





REVIEW

## Clinical Description of Pulmonary Tuberculosis in Cuba

### Descripción clínica de la tuberculosis pulmonar en Cuba

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**Cite as:** Cabrera Rodríguez D, Yon Wong ML, Chiappini Zayas S, Carbonell M. Clinical Description of Pulmonary Tuberculosis in Cuba. South Health and Policy. 2025; 4:343. <https://doi.org/10.56294/shp2025343>

Submitted: 29-03-2025

Revised: 15-06-2025

Accepted: 09-08-2025

Published: 10-08-2025

Editor: Dr. Telmo Raúl Aveiro-Róbalo 

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#### ABSTRACT

**Introduction:** tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. The World Health Organization in 2023 states that it is the leading cause of death from infectious diseases worldwide. Cuba is among the countries with low incidence in the Americas. Efforts are ongoing to achieve the goals of the End Tuberculosis Strategy.

**Objective:** to describe the clinical aspects of pulmonary tuberculosis in Cuba.

**Method:** the historical-logical method was used. Data were obtained through the review of 20 publications from 2020 to 2025.

**Development:** *Mycobacterium tuberculosis* has virulence factors supported by cell wall characteristics that aid its survival and spread. Tuberculosis is contracted through inhalation of aerosol droplets containing *Mycobacterium tuberculosis* from a susceptible person. Symptoms include fever, cough, weight loss, fatigue, night sweats, and hemoptysis. In Cuba, diagnostic techniques include sputum smear microscopy, bacteriological culture, and the tuberculin test. Multidrug therapy is systematically administered in 100 % of diagnosed cases.

**Conclusions:** for decades, changes have been incorporated into the National Program to improve disease management. The association of tuberculosis and Human Immunodeficiency Virus has increased in recent years in the country. Efforts continue to refine both knowledge and management of the disease.

**Keywords:** National Tuberculosis Prevention And Control Program; Tuberculosis; Human Immunodeficiency Virus.

#### RESUMEN

**Introducción:** la tuberculosis es una enfermedad infecciosa causada por *Mycobacterium tuberculosis*. La Organización Mundial de la Salud en 2023 afirma que es la principal causa de muerte por enfermedades infecciosas en todo el mundo. Cuba se encuentra entre los países con baja incidencia en América. Se están realizando esfuerzos para alcanzar los objetivos de la Estrategia para acabar con la tuberculosis.

**Objetivo:** describir los aspectos clínicos de la tuberculosis pulmonar en Cuba.

**Método:** se utilizó el método histórico-lógico. Los datos se obtuvieron mediante la revisión de 20 publicaciones entre 2020 y 2025.

**Desarrollo:** *Mycobacterium tuberculosis* tiene factores de virulencia respaldados por características de la pared celular que favorecen su supervivencia y propagación. La tuberculosis se contrae mediante la inhalación de gotículas en aerosol que contienen *Mycobacterium tuberculosis* de una persona susceptible. Los síntomas incluyen fiebre, tos, pérdida de peso, fatiga, sudores nocturnos y hemoptisis. En Cuba, las técnicas de diagnóstico

incluyen el frotis de esputo, el cultivo bacteriológico y la prueba de tuberculina. La terapia multimedicamentosa se administra sistemáticamente en el 100 % de los casos diagnosticados.

**Conclusiones:** durante décadas, se han incorporado cambios al Programa Nacional para mejorar el manejo de la enfermedad. La asociación de la tuberculosis y el virus de la inmunodeficiencia humana ha aumentado en los últimos años en el país. Se siguen realizando esfuerzos para perfeccionar tanto el conocimiento como el manejo de la enfermedad.

**Palabras clave:** Programa Nacional de Prevención y Control de la Tuberculosis; Tuberculosis; Virus de la Inmunodeficiencia Humana.

