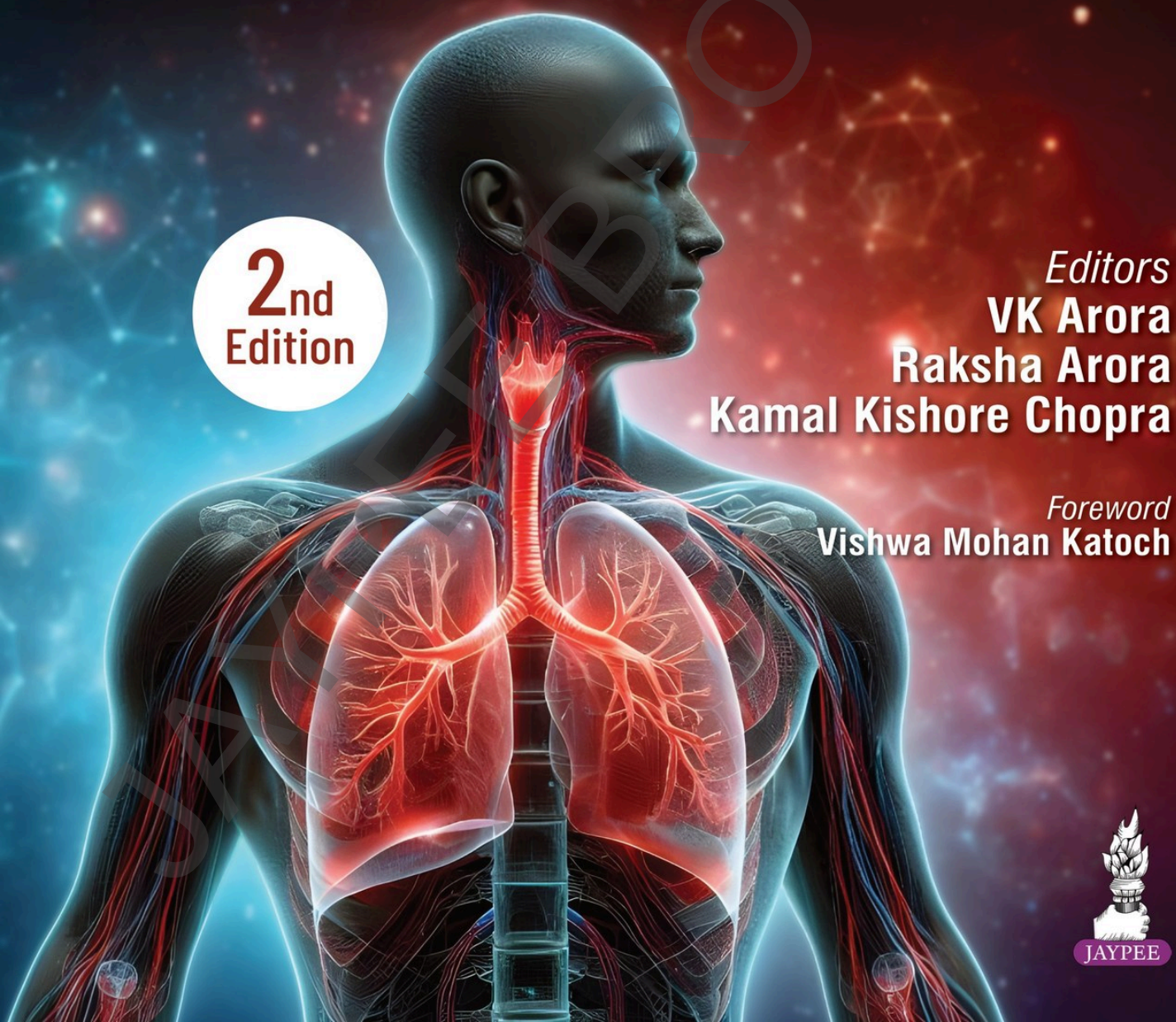
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The Tuberculosis Association of India

#आस TAAS

PRACTICAL APPROACH TO MANAGEMENT OF TUBERCULOSIS AND RESPIRATORY DISEASES



2nd Edition

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Foreword
Vishwa Mohan Katoch

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Contents

Section 1: Epidemiology of Tuberculosis

1. **Disease Prevalence Survey in India** 3
   Shanker Matta, Sanjay Rajpal, Shivani Pawar

2. **Drug Resistance in Tuberculosis** 6
   Zeeshan Sidiq, Kamal Kishore Chopra, Sanjay Rajpal

3. **Epidemiology and Diagnosis of Infections Due to Mycobacteria Other Than Tubercle Bacilli** 10
   Ajoy Kumar Verma, Gavish Kumar, Raj Narayan Yadav, Mohd Jaseem Khan, Ashish Ranjan

4. **Scientific Advances in Tuberculosis and Equitable Distribution Challenges** 20
   Radha P Munje, Gyanshankar P Mishra

5. **Clinical Epidemiology of Pulmonary and Extrapulmonary Tuberculosis in Adults—A Clinician's Perspective** 40
   Nikhil Sarangdhar

6. **Timetable and Classification of Tuberculosis** 57
   Anil Kumar Jain, Kanishk Sinha

7. **Drug-Resistant Tuberculosis in Children: The Indian Perspective** 64
   Ankita Anand

8. **Merits of Chest X-Ray and Sputum Examination at Tertiary/Peripheral Centers for the Diagnosis of Pulmonary Tuberculosis** 69
   VK Arora, Anand Jaiswal

9. **Changing Trends in Chronic Obstructive Pulmonary Disease and Management** 77
   PT James, Durga Balagopalan, Harsha PV

Section 2: Clinical Presentations of Pulmonary and Extrapulmonary Tuberculosis

10. **Critically Ill Tuberculosis Patient** 87
    Gousmahammad Myageri, Ajith Kumar AK, Pooja R Murthy

11. **Cryptogenic Tuberculosis** 99
    OP Sharma, Jatin Ahuja

JAYPEE BROTHERS

12. Extrapulmonary Tuberculosis Diagnosis and Treatment 102
Priya B, Rajeswari Ramachandran, Banurekha Velayutham, G Narendran, Rani Balasubramanian, AR Adhilakshmi, Malaisamy Muniyandi

