

# RE-DEFINING CARE: TB, CRITICAL CARE AND BEYOND

81st NATCON 2026 | NEWSLETTER

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## CRITICAL CARE

Critical care for active TB in India

## CRITICAL CARE

Respiratory failure: past, present, future

## DIAGNOSIS

Sputum-negative pulmonary TB

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India's defence against DR-TB

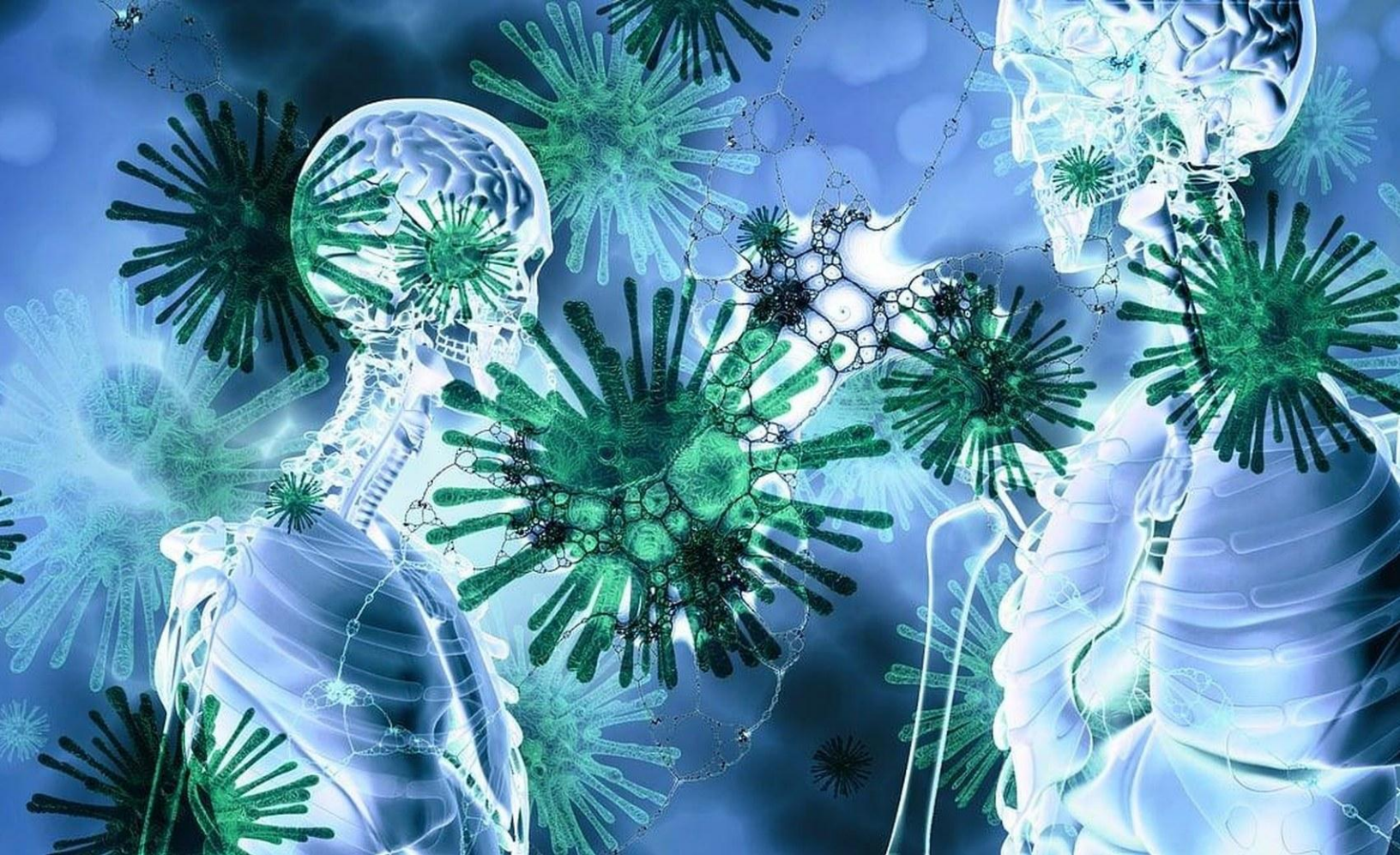
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## About NATCON 2026

The 81st National Conference on Tuberculosis & Chest Diseases, NATCON 2026, is being held in Patiala under the aegis of the Tuberculosis Association of India (TAI). The conference is hosted by the Department of Pulmonary Medicine, Government Medical College, Patiala, in collaboration with the Punjab State TB Association. NATCON 2026 brings together leading experts, clinicians, academicians and researchers to discuss advancements in tuberculosis care, respiratory medicine and public health strategies. Building on the momentum of NATCON 2025 in Kolkata, the conference aims to foster collaboration, innovation and knowledge exchange – uniting minds and igniting ideas that will strengthen India's fight against TB and chest diseases.