## INTRODUCTION

Tuberculosis (TB) is a disease caused by infection of humans with Koch's bacillus or *Mycobacterium tuberculosis*. Transmission occurs from person to person via airborne droplets expelled by the sick person when coughing, expectorating, or talking.<sup>(1)</sup>

It is also known as consumption, a term coined by Hippocrates meaning wasting; it is also called scrofula and white plague. The disease is as old as humanity itself.<sup>(2)</sup> March 24 has been designated World Tuberculosis Day since 1982, in honor of Dr. Robert Koch.<sup>(3)</sup> It has been an important cause of morbidity and mortality throughout history.

The World Health Organization (WHO) in 2023 states that it is the leading cause of death from infectious diseases globally, with approximately 10,8 million new cases and 1,25 million deaths, with the highest incidence of new cases in the Southeast Asia Region (45 %), Africa (24 %), and the Western Pacific (17 %).<sup>(3,4)</sup>

Cuba, a low-incidence country, continues efforts to meet the goals of the "End TB Strategy"<sup>(5)</sup> and has the National Tuberculosis Prevention and Control Program (PNPC-TB), started in 1962. Its main objective is to reduce morbidity and transmission of the disease until reaching its pre-elimination as a public health problem (5 cases per 100,000 inhabitants).<sup>(6,7)</sup>

To describe the clinical aspects of pulmonary tuberculosis in Cuba.

## METHOD

This study used the historical-logical method. Data were obtained through a review of 20 publications from 2020 to 2025. The criteria for selecting sources were scientific articles, both national and international, as well as the current National Tuberculosis Prevention and Control Program in Cuba, basic and complementary textbooks of General Integral Medicine and Public Health.

## DEVELOPMENT

### Microbiology and pathogenesis<sup>(8,9)</sup>

The genus *Mycobacterium* (M.) includes species such as *M. tuberculosis*, *M. bovis*, *M. Bovis* Bacille-Calmette-Guérin (BCG), *M. africanum*, *M. caprae*, and *M. microti*.

From a cellular perspective, organisms of the genus *Mycobacterium* have a peptidoglycan layer and two additional macromolecules forming the core of the cell wall: arabinogalactan acids and mycolic acids, which are covalently bound to each other and to the peptidoglycan.

These components give the genus its unique staining properties. The most specific methods for detecting mycobacteria that reveal the acid-fast characteristics of the cell wall are Ziehl-Neelsen and Kinyoun staining (figure 1).

A characteristic of *M. tuberculosis* is its relatively slow growth rate. In artificial media, the estimated generation time ranges from 20 to 24 hours. Cultures may require two to six weeks to grow depending on the culture method used.

*Mycobacterium tuberculosis* harbors several virulence factors, supported by its cell wall characteristics, which aid its survival and propagation by delaying desiccation and allowing airborne transmission. Furthermore, due to its survival within antigen-presenting cells, respiratory tract cells, and other cell types, it evades detection by the immune system. These factors facilitate phagocytosis, promote the arrest of phagosome maturation, subvert autophagy, and prevent the death of *M. tuberculosis* inside the cell. Additionally, it manipulates apoptotic, pyroptotic, and ferroptotic pathways to its advantage.

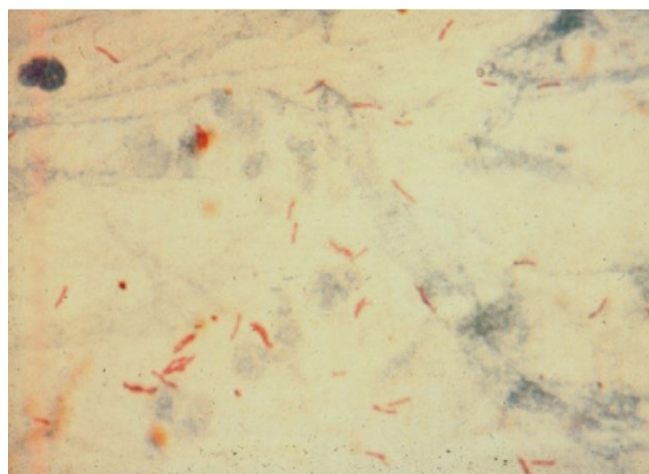
Regarding transmission, one mechanism is necrosis at sites of bacterial proliferation (active tuberculosis disease), which allows bacilli to escape from the lungs into the airways, where they can be aerosolized.