13. Nontuberculous Mycobacteria Clinical Issues 113
VK Arora, SK Agarwal

14. Ocular Tuberculosis 120
Amod Gupta, Reema Bansal

15. Pregnancy and Tuberculosis 124
Namita Chopra

16. Neutrophilic Asthma: An Emerging Corticosteroid-Resistant Phenotype in Adults 132
Sonisha Gupta

17. Clinical Issues in Tuberculosis—Pathologist Point of View 145
VK Arora, Kumud Gupta, Amita Saigal

18. Hypersensitivity Reactions to Antitubercular Agents: Recognition, Pathophysiology, and Modern Management Strategies 154
Monika Rajpal, Zeeshan Sidiq, Sanjay Rajpal

19. Genetic Mapping of Tubercular Bacillus: Clinical Issues of the Future 163
VK Arora, Devendra Bansal, Devanshi Bansal, Rakesh Sehgal

20. Post-tuberculosis Lung Disease 171
VK Arora, Srikanti Raghu, Bavithra B, Jaya Suriya S

21. Hemoptysis in Tuberculosis 180
VK Arora, Vivek Nangia

Section 3: Tuberculosis Diagnosis

22. Practical Approach to Diagnose a Presumptive Tuberculosis Case 191
Kaushal Kumar Dwivedi, Kamal Kishore Chopra

23. New Diagnostic Techniques for Tuberculosis and Their Clinical Relevance 197
Ankita Anand, Sanjay Rajpal

24. Diagnosis and Management of Nontuberculous Mycobacterial Diseases 203
Ashish Ranjan, Ajoy Kumar Verma, Rajnish Gupta, Raj Narayan Yadav

25. Miliary Tuberculosis—Diagnostic Difficulties 214
Surendra Kumar Sharma, Alladi Mohan, Vishwanath Upadhyay

JAYPEE BROTHERS

26. Next-Generation Sequencing for Diagnosis of Tuberculosis **218**
Manpreet Bhalla, Raj Narayan Yadav

27. Role of Molecular Diagnostics Tools in Accurate Diagnosis of Tuberculosis **225**
DS Chauhan

28. Acid-Fast Bacilli Culture and Susceptibility Testing: A Clinician Point of View **231**
Ajoy Kumar Verma, Mohd Jaseem Khan, Gavish Kumar, Raj Narayan Yadav, Ashish Ranjan

29. Role of Lung Ultrasound in Respiratory Diseases **245**
Surya Kant, Ankit Kumar, Shubham Shukla

Section 4: Treatment

30. Approach to Management of Tuberculosis Infection and Subclinical Infection **253**
Vinod Kumar Viswanathan, VK Arora

31. Antitubercular Therapy-Induced Liver Injury: An Update **257**
Ashish Ranjan, Rajnish Gupta, Upasna Agarwal

32. Current Issues in the Diagnosis and Treatment of Multidrug-Resistant Tuberculosis **264**
Rajendra Prasad, Harshita Rani, Rishabh Kacker, Rachit Sharma, Nikhil Gupta

33. Latent Tuberculosis Infection Dormancy and Treatment **269**
Malaisamy Muniyandi, Priya B, Rani Balasubramanian, Banurekha Velayutham, AR Adhilakshmi, Bharathidasan Palani, Rajeswari Ramachandran

34. Treatment of Tuberculosis in Special Situations **278**
Rajendra Prasad, Harshita Rani, Rishabh Kacker, Nikhil Gupta

35. Neurotuberculosis: Clinical Presentation and Current Management **287**
VK Arora, FU Ahmad, A Gupta, VS Mehta

36. BPaLM Regimen for Treatment of Drug-Resistant Tuberculosis **300**
Man Mohan Puri, Lokender Kumar, Prabhpreet Sethi, Neeraj Mumwalia

37. Pharmacotherapeutics of Antituberculous Drugs **312**
Ankita Anand

38. New and Future Antituberculosis Drugs **317**
Kamal Kishore Chopra, Kaushal Kumar Dwivedi

JAYPEE BROTHERS

Section 5: Tuberculosis with Associated Disease

39. Clinical Issues in Tuberculous Meningitis 331
Rajeswari Ramachandran, Priya B, Rani Balasubramanian, Bharathidasan Palani, Malaisamy Muniyandi

40. Management of Critical Situations in Pulmonary Tuberculosis: A Practical Case-Based Approach 349
Shivani Pawar, Sanjay Rajpal, Shanker Matta

41. Psychological Comorbidities in Tuberculosis and Respiratory Diseases: A Case-Based Approach 353
Kranti Garg, Vishal Chopra

42. Tuberculosis and Nontuberculous Pulmonary Diseases in HIV-Infected Children 357
Mamatha Murad Lala

43. Tuberculosis in People Living with Human Immunodeficiency Virus 367
Upasna Agarwal, Poulomi Chatterjee

44. Tuberculosis of the Skeletal System: Case-Based Approach 381
Sumit Sural

Section 6: Tuberculosis Control

45. Clinical Issues in Implementation of Directly Observed Treatment, Short-Course 389
VK Arora, SK Munjal

46. Active and Intensified Case Finding in Tuberculosis 395
Nikhil Sarangdhar

47. Artificial Intelligence for Tuberculosis Control: Practical Applications in Diagnosis, Treatment, and Surveillance 406
Sanjay Rajpal, Ankita Anand

48. Statistical Tools, Artificial Intelligence, and Operational Research—Way Forward 410
VK Arora, Nishi Aggarwal, Sanjay Rajpal

49. Healing Beyond Hospitals: Medical Colleges as Pillars of Tuberculosis Elimination 417
Bineeta Kashyap, Aaradhana, Nilesh Saini

50. Engineering and Other Technological Approaches for Prevention of Nosocomial Transmission of Tuberculosis 422
Kiran Katoch

JAYPEE BROTHERS

51. Stigma and Human Rights in Tuberculosis 427
Kamal Kishore Chopra, Sanjay Rajpal, Shanker Matta, Shivani Pawar

52. The Way Forward in Tuberculosis Genomics 431
Chaitali Nikam

53. Role of Medical Colleges in Revised National Tuberculosis Control Program 436
VK Arora, Rajesh Solanki

54. The Role of Nutrition in Tuberculosis 443
Harleen Grewal, Henrik Friis, VK Arora, Nishi Aggarwal

55. Vaccination in Tuberculosis, Operational Research, and Way Forward 450
Thomas Vadakkan Devassy

56. Tobacco and Its Impact on Lung Health: Indian Guidelines and Way Forward 453
Sonu Goel, Chirag Goel, Diksha Walia

57. Inherited Determinants of Tuberculosis Risk, Severity, and Treatment Response 461
Sanjay Rajpal, Zeeshan Sidiq, Monika Rajpal