**Dignitaries at the inauguration ceremony of the 81st NATCON 2026, Government Medical College, Patiala (1–4 October 2026)**



**Lighting of the ceremonial lamp to mark the opening of the 81st NATCON 2026**

## R.C. Jain Lifetime Achievement Award

81st NATCON 2026, Patiala



**Prof. Dr. R.S. Bedi**

awarded R.C. Jain Lifetime Achievement Award  
(Posthumously)



**Dr. S. K. Katiyar**

awarded R.C. Jain Lifetime Achievement Award

# Re-defining Critical Care for Active Tuberculosis in India: Tracing the Evolution of Tuberculosis Management

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## ■ Introduction

For much of the twentieth century, the management of active tuberculosis (TB) relied predominantly on conservative measures. Patients were commonly referred to sanatoria, where rest, nutritional support, fresh air, prolonged observation, and physical separation from the wider community constituted the principal components of care. This approach reflected the absence of effective antimicrobial therapy and the prevailing understanding that recovery depended substantially on rest and containment. The sanatorium model also established a longstanding association between tuberculosis and institutional isolation, an approach that subsequently influenced the organization of hospital services.

Surgical treatment later assumed an important role in selected patients. Procedures such as artificial pneumothorax, thoracoplasty, and pulmonary resection were undertaken with the objective of reducing bacillary burden or collapsing areas of diseased lung. Although these interventions could provide benefit in carefully selected cases, they were invasive and resource-intensive and could not adequately address the systemic, infectious, and respiratory complications associated with advanced disease. The introduction of effective chemotherapy brought about a significant change in the management of tuberculosis. Multidrug treatment transformed TB from a predominantly chronic and frequently fatal illness into a curable infectious disease and, when initiated promptly and appropriately, substantially reduced infectiousness. Contemporary treatment strategies further support shorter, all-oral regimens for appropriately selected patients when

reliable diagnostic and drug-susceptibility information is available.

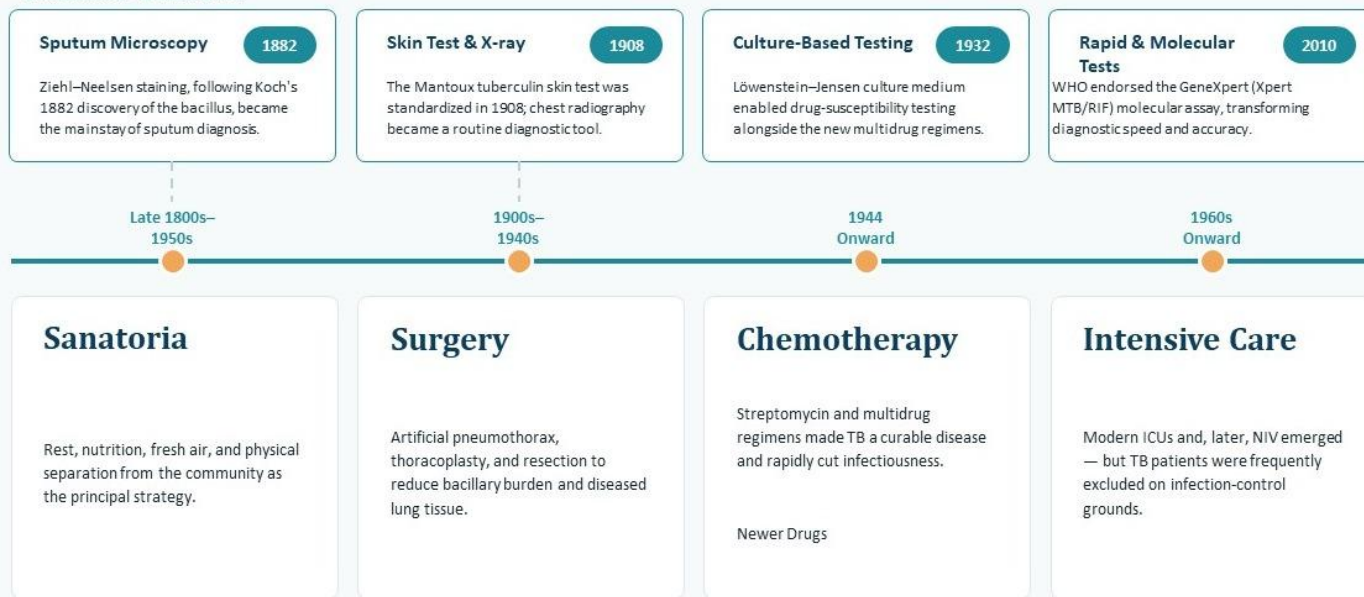
## ■ From Sanatoria and Surgery to Chemotherapy

The pre-chemotherapy era was characterized by significant therapeutic limitations. Sanatoria offered physical separation and supportive care but could not reliably halt progressive pulmonary destruction, disseminated disease, or respiratory failure. Surgical interventions represented an attempt to address localized disease in the absence of effective antimicrobial treatment. With the introduction of streptomycin and, subsequently, multidrug chemotherapy, the basic approach to TB management shifted from physical containment and mechanical modification of diseased lung tissue towards microbiological treatment, eradication of infection, and prevention of drug resistance through combination therapy.

The development and widespread adoption of short-course chemotherapy during the later part of the twentieth century resulted in substantial improvements in treatment success and survival. It also influenced hospital infection-control policies. As effective treatment was capable of reducing infectiousness relatively rapidly, dedicated TB isolation facilities and other infection-control measures were, in some settings, given lower priority. This assumption was subsequently challenged by the emergence of drug-resistant TB, the HIV epidemic, overcrowded healthcare facilities, and increasing recognition of healthcare-associated transmission. These developments demonstrated that effective treatment and appropriate infection-prevention measures must operate together.