### Important definitions<sup>(10,11)</sup>

#### *Suspected Tuberculosis*

Any person presenting symptoms or signs suggestive of TB. The most common symptom of pulmonary TB

is a productive cough lasting more than 3 weeks, which may be accompanied by other respiratory symptoms (dyspnea, chest pain, hemoptysis) and/or general symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).



**Figure 1.** Sputum, decontaminated and concentrated, stained by the Ziehl-Neelsen method. Courtesy of John Bernardo, MD

### *Confirmed Tuberculosis Case*

A patient with *Mycobacterium tuberculosis* complex identified in a clinical sample, either by culture or by a newer molecular method.

### *Case Detection*

The process of identifying and diagnosing the disease carried out in all units of the National Health System and penal institutions. It requires considering the location of the disease; the results of bacteriological and other investigations that may complement the clinical suspicion, including Human Immunodeficiency Virus (HIV); the epidemiological aspects related to the vulnerable group or critical settlement from where the suspected person originates; and epidemiological investigation of cases and their contacts.

### *Severity of Disease*

Described according to the level of life threatening or presence of a tuberculous lesion that could leave significant sequelae. Severe cases include tuberculous meningitis, tuberculous pericarditis, bilateral pleural effusion, miliary TB, vertebral, intestinal, and genitourinary TB, and tuberculous pneumonia in the elderly.

### *Latent Tuberculous Infection*

The state in which the tuberculous bacillus remains latent or dormant in the body. Demonstrated through serological diagnostic means or tuberculin skin test response.

### **Vulnerable groups<sup>(10)</sup>**

Those with a higher probability of developing TB than the general population. They are prioritized as follows:

1. Contacts of pulmonary TB cases AFB-positive
2. Former inmates and current inmates
3. People living with HIV or other immunodeficiencies
4. Children under 5 years and adults  $\geq 60$  years
5. Alcoholics
6. Diabetics
7. Malnourished individuals
8. People with other chronic diseases (asthma, COPD, renal failure, or others)
9. Socially and economically vulnerable cases: homeless, drug addicts, and residents of critical settlements
10. People in health units with prolonged hospitalization (nursing homes and homes for physically or mentally disabled)
11. People with extensive old pulmonary radiographic lesions
12. Cuban collaborators providing services in countries with high TB burden
13. Foreign residents, temporary and permanent, from high TB burden countries
14. Healthcare workers related to patient care

15. Miners
16. Smokers

### **Tuberculosis classification**

According to location, it is classified as Pulmonary Tuberculosis (PTB) and Extrapulmonary Tuberculosis (EPTB).<sup>(11)</sup>

### **Clinical manifestations**

Tuberculosis is contracted by inhalation of aerosol droplets containing *M. tuberculosis* from a previously uninfected susceptible person, leading to deposition in the lungs, with one of the following possible outcomes: immediate elimination before adaptive response develops, or infection.<sup>(11,12)</sup>

#### *Primary Tuberculosis Disease*

Presents with fever. It is usually not accompanied by other symptoms, although pleuritic or retrosternal pain may occur due to pleural effusion and/or lymph node enlargement. Less common symptoms include fatigue, cough, arthralgia, and pharyngitis. Chest X-rays are usually normal. Common radiographic manifestations include hilar and/or mediastinal lymphadenopathy, pleural effusion, and pulmonary consolidation. Consolidation in primary TB may be segmental or lobar, affecting any lobe and is usually homogeneous.<sup>(13,14)</sup>