58. Compliance in Tuberculosis: Integrating Direct Observation and Digital Technologies 468
Neeta Singla

59. Newer Radiological Modalities in Management of Tuberculosis and Respiratory Diseases 472
Harsh Mahajan, Pooja Jain

Annexure I: Programmatic Management of Drug-Resistant Tuberculosis Guidelines 484

Annexure II: Tuberculosis Preventive Treatment Guidelines in India 487

Annexure III: BPaLM Guidelines in India 489

Annexure IV: Four-Months Drug-Sensitive Tuberculosis Regimen (as per Recent WHO Recommendations) 491

Index 493

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8

Merits of Chest X-Ray and Sputum Examination at Tertiary/Peripheral Centers for the Diagnosis of Pulmonary Tuberculosis

VK Arora, Anand Jaiswal

ABSTRACT

Chest X-ray (CXR) and sputum microscopy remain foundational, albeit with defined merits and limitations. CXR is an irreplaceable screening and triage tool due to its speed, wide availability, and ability to detect suggestive parenchymal abnormalities, cavities, and effusions, even in smear-negative cases. Its major merit lies in its public health utility for mass screening in high-prevalence settings. Sputum smear microscopy, the century-old cornerstone, offers direct, low-cost visualization of acid-fast bacilli (AFB), providing rapid, point-of-care infectiousness confirmation critical for initiating treatment and interrupting transmission. However, both techniques suffer from poor specificity (CXR findings overlap with other diseases) and critically low sensitivity, with microscopy missing up to 50% of cases and being unable to detect drug resistance, representing a significant diagnostic gap.

INTRODUCTION

Newer developments are revolutionizing this landscape by augmenting or bypassing these traditional tools. Artificial intelligence (AI)-assisted chest X-ray (CXR) interpretation, using deep learning algorithms, now enhances accuracy and consistency, serving as a powerful computer-aided triage tool in resource-limited settings. The most transformative developments, however, are molecular. Automated, cartridge-based nucleic acid amplification tests (NAATs), such as the World Health Organization (WHO)-recommended GeneXpert MTB/RIF Ultra, have dramatically increased sensitivity, especially in paucibacillary disease, and simultaneously detect rifampicin resistance within hours. Next-generation sequencing (NGS) directly from sputum is emerging to provide comprehensive drug resistance profiles, moving diagnostics toward precision medicine and outbreak investigation, rendering microscopy increasingly adjunctive.

Chest X-rays and sputum smear examination for acid-fast bacilli (AFB) are two important tools used for the diagnosis of pulmonary tuberculosis (TB). Over the past several decades, CXRs have received a rather undue status, surpassing sputum microscopy. With reports from the radiology department labeling the "images" as TB, the process of making a differential diagnosis and undertaking further diagnostic work-up is rather cut short by the physicians. It is but common, though late, to experience errors in the diagnosis. It has been well-documented by scientific studies that no radiological picture is diagnostic of TB.

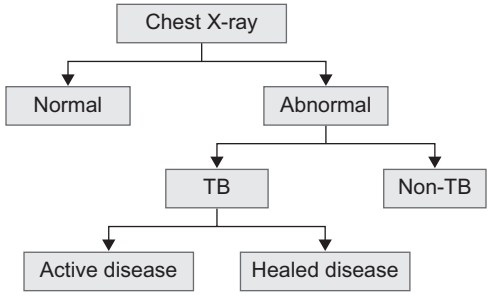
The present chapter shall elaborate on the technical (scientific database) as well as operational issues comparing CXRs and sputum microscopy (AFB smear) for the diagnosis of pulmonary TB at a tertiary-level institute and peripheral centers.

CHEST X-RAY

Chest X-ray—Observer Error

Whenever one sees an X-ray of the chest, a diagnostic algorithm is followed while interpreting the film **(Flowchart 1)**.

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FLOWCHART 1: Diagnostic algorithm chest X-ray.
(TB: tuberculosis)

At each of these bifurcations, there are observer errors which are committed.

In one of the earlier studies, Birkelo et al. found that five experts, while reading X-ray films of TB patients, missed 25% of the positive films (each expert underread the film). When the films were reread 3 months later, each expert changed their own opinion in one fifth of cases (20%). Thus, the error in diagnosis is interobserver as well as intraobserver.

Garland and Yerushalmy confirmed these findings in subsequent studies.

Chest X-ray—Observer Error and Experience

A study conducted by the Research Institute of Tuberculosis, Tokyo, evaluated the role of experience in reporting of CXR for TB diagnosis (either in number of years or number of films they were reporting annually).

Fifty X-ray films (70 mm) were selected—25 from confirmed TB patients or those with other chest diseases, 5 from persons with healed TB, and 20 from persons without any clinical abnormality.

A group of 192 physicians classified in terms of experience **(Table 1)** reported these films.

Thus, significant observer errors of underdiagnosis (21.8%) and overdiagnosis (19.5%) were committed even by the most experienced. The investigators estimated that in mass X-ray examination probably one fifth of cases with active TB were being actually missed.

Chest X-ray—Observer Error—Clinical Implications

In a study by the International Union Against Tuberculosis (IUAT), the observer error and its clinical implications were evaluated.

A sample of 1,100 X-ray films (200 of infectious TB cases, 400 with previous TB disease, 300 from normal persons, 100 from patients confirmed to have non-TB disease, and 100 from persons having minimal findings not needing follow-up) were asked to be reported by 90 doctors (both expert radiologists and physicians) across nine countries. They were asked questions as listed in **Table 2**, and their responses (Yes/No) were indexed from 0 to 100 ("0" means total agreement, and "100" means total disagreement).

It is clear that significant disagreement persists even among these international experts to most basic question like cavitation present or not (28 index score on a scale of 0-100) which is crucial for taking decision to start antitubercular treatment (ATT). Further, it was estimated that:

TABLE 1: Experience and observer error X-ray.