# Evolution of TB Management

## DIAGNOSTIC MILESTONES



Evolution of TB management — from sanatoria and surgery to chemotherapy and intensive care. Figure: Dr Rajnish Gupta

## ■ Non-utilization of Intensive Care in TB management

Modern intensive care evolved during the mid-twentieth century, initially in response to poliomyelitis and other causes of acute respiratory failure. Negative-pressure ventilators, popularly known as “iron lungs,” represented an important advance in respiratory support by assisting ventilation without requiring an artificial airway. However, these devices were not developed specifically to address the infection-control challenges associated with contagious pulmonary TB and did not establish a structured model for tuberculosis critical care.

By the 1960s, intensive care units were becoming established, supported by invasive mechanical ventilation, improved physiological monitoring, and organized multidisciplinary care. Despite these advances, patients with active TB were frequently excluded from conventional ICUs. Concerns regarding airborne transmission, inadequate isolation facilities, limited availability of negative-pressure rooms, uncertainty regarding outcomes, and the perception that advanced organ support might be futile in severe TB contributed to this practice. Consequently, patients with respiratory failure were often managed in general wards, infectious-disease units, or improvised clinical areas that

lacked both the monitoring capabilities of an ICU and the engineering controls required for effective respiratory isolation.

This approach had important ethical and clinical implications. A potentially reversible cause of respiratory failure could receive a different standard of care solely because of its transmissibility. In many settings, the risk to healthcare workers and other patients was addressed by limiting access to invasive critical care, which was a compromised option directed more towards saving the healthcare workers rather than the patients themselves.

**Infectiousness must never become a reason for therapeutic neglect.**

## ■ Non-Invasive and Invasive Ventilation: A Change in Clinical Thinking

The increasing availability of non-invasive ventilation (NIV) during the 1990s introduced an important intermediate form of respiratory support for patients with acute respiratory failure. NIV could provide ventilatory assistance before intubation, support selected patients during recovery, facilitate weaning, and in appropriate circumstances, avert the need for invasive airway management. Its use in patients

with active TB was initially cautious and inconsistent because of concerns regarding mask leakage, aerosolization of respiratory secretions, and occupational exposure. As a result, NIV was sometimes provided in makeshift or suboptimal clinical locations.

With advances in infection-prevention practices, appropriate patient selection, improved interface design, respiratory protection, and close clinical monitoring, the realisation came that active TB should not in itself be regarded as an absolute contraindication to NIV. Similarly, endotracheal intubation need not be postponed solely because of concerns regarding infection transmission. Invasive mechanical ventilation may be required in patients with severe hypoxemia, respiratory muscle exhaustion, altered mental status, shock, inability to protect the airway, or failure of non-invasive support. Decisions regarding escalation of respiratory support should therefore be guided by the patient's status without being affected by stigma or assumption that active TB patient should receive less intensive treatment.

Respiratory support is an adjunct to, rather than a substitute for, effective anti-TB therapy. Its primary role is to provide time and physiological support while antimicrobial treatment takes effect and while clinicians address sepsis, organ dysfunction, nutritional needs, coexisting infections, and potentially reversible pulmonary injury. Successful diagnosis and treatment therefore remains central not only to individual patient outcomes but also to public health because effective therapy reduces the period of infectiousness.

### ■ Infection Prevention and Control as key elements of TB ICU and Critical Care

The development of dedicated TB critical-care services should be based on a hierarchy of infection-prevention controls rather than on reliance upon personal protective equipment alone. Early recognition and identification of presumptive infectious cases, appropriate triage, respiratory isolation, prompt initiation of effective treatment, environmental and engineering controls, administrative measures, and respiratory protection should function as an integrated system.

A dedicated TB ICU should provide appropriately designed airflow, suitable pressure relationships, adequate air changes per hour, and high-efficiency filtration or other validated air-cleaning systems. Where feasible, more than 12 air changes per hour may be incorporated into the design

of high-risk clinical areas. However, the performance of the ventilation system should be established through engineering assessment, commissioning, validation, and ongoing maintenance rather than inferred solely from equipment specifications. Correctly designed and maintained HEPA filtration within an HVAC system can reduce the recirculation of infectious aerosols. Portable air-cleaning devices may provide additional benefit in selected circumstances but should not be regarded as substitutes for a properly designed and validated ventilation system.

Respiratory protection remains an essential component of occupational safety. Healthcare workers caring for patients with infectious TB should use fit-tested particulate respirators meeting applicable standards, such as N95 or equivalent respirators. Depending on the procedure and institutional policy, enhanced respiratory protection may be warranted during aerosol-generating procedures. An effective respiratory-protection programme should include fit testing, appropriate training, medical evaluation where required, and monitoring of adherence.

Within the ICU, closed suction systems can reduce circuit disconnection and the dispersal of respiratory secretions during mechanical ventilation. Additional measures include minimizing unnecessary ventilator-circuit breaks, using compatible bacterial or viral filters where appropriate, maintaining meticulous hand hygiene, limiting unnecessary staff exposure, following defined patient-transport procedures, and implementing clear protocols for bronchoscopy, nebulization, airway suctioning, and terminal environmental cleaning. These measures should be reinforced through occupational-health surveillance, continuing staff education, and prompt assessment and management of any unprotected occupational exposure.

### ■ Transmission Risk and the Need for Early Treatment

Transmission risk among patients with TB is heterogeneous and is influenced by factors such as cough frequency, the presence of cavitary disease, sputum bacillary burden, ventilation characteristics, and the duration and intensity of exposure. Cavitary pulmonary disease is generally associated with a higher bacillary burden and greater infectiousness. Effective treatment usually reduces transmission risk, although the time required to achieve a substantially lower level of infectiousness varies according to individual patient characteristics and the treatment regimen.