#### *Reactivation (Post-primary) Tuberculosis*

Symptoms may begin insidiously and be present for weeks or months before diagnosis. They include cough, weight loss, and fatigue; fever and night sweats, chest pain, dyspnea, hemoptysis, vague or nonspecific symptoms. Cough may be absent or mild initially and can be nonproductive or produce only scant sputum. It may occur only in the mornings as secretions accumulated during sleep are expectorated; as disease progresses, cough becomes more continuous throughout the day producing yellow or yellow-green sputum. Frank hemoptysis, due to caseous detachment or endobronchial erosion, usually appears later. Physical findings are nonspecific and may be absent in mild or moderate disease. When large areas of the lung are involved, signs of consolidation with bronchial breathing and amphoric sounds may be heard.<sup>(15)</sup>

### **Tb diagnostic techniques<sup>(10,16,17,18)</sup>**

#### *Bacteriology and Microscopy*

Includes microscopy results of pulmonary cases and identification of *M. tuberculosis* by culture or newer methods. At least two sputum samples should be collected from all patients suspected of pulmonary TB for microscopy. Identifying AFB negative cases is especially important in HIV where mortality is higher.

Microscopy (bacilloscopy) is the main diagnostic technique in Cuba. It is easy, fast, and inexpensive, useful both for detecting the most infectious cases (AFB-positive) and for monthly follow-up of PTB cases in treatment. Possible results include:

- Pulmonary tuberculosis with positive microscopy (AFB-positive PTB) one or more positive sputum smears.
- Pulmonary tuberculosis with negative microscopy (AFB-negative PTB), which can be:
  - ✓ AFB-negative PTB Culture (+): at least two AFB-negative sputum samples.
  - ✓ AFB-negative PTB Culture (-).

For pulmonary TB with negative microscopy (AFB-negative PTB): symptomatic respiratory patients (SRPs) with symptoms persisting 21 days or more (SRPs + 21) and two negative smears should repeat microscopy and culture, perform chest X-ray, HIV testing, and receive a broad-spectrum antibiotic (except quinolones).

#### **Bacteriological Culture**

Reference technique for definitive diagnosis in 15-20 % of total cases and 20-30 % of pulmonary TB patients. Allows early detection, often before becoming highly infectious. Culture results take time but are more sensitive than microscopy. Can detect as few as 10 to 100 acid-fast bacilli (AFB) if properly performed.

#### **Tuberculin Skin Test**

Used for epidemiological purposes in outbreak control and diagnostic purposes in particular cases. Requires high accuracy and standardization and trained personnel. Reading occurs at 72 hours by gentle and thorough palpation.

False negatives are common in HIV- infected individuals, limiting its usefulness. Due to severe immunodeficiency in this group, preventive treatment is suggested regardless of results.

Contraindicated in severely ill patients, with acute infectious processes, widespread eruptions, or receiving

steroid treatment.

### Other Techniques

- **Rapid Mycobacterial Culture:** Performed only at the National Reference Laboratory for TB (LNR-TB) of the IPK, using the automated BacT/ALERT 3D system for rapid mycobacterial diagnosis in liquid media. This system has high sensitivity and specificity. Growth time averages 11-13 days; for rapidly growing mycobacteria, 2-3 days.

Due to supply costs and availability difficulties, it is limited to severe cases, HIV, children, or high-risk patients and depends on resources.

- **Molecular Diagnosis by PCR:** Polymerase Chain Reaction (PCR) detects *M. tuberculosis* by amplifying purified DNA directly from clinical specimens without culture. Used mainly when traditional methods are insufficient to demonstrate infection.

### Tb treatment<sup>(10,11)</sup>

In Cuba, multidrug therapy is used, applied to all diagnosed cases.