Experience	No. of Readers	Underreading* (%)	Overreading† (%)
1–4 years	37	28.0	18
5–9 years	37	19.2	19
>10 years	88	17.6	17
No. of Films Read Annually			
1–5,000 films annually	43	22.4	17.5
5,000–20,000 films annually	48	24.0	18
>20,000 films annually	41	15.2	15.5
Average of all	192	21.8	19.5

*Underreading—When the reader failed to request further investigation (missed TB diagnosis).
†Overreading—Request for further examination made in a person with a normal chest X-ray (wrongly diagnosed TB).
(TB: tuberculosis)

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TABLE 2: IUAT study on X-ray classification: Indices of disagreement on questions.

Question	Index Score
Is the film abnormal	34
Noncalcified abnormality, probably TB	37
Cavity present	28
Abnormality—probably not TB	45
Need for medical action	31
Abnormality in lymph nodes	60

(IUAT: International Union Against Tuberculosis; TB: tuberculosis)

- Five percent of smear-positive patients were reported as having normal X-rays, 17% as having probably non-TB abnormality, and 24% as not in need of clinical action.
- Thus, if treatment is restricted to patients in whom 50% or more of readers report cavitation (active TB), only one third of those having positive sputum would be treated.

It was concluded that radiological criteria alone can not be a confirmatory evidence of pulmonary TB.

Chest X-ray Observer Error—Follow-up Tool

Due to observer error, the CXR cannot be used as a follow-up tool.

In a study done by Garland, 4500 TB patients, each having two serial films (one at the beginning of the TB treatment and another at the end), were evaluated by expert radiologists and chest specialists. They were asked to report improvement, deterioration, or no change. It was noted that inter- and intraobserver errors were significantly high (29–30 and 19–24%, respectively).

In another study among 112 patients who had bacteriological quiescent disease (followed up to 4 years), 35 (31%) were classified as deteriorating on CXRs and thus in need of TB treatment.

Thus, radiography alone cannot be used to adjudge the response to treatment.

Chest X-ray—Observer Error and Human Immunodeficiency Virus Coinfection

Coinfection of human immunodeficiency virus (HIV) and TB further diminishes the reliability of CXR in the diagnosis as atypical presentations occur, e.g., lower lung infiltrates, absence of cavities, and normal or minimally abnormal CXRs. Harries et al. observed that 66 bacteriologically (smear or culture-positive) confirmed cases would have been missed out of 402 adults (HIV-infected) seeking care for symptoms of pulmonary TB. Their X-rays were reported as inconsistent with TB.

Chest X-ray—Operational Constraints

At peripheral units in remote and difficult terrains of the northeast, deserts, and hilly regions of India, there are operational shortcomings in radiology. These units require power, trained staff, maintenance, costly consumables and processors, spare parts, X-ray films, etc., and thus become a difficult proposition in these areas.

As most of the X-ray units are located at district level, the patients shall have to travel at least twice from villages and wait for 2–3 days for the report. This adds to the cost and time factor in the diagnosis.

It is, thus, clear that treating TB just on the basis of "Shadows" does wrong to both individuals as well as to the program. To individuals, we give wrong treatment. As a result, his disease remains either undiagnosed or progresses to end stage. This leads to significant respiratory morbidity, from which he becomes progressively disabled (i.e., lung cancer, bronchiectasis becomes inoperable, fibrosis progresses to end-stage lung disease). The increased mortality is a logical consequence of this misdiagnosis. To the program—it impacts by channeling the resources (drugs, funds, and manpower) to those who either never had TB or are suffering from sequelae of it. Incorrect diagnosis also leads to increased default among this group.

CASE STUDIES

The following five case studies are presented where radiological diagnosis and treatment lead to significant error.

Case 1

A 45-year-old female presented with cough and expectoration for 3 months. Her initial X-ray is as per **Figure 1**. Blood counts were normal. The erythrocyte sedimentation rate (ESR) was 60 mm in the first hour.

- Physician diagnosis—Pneumonia and lung abscess—TB
- Treatment—ATT started (took for 2 months)
- Final diagnosis—Cavitating squamous cell carcinoma of the lung

Comments

Sputum smears for AFB were not asked for. Mere cavitation and a raised ESR are not a sufficient proof for the diagnosis of TB.

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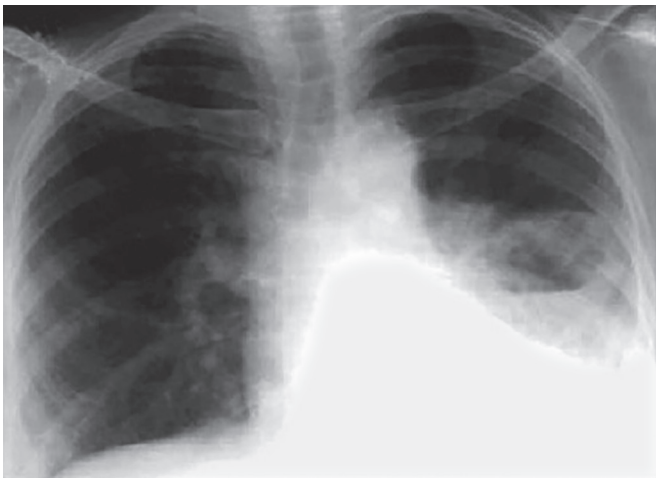


FIG. 1: Chest X-ray showing cavitary lesion initially diagnosed as pneumonia/lung abscess–tuberculosis; later confirmed as cavitating squamous cell carcinoma of the lung.

Case 2

A 52-year-old male presented with a history of cough with mucoid sputum and significant weight loss for 5 months. His X-ray is shown in **Figure 2**.

Blood counts were normal. He was not diabetic; the Mantoux test showed 15 mm of induration. Sputum smears for AFB were negative.