These principles establish two simultaneous priorities for a TB ICU: immediate respiratory and organ support and rapid microbiological diagnosis followed by prompt initiation of an effective treatment regimen. Molecular testing, culture, and drug-susceptibility testing are particularly important because inappropriate or delayed treatment can prolong infectiousness and adversely affect clinical outcomes. Patients with drug-resistant TB require specific/individualized regimens, which may have potential drug toxicity, pharmacokinetic and pharmacodynamic interactions, requiring a prolonged multidisciplinary care and follow-up.

### ■ India's Programme Response and the Case for TB ICUs

India's national TB programme has progressively strengthened diagnostic services, treatment access, surveillance systems, and public-private collaborations. The Revised National Tuberculosis Control Programme (RNTCP), expanded nationally through phased implementation that achieved nationwide coverage in 2006, was built around the DOTS strategy and aimed to improve case detection and treatment success. Its scale demonstrated the capacity of organized public-health infrastructure to deliver standardized TB services across the country. RNTCP was upgraded to National TB Elimination Programme (NTEP) in 2020 that set targets for TB elimination in the country.

However, there exists a need for dedicated critical-care set ups for TB management like TB ICUs and High Dependency Units (HDUs). Severe TB may present with acute respiratory distress syndrome, massive haemoptysis, septic shock, disseminated disease, pulmonary hypertension, or multiorgan failure. Such patients require continuous monitoring and advanced organ-support interventions that cannot be reliably provided in conventional isolation wards. A comprehensive national TB-elimination strategy should therefore incorporate clearly defined referral pathways and create dedicated TB ICUs and HDUs, in appropriately identified areas and regions of the country.

A TB ICU should not be viewed simply as a clinical area containing ventilators. It should function as an integrated clinical, infection-control, and engineering system appropriately supervised by infectious-disease personnel, intensivists, respiratory therapists, nurses, microbiologists, pharmacists, physiotherapists, and nutrition teams. Standardized admission criteria, escalation pathways,

antimicrobial stewardship, drug-toxicity monitoring, rehabilitation, and appropriate end-of-life decision-making should form part of the service framework. Equipment and manpower availability is a key requirement of the set up. Systematic data collection should address illness severity at admission, the mode and duration of respiratory support, complications, drug-resistance patterns, ICU and hospital mortality, ventilator-associated events, healthcare-worker exposures, and functional outcomes.

**A TB ICU is not simply a clinical area containing ventilators – it is an integrated clinical, infection-control and engineering system.**

### ■ Ethical and Clinical Imperative

The development of dedicated TB ICUs is justified not only by advances in technology but also by the fundamental ethical principles. Patients with transmissible disease like TB also remain entitled to a timely, appropriate, and proportionate critical care delivery in a manner similar to those with other critical illnesses. Protecting healthcare workers, other patients, and visitors is essential. Such protection should be achieved through appropriate engineering controls, administrative measures, and personal respiratory protection rather than through therapeutic exclusion. A well-designed TB ICU can transform a historically high-risk clinical setting into a controlled environment, in which both the patient care and infection prevention can be delivered effectively, providing the ethical as well as the clinical solutions.

In short, the evolution of TB management demonstrates that each major therapeutic advance has influenced the organization of care. Sanatoria addressed the need for separation; surgery provided an option for selected localized disease when chemotherapy was unavailable; chemotherapy addressed the underlying infectious process; and modern intensive care provides support for acute physiological failure. The contemporary model should bring these lessons together by integrating infection containment, effective antimicrobial treatment, advanced organ support, and prevention of healthcare-associated transmission within a single coordinated and comprehensive service.

## ■ Conclusion

Critical care for active TB in India has progressed from conservative sanatorium-based management and selected surgical interventions to chemotherapy-supported, technologically advanced organ support. Nevertheless, the full benefits of this evolution have not been uniformly realized, particularly for TB patients with severe respiratory failure who historically faced barriers to conventional ICU care because of infection-control concerns. Non-invasive and invasive mechanical ventilation can be provided to appropriately selected patients when embedded within a robust infection-prevention and control framework.

Dedicated TB ICUs incorporating engineered ventilation, validated high-efficiency filtration, adequate air-change rates, comprehensive respiratory-protection programmes, closed suction systems, and trained multidisciplinary teams should be regarded as an important extension of India's TB response. Such services provide a practical and ethical means of ensuring that infectiousness does not become a reason for therapeutic neglect. Re-defining critical care for active TB therefore requires more than just placing ventilators in isolation wards; it requires a deliberate commitment to integrated, equitable, clinically appropriate, and infection-safe critical care within the broader national TB programme of the country.

## CRITICAL CARE

# Paradigm Shift in the Management of Respiratory Failure: Past, Present and Future

Dr. Ajith Kumar A.K., Lead Consultant, Critical Care Aster Whitefield Hospital, Bengaluru

Respiratory failure has always been one of the defining challenges of critical care. Yet, the way we understand and manage it has undergone a remarkable transformation. The journey has been from "supporting the lungs" to "protecting the patient," and now towards "personalising respiratory support."

## ■ The Past: When More Was Considered Better

Historically, management of respiratory failure was largely focused on correcting hypoxaemia and hypercapnia, often with escalating oxygen concentrations and aggressive mechanical ventilation. The ventilator was primarily viewed as a means of normalising blood gases. High tidal volumes and airway pressures were accepted, sometimes at the cost of additional lung injury.