Treatment regimens depend on case classification as follows:

1. Category I: New cases of AFB-positive PTB, AFB-negative PTB, all extrapulmonary TB forms, and HIV/TB.
2. Category II: Previously treated cases (retreatment), relapses, failures, and abandonments.
3. Category III: New and/or previously treated cases with documented mono- or poly-resistance.
4. Category IV: New and/or previously treated cases with documented multidrug resistance.

In case of documented resistance, treatment regimens are modified accordingly. The drug treatment of tuberculosis in Cuba is based on the following (table 1).

**Table 1.** Drug Treatment of Tuberculosis in Cuba

Drugs	Presentation	Doses		Average modulus
		Daily	Maximum	
Isoniazid (H)	Tab: 150mg	5mg/kg	300mg	120 tabs.
Rifampicin (R)	Tab: 300mg	10mg/kg	600mg	120 tabs.
Pyrazinamide (Z)	Tab: 500mg	20-30mg/kg	1,5-2g	180 tabs.
Ethambutol (E)	Tab: 400mg	15-20mg/kg	2,5g	360 tabs.
Second phase: intermittent 3 times a week (48 doses)				
Isoniazid (H)	Tab: 150mg	15mg/kg	750mg	200 tabs.
Rifampicin (R)	Tab: 300mg	10mg/kg	600mg	120 tabs.
<b>Total:</b> 108 doses				
<b>Source:</b> National Tuberculosis Control Program				

### Contact tracing study<sup>(10,19)</sup>

Contact and case tracing (focus control) is the investigation carried out to understand the epidemiological characteristics of both patients and their contacts to determine infection sources and transmission patterns. It is especially important in bacilliferous (AFB-positive) cases due to the high risk of infection and disease.

- **Close household contacts:** Those living in the same house as the infectious case, sharing space and air.
- **Close non-household contacts:** Persons having regular and prolonged contact with the infectious case but not living in the same house.
- **Second circle of contacts (middle circle):** Those spending less time with the infectious case, including frequent home visitors, friends, relatives, classmates, coworkers, leisure contacts, club or team members, or passengers seated next to the patient on an airplane >8 hours.
- **Third circle of contacts (outer circle):** Those living in the same community or attending the same school, sports center, or workplace who may have had occasional contact.

A TB focus is defined as the TB case plus persons living under the same roof (intimate or household contacts), frequent non-close contacts (social, work, or school contacts), and occasional contacts.

General indications for contact studies must be followed, including a clinical-epidemiological evaluation with



thorough history-taking, physical exam, diagnosis, and follow-up; tuberculin skin test, chest X-rays, and other studies depending on the specifics of each patient and contact.

#### **TB and HIV** <sup>(10,11)</sup>

The association of TB and HIV has increased in recent years in the country. Due to the impact of this dual infection, epidemiological surveillance must be ensured for this association in all TB cases and all HIV-positive or AIDS patients through established diagnostic exams for both entities.

In these cases, disease presentation ranges from subclinical stages to potentially fatal. It is influenced by the degree of immunosuppression. Early in HIV infection, TB clinical presentation is similar to that in HIV-negative patients, including fever, cough, weight loss, fatigue, loss of appetite, night sweats, and hemoptysis. As immunity declines, the frequency of pulmonary cavitation and hemoptysis decreases. Tuberculous meningitis is associated with very high mortality. Septic-type illness with hypotension, anemia, coagulopathy, and organ dysfunction can occur, with high mortality unless diagnosed and treated promptly.

#### **CONCLUSIONS**

Throughout its evolution, the National Program has incorporated changes aiming to eliminate the disease through concrete actions. The association between TB and HIV has increased in recent years in the country<sup>(20)</sup> Given the impact of this dual infection, it is essential to strengthen and update healthcare personnel's capacities in TB prevention and control, increase public knowledge, and develop pertinent research to support TB control and elimination.

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## INFORMED CONSENT

The authors declare they have obtained permission to use the images included in this article.

## FUNDING

There is no funding for this work.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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