- Physician's diagnosis—TB (active cavitary disease)
- Treatment—ATT started (took for 3 months)

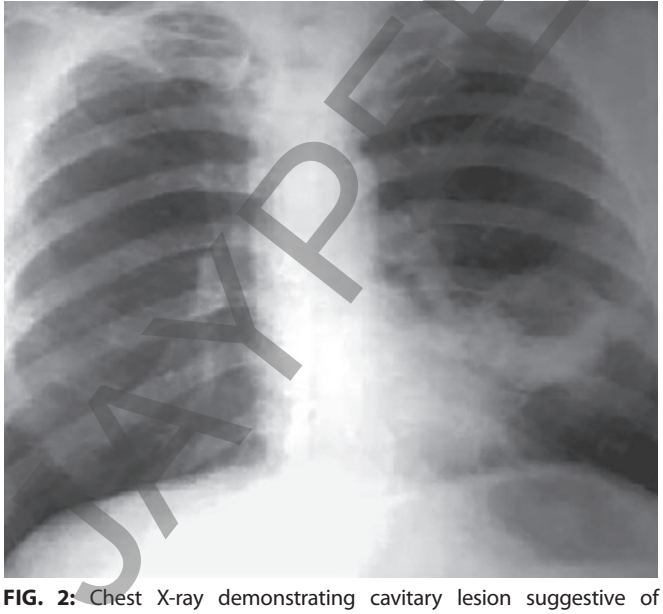


FIG. 2: Chest X-ray demonstrating cavitary lesion suggestive of pulmonary tuberculosis in a patient with chronic cough and weight loss.

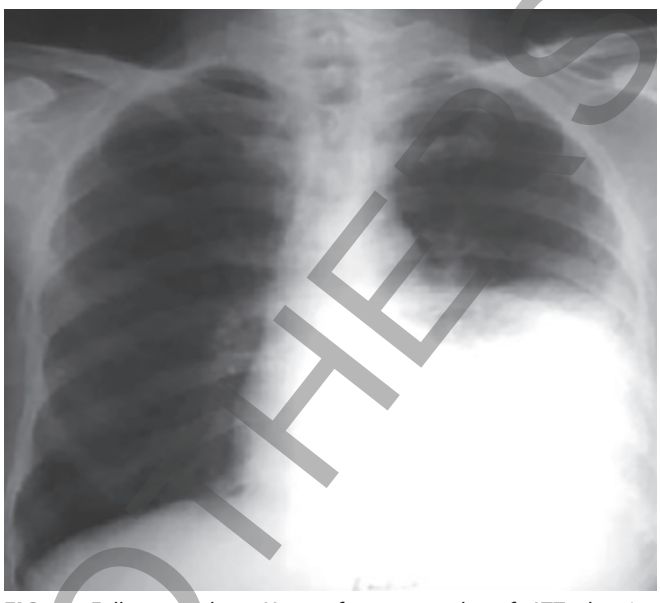


FIG. 3: Follow-up chest X-ray after 3 months of ATT showing persistence/progression of lesion; later diagnosed as squamous cell carcinoma of the lung.
(ATT: antitubercular treatment)

- Repeat X-ray at the end of the third month is shown in **Figure 3**.
- Final diagnosis—Squamous cell lung carcinoma

Comments

- Sputum smears for AFB must be done even if X-ray shows features suggestive of TB (e.g., cavitation).
- Among smokers, cavitary squamous cell carcinoma is quite often misdiagnosed as TB.
- A cavity of 2 cm in size is said to harbor 10^8 bacilli, and the chance of finding AFB in smears is more than 96%.
- Under such circumstances, particularly when sputum examinations remain persistently negative, clinicians should maintain a high index of suspicion for an alternative diagnosis.

Case 3

A 22-year-old female patient presented with worsening cough and expectoration over the past 2 weeks. She was a known case of bronchial asthma for which off-and-on oral and inhaled steroids along with bronchodilators were prescribed.

The expectoration was purulent, and she was febrile.

- *Investigations*: Hemoglobin (Hb) 9.8 g/dL, total leukocyte count (TLC) 12,900/mm^3, and differential

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leukocyte count (DLC) showing polymorphs 48%, lymphocytes 32%, and eosinophils 10%
Her X-ray is shown in **Figure 4**.

- *Physician's diagnosis*: Asthma with bilateral infiltrates and cavitation—TB
- *Treatment*: ATT and asthma management
- *Course*: The patient showed further deterioration over 2 months.
- *Final diagnosis*: Allergic bronchopulmonary aspergillosis (ABPA)

Comments

While interpreting X-ray films, physicians must ask for pertinent clinical history. This case had asthma and eosinophilia. Sputum smears for AFB were negative. Serological testing for Aspergillus was positive. In patients with allergic bronchopulmonary aspergillosis (ABPA), persistent and transient (fleeting) radiographic opacities often lead to diagnostic confusion, resulting in some patients being incorrectly labeled as having multidrug-resistant tuberculosis (MDR-TB).

Further Course

Antitubercular treatment was stopped, and she was started on steroids. The CXR cleared in 3 weeks **(Fig. 5)**.

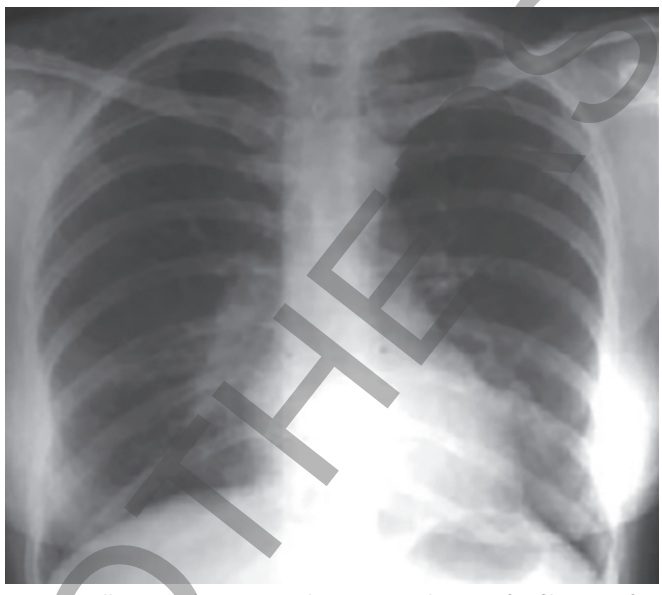


FIG. 5: Follow-up chest X-ray showing resolution of infiltrates after steroid therapy in allergic bronchopulmonary aspergillosis (ABPA).

Case 4

A 38-year-old male patient presented with a history of weight loss, cough with mucoid expectoration, and hemoptysis for 2 years duration.

