TPS >12 that will not have TB, but this chance is much lower than patients with a TPS 6 –11.

For patients who need a follow-up, the risk is always that many of them do not return and the health services are subsequently unable to trace them. With the distinction between TPS 6-11 and TPS 0-5, the health staff can prioritize actions for those patients who really need follow-up.

References and Further Reading

Documents

World Health Organization (WHO). Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis among adults and adolescents.
http://whqlibdoc.who.int/hq/2007/WHO_HTM_TB_2007.379_eng.pdf

World Health Organization (WHO). Global Tuberculosis Control - Surveillance, Planning, Financing. WHO Report 2008. WHO/HTM/TB/2008.393.
http://www.who.int/tb/publications/global_report/2008/pdf/fullreport.pdf

World Health Organization (WHO). 2004. Interim policy on collaborative TB/HIV activities. WHO/HTM/TB/2004.330. http://whqlibdoc.who.int/hq/2004/WHO_HTM_TB_2004.330_eng.pdf

International Standards for Tuberculosis Care. Tuberculosis Coalition for Technical Assistance. 2006.
http://www.who.int/tb/publications/2006/istc_report.pdf

Scientific Papers

- van Cleeff MR, Kivihya-Ndugga LE, Meme H, Odhiambo JA, Klatser PR. The Role and Performance of Chest X-ray for the Diagnosis of Tuberculosis: A Cost-effectiveness Analysis in Nairobi, Kenya. BMC Infect Dis 2005 Dec 12;5:111
- Tattevin P, Casalino E, Fleury L, Egmann G, Ruel M, Bouvet E. The Validity of Medical History, Classic Symptoms and Chest Radiographs in Predicting Pulmonary Tuberculosis: Derivation of a Pulmonary Tuberculosis Prediction Model. Chest 1999;115(5):1248-53.
- Colebunders R, Bastian I. A Review of the Diagnosis and Treatment of Smear-Negative Pulmonary Tuberculosis. Int J Tuberc Lung Dis 2000;4(2):97-107.
- Campbell IA, Bah-Sow O. Pulmonary Tuberculosis: Diagnosis and Treatment. BMJ 2006 20;332(7551):1194-7.
- Andreu J, Cáceres J, Pallisa E, Martinez-Rodriguez M. Radiological Manifestations of Pulmonary Tuberculosis. Eur J Radiol 2004 Aug;51(2):139-49.
- Van Dyck P, Vanhoenacker FM, Van den Brande P, De Schepper AM. Imaging of Pulmonary Tuberculosis. Eur Radiol 2003 Aug;13(8):1771-85.
- Banda HT, Harries AD, Welby S, Boeree MJ, Wirima JJ, Subramanyam VR, Maher D, Nunn PA. Prevalence of Tuberculosis in TB Suspects with Short Duration of Cough. Trans R Soc Trop Med Hyg 1998;92(2):161-3.
- Harries AD, Banda HT, Boeree MJ, Welby S, Wirima JJ, Subramanyam VR, Maher D, Nunn P. Management of Pulmonary Tuberculosis Suspects with Negative Sputum Smears and Normal or Minimally Abnormal Chest Radiographs in Resource-Poor Settings. Int J Tuberc Lung Dis 1998;2(12):999-1004.
- Den Boon S, Bateman ED, Enarson DA, Borgdorff MW, Verver S, Lombard CJ, Irusen E, Beyers N, White NW. Development and Evaluation of a New Chest Radiograph Reading and Recording System for Epidemiological Surveys of Tuberculosis and Lung Disease. Int J Tuberc Lung Dis 2005; 9(10): 1088-96.
- Tostmann A, Kik SV, Kalisvaart NA, Sebek MM, Verver S, Boeree M, van Soolingen D. Tuberculosis transmission by patients with smear-negative pulmonary tuberculosis in a large cohort in the Netherlands. Clin Infect Dis 2008; 47: 1135-42.
- Behr MA, Warren SA, Salamon H, Hopewell PC, Ponce L, Daley CL, Small PM. Transmission of M tuberculosis from Patients Smear-Negative for Acid-fast Bacilli. Lancet 1999; 353: 444-9.
- Reid MJA, Shah NS. Approaches to Tuberculosis Screening and Diagnosis in People with HIV in Resource-Limited Settings. Lancet Infect Dis 2009; 9: 173–84.

– Goodman L.R., Felson's Principles of Chest Roentgenology, 2nd edition 1999
– Were W. Et al, A Simple Screening Tool for Active Tuberculosis in HIV - Infected Adults Receiving Antiretroviral Treatment in Uganda. IJTLD 2009;13(1):47-53