The emergence of the concept of ventilator-induced lung injury (VILI) fundamentally changed this philosophy. The landmark ARDSNet trial demonstrated that lower tidal-volume ventilation could improve outcomes in ARDS, establishing lung-protective ventilation as a cornerstone of modern critical care. Subsequently, prone positioning,

appropriate PEEP strategies and conservative fluid management further reinforced the principle that how we ventilate may be as important as whether we ventilate.

## ■ The Present: From Numbers to Physiology

Today, respiratory failure is no longer viewed simply as an abnormal blood-gas report. We increasingly recognise it as a heterogeneous physiological syndrome requiring an individualised approach.

High-flow nasal oxygen (HFNO) and non-invasive ventilation (NIV) have expanded our ability to provide effective respiratory support while avoiding or delaying invasive mechanical ventilation in appropriately selected patients. At the same time, modern invasive ventilation emphasises driving pressure, mechanical power, patient-ventilator interaction, respiratory effort and lung recruitability, rather than tidal volume or plateau pressure alone.

Perhaps the most important paradigm shift is the recognition that oxygen itself is a drug. Both inadequate and

excessive oxygenation may be harmful. Similarly, “normalising” carbon dioxide or respiratory rate at all costs may not always be appropriate. The contemporary approach therefore seeks the right target for the right patient, rather than a universal numerical target.

**Oxygen itself is a drug — both too little and too much may be harmful.**

We have also moved from ventilator-centred care to patient-centred respiratory support. Awake proning, early mobilisation, sedation minimisation and liberation from mechanical ventilation are now integral components of respiratory care.

#### ■ The Future: Precision Respiratory Medicine

The next revolution is likely to be one of precision respiratory support. Respiratory failure will increasingly be characterised by continuous, multimodal physiological data rather than intermittent measurements. Artificial intelligence may help integrate ventilator waveforms, imaging, blood gases, biomarkers and clinical trajectories to predict deterioration, optimise settings and identify the ideal time for escalation or weaning.

Closed-loop and adaptive ventilation systems may increasingly adjust support according to the patient's changing physiology. Non-invasive technologies may become more sophisticated, while extracorporeal support—including ECMO—may evolve from rescue therapy towards a

more strategically integrated component of selected severe respiratory failure.

The future, however, should not be defined merely by increasingly sophisticated machines. The greatest advance will be knowing when not to use them.

#### ■ The New Paradigm

The evolution of respiratory failure management can therefore be summarised in three transitions:

- 1 From oxygenation to lung protection.
- 2 From protocol-driven ventilation to physiology-driven care.
- 3 From “one-size-fits-all” respiratory support to precision, patient-centred therapy.

The ultimate goal is no longer simply to achieve acceptable blood gases. It is to restore physiological stability while minimising iatrogenic injury, preserving diaphragmatic and systemic function, and helping the patient return to a meaningful life.

The future of respiratory failure management will belong not to the most powerful ventilator, but to the clinician who can best integrate physiology, technology, biology and human judgement.

In respiratory failure, the paradigm has shifted from “How much support can we provide?” to the far more important question: “What is the least harmful support this patient needs—and when should we change it?”

#### DIAGNOSIS

## Sputum-Negative Pulmonary Tuberculosis: A Persistent Diagnostic Dilemma

**Dr. H. J. Singh, MBBS, MD (Chest & TB)**  
Fellow: FIAB, FNCCP, ICAAI

important diagnostic challenge because a negative sputum smear does not exclude active pulmonary TB. Patients may have persistent symptoms and radiological findings suggestive of TB despite negative microscopy. Low bacillary burden, inadequate specimens and technical factors can all

contribute to sputum negativity. This article reviews the key clinical, radiological and microbiological principles needed for systematic evaluation.

### ■ 1. Why Can Sputum Smear Be Negative?

The main reason is a low concentration of *Mycobacterium tuberculosis* in respiratory secretions. Conventional smear microscopy requires a relatively high bacillary concentration for reliable detection. Patients with early disease, minimal pulmonary involvement or non-cavitary lesions may therefore have bacillary loads below the detection threshold.

Sputum negativity may be more frequent in individuals living with HIV, elderly patients and those with immunosuppressive conditions. Patients who cannot produce sputum or provide only a small-volume specimen may also have inadequate samples. In addition, improper collection, delayed transportation, inadequate processing or laboratory errors can reduce diagnostic yield. A good-quality specimen and appropriate laboratory handling are therefore essential.

### ■ 2. Clinical Presentation and Risk Factors

Symptoms of SNPT are often nonspecific and may resemble other respiratory diseases. Common complaints include persistent cough, low-grade fever, fatigue, weight loss, reduced appetite and night sweats. Productive cough and expectoration may be less prominent because of the lower bacillary burden.

Suspicion should increase when symptoms persist despite appropriate treatment for presumed bacterial respiratory infection. Important risk factors include close contact with a TB patient, previous tuberculosis, diabetes mellitus, malnutrition, chronic kidney disease, HIV infection and residence in an area with high TB prevalence.

Tuberculin skin testing and interferon-gamma release assays can provide supportive evidence of TB infection, but they cannot distinguish active disease from latent infection. They should therefore be interpreted together with the clinical picture, imaging and microbiological findings.