The patient had a history of receiving multiple courses of antitubercular treatment (ATT). His erythrocyte sedimentation rate (ESR) was 30 mm in the first hour, while the complete blood count (CBC) was within normal limits.
His X-ray is shown in **Figure 6**.

- *Physician's diagnosis*: Drug-resistant TB
- *Treatment*: Second-line drugs prescribed
- *Final diagnosis*: Silicosis

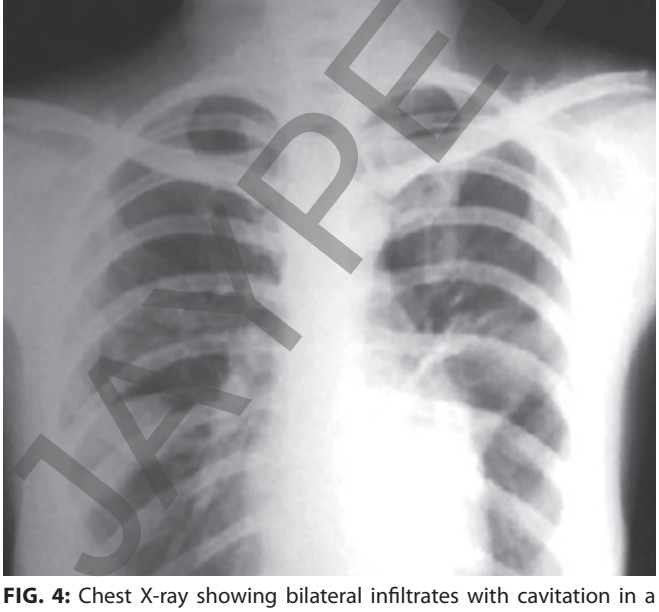


FIG. 4: Chest X-ray showing bilateral infiltrates with cavitation in a patient with bronchial asthma; initially misdiagnosed as tuberculosis.

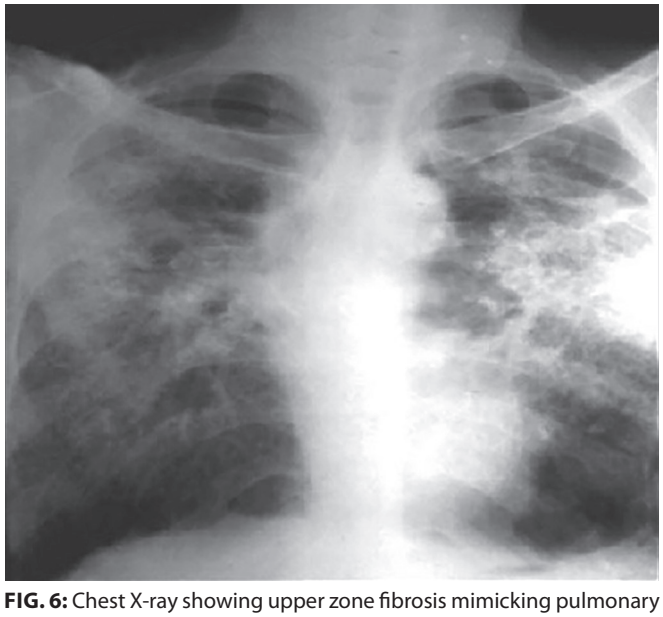


FIG. 6: Chest X-ray showing upper zone fibrosis mimicking pulmonary tuberculosis; final diagnosis silicosis.

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Comments

- Silica causes progressive fibrosis in upper zones and mimics TB on X-ray films.
- Sputum examination is persistently negative in fibrosis due to silica.
- These patients always have a history of working in stone crushing units or in silica mines.
- Though silicosis is a predisposing risk factor for developing TB, quite often these patients are put on ATT without confirmation of active disease.
- The persistent radiological shadows (progressive massive fibrosis) often mislead physicians.

Case 5

A 45-year-old patient presented with respiratory failure. The patient has been on ATT for 2 years. She was diagnosed as having pulmonary TB after CXR showed bilateral infiltrates **(Fig. 7)**. Sputum examination was done repeatedly and was negative for AFB.

- Physician's diagnosis: MDR-TB
- Final diagnosis: Interstitial lung disease (ILD) with honeycomb lung (end-stage lung disease—**Fig. 8**)

Comments

- Interstitial lung disease is another group of disorders that is misdiagnosed and treated as TB.

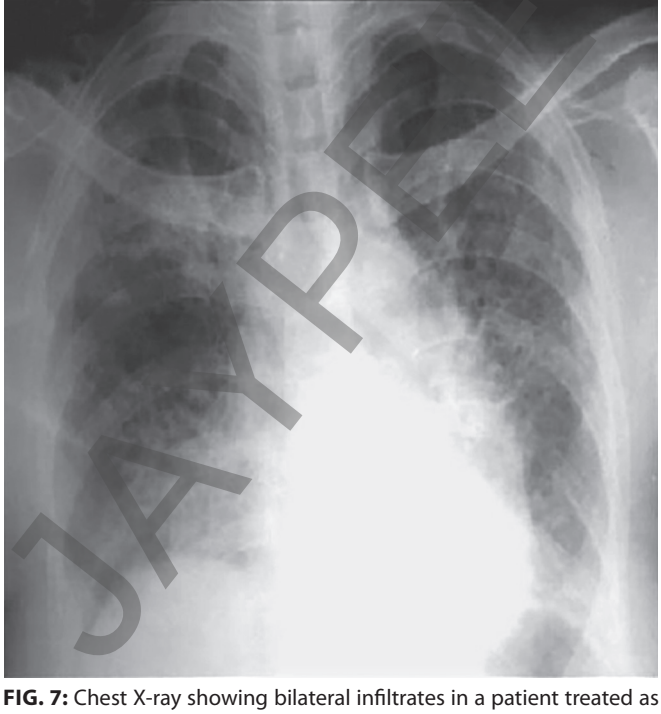


FIG. 7: Chest X-ray showing bilateral infiltrates in a patient treated as pulmonary tuberculosis.

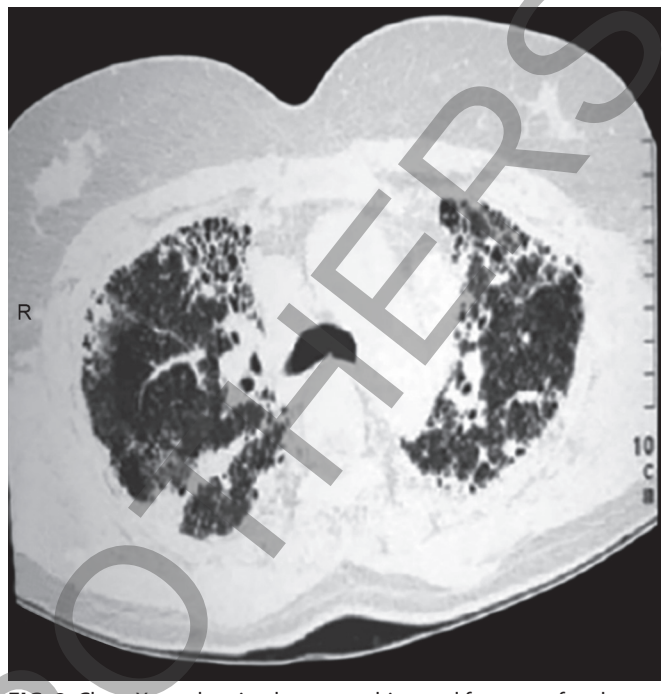


FIG. 8: Chest X-ray showing honeycombing and features of end-stage interstitial lung disease (ILD), misdiagnosed as multidrug-resistant tuberculosis (MDR-TB).

- Clinical history (progressive dyspnea and dry cough) and examination (clubbing, end-inspiratory crackles) are helpful in diagnosis.
- In the presence of clinicoradiological deterioration, a persistent negative sputum smear for AFB should alert the physician for an alternative diagnosis.
- Delay in diagnosis leads to end-stage lung disease.
- A course of steroids would have prevented rapid deterioration to respiratory failure.

SPUTUM MICROSCOPY FOR ACID-FAST BACILLI

Sputum microscopy is a reliable diagnostic tool for pulmonary TB. It not only aids the diagnosis but also serves as a useful monitoring tool. The reliability of sputum microscopy is dependent on the following:

1. Probability of finding AFB in smears
2. Probability of false-positive or false-negative results
3. Frequency of agreement between microscopists

1. In a study by David et al. (involving eight laboratories), it was shown that the number of bacilli per mL of sputum determines the probability of finding or not finding AFB on smears. With an estimated 50,000 bacilli per mL of sputum, the probability of finding a positive result is as high as 90%. A cavity of 2 cm in size is known to harbor as high as 10^8 bacilli.

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The study was carried out at the National TB Institute (NTI), India, to determine the additional case yield by examining up to eight consecutive sputum smears in patients with pulmonary TB. The first two samples were found to provide a diagnostic yield of 85% to 89% positivity. Rest six samples add little to the total diagnostic percentage. If three properly collected sputum samples were examined, as per guidelines (grading system), the percentage of sputum-positive patients would increase.

After adopting the DOTS (directly observed treatment, short-course) strategy, the new smear-positive detection has increased from 25% under the National TB Programme (1962) to 59% in 2002 under the Revised National TB Control Programme (RNTCP). The yield has further improved to 69% in 2003 (TB India 2004, DGHS).

It is thus prudent to ask for sputum tests for diagnosis.

2. It is wise to understand the limitations of the test and the consequences. The result of sputum smears (AFB) may not be positive in all patients. Thus, there is a need for X-rays and/or sputum cultures to increase the sensitivity. False-positive smears have been reported due to acid-fast particles and other microorganisms (waxes, precipitates of stain, nocardia, environmental mycobacteria, spores of *Bacillus subtilis*, fibers and pollens, food particles, yeast, and artifacts such as scratches on slides). Occasionally, AFB may be transferred from one slide to another during staining, by wire loops, glass rods, oil dropper, or microscope lens. If proper care is taken, most of the causes of false-positive smears can be avoided. The consequences of the results, both to individuals and to the national programs, are well-understood.

   False-negative smear results are more commonly attributed to inadequate sputum collection, failure to select suitable sputum particles for making smears, poor smear preparation, and inadequate examination of the smears. The laboratory technicians must be properly trained to develop a methodology. Strict supervision and monitoring go a long way in delivering desired results.

3. There appears to be better agreement between microscopists in reporting positive (AFB) smear and negative smear results (92.8 and 93% agreement, respectively). The disagreement was mostly in reporting scanty bacilli in smears. Further, it is to be noted that if a simple training is imparted to the health workers for 2 to 4 weeks, their results can match closely with those of experts.

Case 6

A 45-year-old female presented with fever and cough for 3 months. CXRs showed right lower zone pneumonia. The patient was given a 10-day course of antibiotics with no relief.

The patient was referred to the respiratory institute. Routine blood–urine examination along with results of blood sugar, liver function test (LFT), and kidney function test (KFT) were in normal range. Sputum smears were negative for AFB. HIV serotesting was also negative. X-ray is shown in **Figure 9**. A percutaneous ultrasound-guided needle aspiration showed smear positivity for AFB. ATT was started. The patient showed further deterioration **(Fig. 10)**. A repeat procedure (needle aspiration) revealed that acid-fast structures were filamentous, beaded, and weakly acid-fast positive, suggestive of *Nocardia* infection. The culture confirmed the organism. The patient responded to cotrimoxazole and minocycline.

Comments

- Chronic necrotizing infection due to anaerobic organisms, other bacteria (*Actinomyces* and *Nocardia*), or fungal etiology (invasive aspergillosis) occurs frequently in elderly or immunocompromised hosts (diabetic, HIV, renal transplants, on drugs like steroids).
- Quite often, radiological pictures suggest TB, but persistent negative results for AFB prompt further investigative work-up.
- *Nocardia* is typically seen as beaded, acid-fast filament.
- However, broken filament fragments can appear as acid-fast rods and mimic *Mycobacterium tuberculosis* on smears.



FIG. 9: Chest X-ray showing right lower zone consolidation; initial suspicion of tuberculosis with negative sputum smears.