### ■ 3. Role of Chest Imaging

Chest radiography is usually the first imaging investigation. Findings that may suggest TB include upper-lobe infiltrates, nodular opacities, fibrotic changes and cavities. However, SNPT may have less characteristic appearances, including non-cavitary infiltrates, lower-lobe disease, hilar or mediastinal lymphadenopathy and diffuse infiltrates, particularly in immunocompromised patients.

HRCT can provide additional information when chest radiography is inconclusive. Centrilobular nodules, tree-in-

bud opacities, bronchogenic spread and small cavities can be highly suggestive of active TB. HRCT may also identify subtle abnormalities not readily visible on standard radiographs and can help select sites for microbiological sampling.

Imaging alone is not diagnostic because malignancy, fungal infection, organizing pneumonia and sarcoidosis may produce similar patterns. Radiological findings must therefore be integrated with clinical and microbiological evidence.

### ■ 4. Microbiological Diagnosis

*Mycobacterial* culture remains an important method for confirming pulmonary TB and can detect low numbers of bacilli. Liquid culture systems such as the *Mycobacteria* Growth Indicator Tube (MGIT) have improved recovery and shortened detection time. Culture also permits drug-susceptibility testing, which is particularly important when drug resistance is a concern. Its major limitation is the time required before results become available.

Rapid molecular tests have transformed TB diagnosis. Xpert MTB/RIF can detect *M. tuberculosis* genetic material and simultaneously identify rifampicin resistance. Molecular testing is particularly valuable in sputum-negative disease because genetic material may be detected when the bacillary burden is insufficient for smear positivity. Rapid results can support earlier diagnosis and treatment decisions.

Microscopy, molecular testing and culture should be regarded as complementary investigations. Test selection should reflect the patient's clinical status, specimen quality, imaging findings and available resources.

### ■ 5. Induced Sputum

Some patients with suspected pulmonary TB cannot produce an adequate spontaneous sputum specimen. In such cases, sputum induction using nebulized hypertonic saline is a practical and minimally invasive alternative. Induced sputum can improve the chance of microbiological confirmation and may reduce the need for more invasive diagnostic procedures.

The technique can often be performed in an appropriately equipped outpatient or clinical setting with suitable infection-control measures. It is therefore a useful intermediate step when spontaneous sputum is inadequate,

provided the patient's clinical circumstances permit the procedure.

### ■ 6. Fibreoptic Bronchoscopy

When non-invasive investigations fail to establish the diagnosis, fibreoptic bronchoscopy becomes an important diagnostic modality. It permits direct airway examination and collection of lower respiratory tract specimens, including bronchial washings, bronchoalveolar lavage fluid, brushings and transbronchial biopsy tissue. These specimens can undergo smear microscopy, molecular testing and culture.

Biopsy tissue may show granulomatous inflammation with caseation, providing strong supportive evidence for TB even when microbiological confirmation is not immediately available. Bronchoscopy can substantially improve diagnostic yield, but it is invasive and requires trained personnel, infrastructure and patient monitoring. It is generally reserved for cases in which less invasive methods are inconclusive or when an alternative diagnosis also needs evaluation.

### ■ 7. Practical Diagnostic Approach

A systematic approach is essential. Obtain at least two or three high-quality sputum samples whenever feasible. Perform sputum smear microscopy and rapid molecular testing. Obtain chest radiography and consider HRCT when indicated. Send respiratory specimens for mycobacterial culture.

**A negative sputum smear should not, by itself, be used to exclude active pulmonary TB.**

If the patient cannot produce adequate sputum, consider induced sputum. If non-invasive investigations remain inconclusive, bronchoscopy with BAL and, when appropriate, biopsy may be required. The final assessment should integrate symptoms, epidemiological risk factors, imaging and laboratory findings.

In selected high-risk patients with strong clinical and radiological evidence of TB, treatment may be initiated empirically while microbiological confirmation is awaited, particularly when diagnostic delay could result in serious consequences. Such decisions require careful clinical judgment and follow-up.

### ■ 8. Key Takeaway

A negative sputum smear should not by itself be used to exclude active pulmonary TB. SNPT remains an important diagnostic dilemma because low bacillary burden, atypical disease patterns and inadequate specimens can reduce smear sensitivity. Clinical vigilance is particularly important in patients with persistent constitutional symptoms, relevant risk factors and suggestive imaging.

Rapid molecular assays, liquid culture, induced sputum and bronchoscopy have improved the ability to identify SNPT. The most effective strategy is to combine clinical assessment with epidemiological information, imaging and microbiological evidence. Early recognition and timely treatment can help prevent disease progression, reduce morbidity and limit ongoing community transmission.



Image Credit: Getty Images

# From Genome to Action: Building India's Genomic Defence Against Drug-Resistant Tuberculosis

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## ■ Introduction

India carries the largest share of the global tuberculosis burden and, consequently, a substantial burden of drug-resistant disease. For tuberculosis researchers, one of the most important questions in the era of drug-resistant TB is deceptively simple: how rapidly and accurately can we determine which drugs are likely to remain effective against a given strain, and which resistance that strain already carries? For much of the past century, answering that question meant waiting weeks for culture and then longer for phenotypic drug-susceptibility testing. Molecular diagnostics have shortened this interval considerably, but most assays interrogate a limited number of resistance-associated targets and do not cover every drug of clinical importance. The challenge, therefore, is to bridge the gap between the genetic information carried by *Mycobacterium tuberculosis* and the treatment decisions that clinicians need to make.