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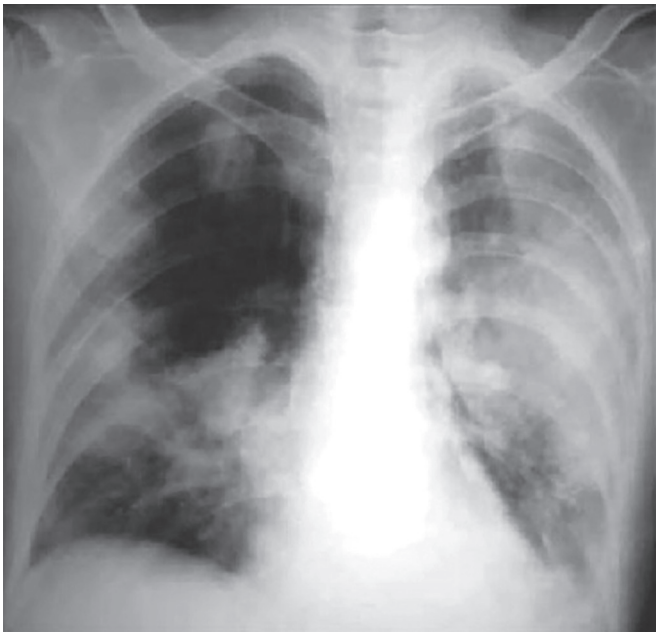


FIG. 10: Follow-up imaging showing progression of lesion; final diagnosis of nocardiosis confirmed on culture.

COMPARING X-RAY AND SPUTUM MICROSCOPY (ACID-FAST BACILLI) WITH CULTURE

In a landmark study by NTI (India), the two diagnostic tools were compared with the gold standard—culture positivity for *M. tuberculosis*.

It was found that 20 of 162 (12%) culture-positive TB patients would have been missed because they were classified on X-ray as normal or having non-TB disease. On the other hand, among 227 patients classified radiologically as TB, 37% were not confirmed by culture. Of the 145 patients positive by smear for AFB, 130 (90%) were confirmed by culture. However, 20% of culture-positive patients may be missed on smear results. In this subgroup, one has to rely on X-rays for the diagnosis, as a culture facility is not available at most of the peripheral/district centers. Moreover, culture causes an inadvertent delay of 6–8 weeks for the diagnosis.

Scenario at Tertiary Level Institute

Tertiary level institutes usually deal with serious cases, those having diagnostic dilemmas, complications, or not responding. At these centers, there is a need for facilities such as chest radiography, mycobacterial culture (using both conventional and rapid techniques), and specialized diagnostic procedures such as bronchoscopy, computed tomography (CT), and ultrasonography to establish a tissue diagnosis or obtain bacteriological confirmation. At times, an alternative diagnosis may emerge. The need for therapeutic intervention such as intercostal tube drainage and surgical considerations may mandate early need for imaging techniques.

On a program basis, if one has to select an ideal diagnostic tool, then it has to qualify in the following respect: It should be simple, easy to perform and read, quick, and require minimal equipment and maintenance. It should be scientifically correct, confirmatory, and overall cheap. If reviewed, sputum microscopy scores on all fronts over and above CXR as a diagnostic and monitoring tool.

As the national programs reach the remote areas of India, it is evident that sputum microscopy is a more sustainable and viable tool for TB diagnosis and follow-up. If two to three smears are correctly performed on a properly collected sputum sample, about 50–70% of patients with active pulmonary TB will have positive smears.

MESSAGES

- Sputum microscopy is a superior diagnostic tool in TB because it is a scientifically correct, confirmatory, and operationally viable method in diagnosing majority of TB cases.
- Chest X-ray can be the initial modality of investigation under emergencies such as hemoptysis, pneumothorax, or pyopneumothorax or in a moribund patient.
- Chest X-ray cannot replace the importance of sputum microscopy; it can be a useful adjunct in the diagnosis.

SUGGESTED READINGS

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VK Arora is a distinguished pulmonologist and a leading authority in the field of tuberculosis (TB) and respiratory diseases in India. He has made significant contributions to TB control, research, and clinical practice over several decades. Dr Arora served as the Director of the National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, and also held the position of Additional Director General of Health Services in the Government of India. He has been actively involved in national and international efforts for TB control and has contributed extensively to policy development, research, and capacity building in TB management. Dr Arora has also served as Chairman of the Tuberculosis Association of India and has played a pivotal role in strengthening advocacy, awareness, and community engagement for TB elimination in the country. A prolific academician and editor, Dr Arora has authored and edited several books, scientific papers, and guidelines on TB and respiratory medicine. His work focuses particularly on practical approaches to TB diagnosis, treatment, program implementation, and emerging advances in the field. Through his academic leadership and editorial contributions, he continues to guide clinicians, researchers, and public health professionals in improving the management and control of TB.



Raksha Arora is a distinguished academician, clinician, and health expert with an extensive experience in the field of gynecology and obstetrics. With decades of dedicated service in medical education, patient care, and control initiatives, she has made significant contributions to strengthening evidence-based clinical practices and programmatic management of issues in the field of maternal health in India. She has been Director–Professor in the Gynecology Department of Maulana Azad Medical College, New Delhi. She is a WHO Fellow in Gynecologic Oncology from London. She has been actively involved in training healthcare professionals, mentoring postgraduate students, and supporting implementation of national guidelines. Her work reflects a strong commitment to integrating clinical excellence with public health strategies for effective maternal disease control. She is very active in national teaching and training program. She has got good experience in editing books and research paper and authored many research papers published in national and international journals. As Editor of Practical Management of Tuberculosis and Respiratory Diseases, Professor Dr Arora brings valuable academic insight and field experience to ensure that the book serves as a practical, reliable, and user-friendly resource for clinicians, program managers, and healthcare workers involved in patient care.



Kamal Kishore Chopra is a senior public health expert and tuberculosis (TB) specialist with extensive experience in the programmatic management and control of TB in India. Over the last 40 years, he has been actively involved in strengthening TB services through training, program implementation, and operational guidance for healthcare providers. Dr Chopra has contributed significantly to capacity building of medical officers and TB program staff, with a focus on translating national guidelines into practical, field-oriented clinical practice. His areas of interest include case-based management of tuberculosis, community engagement, and improving adherence to standard treatment protocols. Through his academic and programmatic work, Dr Chopra has remained committed to enhancing the quality of TB care and supporting India's efforts toward TB elimination. As editor of this book, he brings together practical insights and real-world clinical experiences to help clinicians manage tuberculosis more effectively. He has 225 research papers published in national and international journals.

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