## ■ An Indian catalogue for Indian strains

Whole-genome sequencing offers a comprehensive view of genetic variation in a single assay. Its clinical value, however, depends on how accurately that variation can be interpreted. The World Health Organization addressed this need in 2021 with the first global catalogue of mutations in the *M. tuberculosis* complex and their association with drug resistance, drawing on more than 38,000 isolates from over 40 countries, and expanded it in a second edition in 2023. Valuable as these global references are, they also carry a clear implication: because lineage distributions, mutation frequencies and treatment histories differ between settings, countries with a high burden of drug-resistant disease benefit from generating and interpreting their own national data alongside the global evidence.

The Indian Catalogue of *Mycobacterium tuberculosis* Mutations and their Association with Drug Resistance (Version 1.0, 2022), developed by ICMR-NIRT in collaboration with the US Centers for Disease Control and

Prevention and the National Tuberculosis Elimination Programme, was an important step in that direction. Whole-genome sequences from 2,112 clinical isolates, each linked to phenotypic drug-susceptibility results, were used to characterise more than 8,000 mutations across 15 first- and second-line anti-tuberculosis drugs. By grading variants according to their association with resistance, the catalogue provides Indian laboratories with an interpretive framework grounded in Indian clinical isolates. It also raises questions worth pursuing further — among them, the extent to which particular variants reflect genuine resistance rather than the lineage background of the strain in which they occur, a distinction that future analyses may be able to resolve.

**The mutation catalogue provided an important national reference for interpreting genomic variants and their association with drug resistance in Indian isolates.**

The catalogue was designed to evolve, and it has. Version 2.0, released subsequently by ICMR-NIRT with national and international partners, substantially expands the dataset, incorporates a larger proportion of drug-sensitive strains and refines the grading of variants across the anti-tuberculosis drugs in current use. As new resistance patterns emerge from the field, successive versions allow genomic surveillance in India to remain aligned with the changing epidemiology of drug-resistant tuberculosis.

## ■ The laboratory network behind the data

Genomic surveillance is only as dependable as the laboratory network that generates the underlying data. Every genomic result begins with an isolate that has been correctly collected, cultured, tested and documented. India's National Reference Laboratory network plays a critical role through external quality assurance, proficiency testing, biosafety supervision, accreditation and laboratory training. This infrastructure may receive less attention than sequencing

itself, but it is fundamental: without high-quality microbiology and quality-assured laboratories, sequencing can produce high-resolution information without reliable clinical meaning.

This lesson is not unique to genomics. Earlier molecular diagnostic technologies also demonstrated that the impact of a new test depends not only on analytical performance, but on how effectively it can be integrated into real-world laboratory and programme settings. Multicentric evaluation of upfront Xpert MTB/RIF testing across Indian sites demonstrated both the potential and the operational limitations of rapid molecular testing, contributing to the evidence base that informed WHO guidance on tuberculosis care.

### ■ Protecting bedaquiline

The need for genomic surveillance is particularly urgent for bedaquiline. Its introduction and subsequent incorporation into shorter, all-oral regimens have transformed the treatment landscape for drug-resistant tuberculosis. The drug is now indispensable – and therefore its emerging resistance is a major concern. Resistance-associated variants in Rv0678 (mmpR5), and less commonly in *atpE* and *pepQ*, have been reported, with some mutations also associated with cross-resistance to clofazimine.

Phenotypic susceptibility testing for bedaquiline is technically demanding, slow and available at relatively few centres. Systematic genomic profiling therefore offers an important opportunity for early warning. Work at ICMR-NIRT is characterising bedaquiline resistance-associated mutations among Indian clinical isolates and examining their relationship with phenotypic susceptibility and treatment history. The aim is not simply to document resistance after it appears, but to generate the evidence and the baseline against which emerging resistance can be recognised early enough to inform patient management – ensuring that each patient receives a regimen to which their organism is genuinely susceptible, and that a drug on which the entire drug-resistant TB programme depends is not eroded by avoidable misuse.

### ■ Watching treatment, not just diagnosing disease

Diagnosis is only the beginning. Once treatment is initiated, assessing whether a patient is responding remains a significant challenge. Rapid molecular tests such as CBNAAT/GeneXpert have transformed tuberculosis diagnosis by enabling early detection of *Mycobacterium*

tuberculosis and key drug-resistance markers. However, because these assays detect mycobacterial DNA rather than viable bacilli, detection of DNA may persist even after bacterial clearance and therefore does not reliably reflect treatment response. Assessment of response consequently relies on a combination of clinical, radiological and, where feasible, microbiological findings. These approaches have important limitations, particularly in paucibacillary disease, as seen in children and extrapulmonary tuberculosis, where bacillary loads are low, specimens are often difficult to obtain and many patients cannot produce sputum. Treatment monitoring therefore remains an important unmet need.

Rapid molecular tools that can more meaningfully reflect the presence or clearance of viable *M. tuberculosis* during therapy could help address this gap. An assay capable of indicating, within weeks rather than months, whether a patient is responding—using accessible specimens and chemistry suited to laboratories with limited infrastructure—could enable earlier identification of non-response and timely modification of therapy. Such tools may also help reduce the period during which poorly suppressed bacterial populations can persist and potentially acquire additional resistance. Developing and validating approaches for treatment-response monitoring, particularly for paediatric and extrapulmonary tuberculosis, is therefore an important research priority.

### ■ The host side of the equation

Resistance is a property of the bacillus, but clinical outcome reflects the interaction between the bacillus and its host. Studies of monocyte subsets, plasma chemokines such as CXCL9 and CXCL10, and monocyte microRNA profiles have identified distinct inflammatory signatures in patients with drug-resistant tuberculosis. These markers are unlikely to replace microbiological testing, but they may help stratify patients according to risk and provide complementary measures of disease severity and treatment response.

### ■ Beyond cure: post-tuberculosis lung health

Microbiological cure is not always the end of the illness. A substantial proportion of patients complete treatment successfully and are nonetheless left with persistent respiratory symptoms, impaired lung function, bronchiectasis or fibrotic damage – a spectrum now recognised as post-tuberculosis lung disease. For these patients, breathlessness, reduced exercise capacity,

recurrent infection and loss of livelihood may continue long after the last dose, and the same inflammatory processes that cause tissue damage during active disease are likely to shape what remains afterwards. Until recently, post-tuberculosis lung health has received relatively little attention, but this is now changing. Understanding who is at risk, and why, is an important first step towards a model of care that recognises a cured patient's lung health as an integral part of treatment outcome, rather than something outside it.

**Patients who survive TB must recover their quality of life not merely their negative culture.**

### ■ Conclusion

Tuberculosis elimination in India will not be achieved by a single technology. Progress will come from bringing genomics, immunology, diagnostics and programme practice together: interpreting sequences against an Indian resistance catalogue; ensuring that the laboratories generating the data are quality-assured; detecting resistance to critical drugs before it becomes widespread; and recognising treatment failure early enough to act. Accurate diagnosis and the appropriate use of the drugs already available are crucial not only for curing the patient in front of us, but also for preventing the resistance of tomorrow – antimicrobial stewardship is, in this sense, inseparable from good tuberculosis care.

Equally, the responsibility does not end at microbiological cure. Investigating and addressing post-tuberculosis lung health is essential if patients who survive tuberculosis are to recover their quality of life, and not merely their negative culture.

The journey from genome to action is therefore not simply about generating more data. It is about converting reliable genomic, microbiological and immunological evidence into knowledge that strengthens diagnosis, surveillance, treatment and long-term care. That convergence is increasingly within reach – and it is where research can make a tangible contribution to tuberculosis control in India.

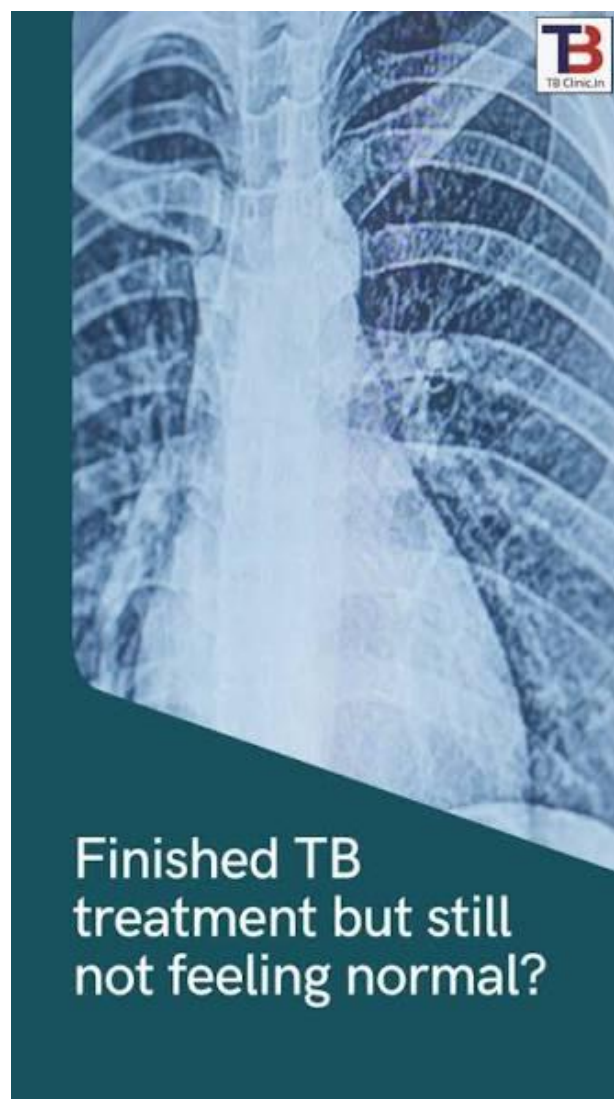


Image Credit: TB Clinic.in



Full house workshop on “Gender equality - break the bias”



Union-SEAR panel discussion at the 81st NATCON 2026, Patiala

#### UNION-SEAR SESSION

**PAN-TB Regimens: Toward a Universal, All-Oral Treatment for Drug-Susceptible and Drug-Resistant Tuberculosis**

**Moderator: Dr. Nibedita Rath, President, Union SEAR**

**Panellists: [Dr. V.K. Arora, Dr. S.K. Katiyar, Dr. Sanjeev Nair and Dr. Chaitali Nikam]**

**Chairperson: [Dr. Jai Kishan]**

## Glimpses from NATCON 2026



Release of the NATCON 2026 Souvenir by dignitaries at the inauguration ceremony



Dignitaries releasing 77th TB Seal Campaign 2026 at the 81st NATCON 2026, Patiala

The Union

International Union Against  
Tuberculosis and Lung Disease  
South East Asia Region Membership Group



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