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AI in Healthcare: Drug Delivery in Tuberculosis

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Abstract

Tuberculosis (TB), mainly caused by Mycobacterium tuberculosis, remains a major global health burden, accounting for millions of new infections and deaths each year. Although progress has been made in diagnosis and treatment, the growing threat of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB makes disease control increasingly difficult. Conventional diagnostic approaches such as chest X-rays, sputum smear microscopy, and culture methods continue to play an important role, but they face limitations in sensitivity, turnaround time, and accessibility, particularly in low-resource settings. In this context, artificial intelligence (AI) is emerging as a powerful tool for TB management by improving screening precision, accelerating diagnosis, strengthening public health surveillance, and assisting in treatment monitoring. AI-based advances are also shaping drug delivery systems, where machine learning supports nanocarrier design, targeted release, and personalized dosing, leading to safer and more effective therapies. Still, barriers such as limited datasets, high implementation costs, technical challenges, and unresolved regulatory and ethical issues persist. Looking ahead, AI applications in TB are expected to expand further, with integration into clinical workflows, smartphone-based adherence monitoring, real time tracking of treatment response, and predictive models for patient outcomes. Ultimately, incorporating AI into TB prevention and care offers great promise for advancing global control strategies and improving health outcomes provided there is sustained investment, equitable access, and strong validation frameworks.

Keywords: Artificial Intelligence, healthcare, drug delivery, tuberculosis, *Mycobacterium tuberculosis*

INTRODUCTION

Tuberculosis (TB) is an infectious disease mainly caused by *Mycobacterium tuberculosis* and some closely related species. It continues to be a serious health threat worldwide because of its high levels of illness and death. In 2022**,** TB claimed about 1.3 million lives**,** and predictions warn that the disease could result in nearly 31 million deaths in the coming years. Although TB usually affects the lungs, it can also involve other parts of the body, leading to extra pulmonary disease. Nearly 15–20% of all TB cases are extra pulmonary, particularly in people who are co-infected with HIV**.** Moreover, *M. tuberculosis* has been reported to cause tumor-like growth, and some studies have suggested a link between pulmonary TB and lung cancer**,** highlighting the need for better management and control [1].

TB is caused by members of the species *Mycobacterium tuberculosis* complex (MTBC), which includes: M. tuberculosis (M. TB), the primary cause of TB in humans; *M. africanum*, which causes TB in humans but is largely restricted to certain regions of Africa; and *M. bovis*, *M. caprae*, and *M. pinnipedii*, which are responsible for TB in wild and domesticated animals [2].

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Tuberculosis (TB), commonly known as the "white death" is an infectious disease usually caused by *Mycobacterium tuberculosis* (M. TB). It primarily targets the lungs, although it can also affect other parts of the body. The term "latent TB" describes infections that generally do not show symptoms. About 10% of these dormant infections may develop into active disease if left untreated, and roughly half of those affected can die. Typical signs of active TB include fever, night sweats, weight loss, and a persistent cough that may produce blood-stained sputum. When TB involves other organs, it can cause a range of different symptoms. People with active pulmonary TB can pass the infection on others through coughing, sneezing, spitting, or even speaking. Those living with HIV/AIDS and smokers are at higher risk of infection.

TB is diagnosed using conventional methods such as chest X-rays, microscopic examination, and culturing body fluids**.** For latent TB, blood tests and the tuberculin skin test (TST) are commonly employed. Prevention measures include screening high-risk populations, early detection and treatment of cases, and vaccination with Bacillus Calmette–Guerin (BCG).

TB has long been a major contributor to illness and death worldwide, but for many decades it remained neglected in both developed and developing countries. Recently, it has gained renewed focus**,** with substantial efforts underway to strengthen control programs. This renewed attention is driven by the rising TB incidence in HIV-affected regions**,** the proven effectiveness of short-course chemotherapy, and the understanding that TB control is one of the most cost-effective health interventions in developing countries [3].

Current treatment regimens for adults with drug-susceptible or drug-resistant TB are lengthy, can lead to serious drug-related side effects**,** and impose a considerable financial burden on patients. Past attempts to shorten these treatment regimens have increased the risk of treatment failure and relapse**.** Additionally, the technical challenges of monitoring treatment using sputum culture make accurate patient follow-up difficult in both programmatic and clinical trial settings, and these methods are not suitable for all populations. The growing prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, along with the emergence of bed aquiline resistance, poses serious public health threats and may reduce treatment success rates. The limitations in current diagnostics, treatment options, and vaccination strategies are evident, and urgent interventions are needed to keep the WHO End-TB targets within reach.

Commonly employed methods for TB diagnosis include immunological, radiographic, microscopic, bacterial culture, and clinical approaches. Immunological tests**,** such as QuantiFERON-TB Gold (QFT) and the Tuberculin skin test (Mantoux test), are primarily used for screening and ruling out TB infection. Similarly, radiography (chest X-rays) serves as a screening tool to detect active pulmonary TB, but it cannot identify latent TB infections [4].

HISTORY

In 1882, Robert Koch discovered the tubercle bacillus, today known as *Mycobacterium tuberculosis* (M. TB), and proved it to be the cause of tuberculosis (TB). Since that time, the TB epidemic has continued to spread across the world, showing little sign of decline. TB is an airborne infectious disease and remains one of the leading causes of death globally. Although it most often attacks the lungs (called pulmonary TB), it can also spread to other organs of the body (known as extra pulmonary TB).

M. tuberculosis can stay dormant inside the human body for many years, causing no signs of illness, which makes many people silent carriers of the infection **(**inactive TB). According to the 2022 report from the World Health Organization (WHO)**,** nearly one-quarter of the global population (around 2 billion people) carry the latent form of the infection. For people with latent TB infection (LTBI**)**, the estimated lifetime chance of developing active TB disease is about 5–10%. Bacteria are especially likely to reactivate in people with weakened immune systems, such as those living with HIV co-infection, where dormant TB can progress into active disease [4].

- *Ancient Times:* Evidence from Egyptian mummies (≈ 2400 BC) reveals skeletal damage typical of tuberculosis, such as Pott's disease. Hippocrates (5th–4th century BC) described the illness known as "phthisis" (consumption), characterized by symptoms like coughing and fever.
- *Middle Ages & Renaissance:* Tuberculosis appeared in several forms, such as scrofula (swelling of the cervical lymph nodes), which was often referred to as the "king's evil." Medical treatments during this time were basic and largely rooted in superstition. The concept that TB was a contagious disease had still not been clearly recognized.
- *17th–18th Centuries:* More detailed pathological descriptions emerged during this period. In 1679, Francis Sylvius described the presence of tubercles and explained how they developed in the lungs and throughout the body. Later, in 1720, Benjamin Marten suggested that consumption might be caused by "tiny living creatures" (a forerunner of germ theory) and also noted that close contact could spread TB.
- *19th Century:* This period saw major progress: the term "tuberculosis" was introduced. In 1865, Jean-Antoine Villemin proved the transmissibility of TB through inoculation experiments. In 1882, Robert Koch identified *Mycobacterium tuberculosis* as the causative bacillus. The sanatorium movement also began, promoting fresh air, rest, and good nutrition as treatment approaches.
- *20th Century Onwards:* This era marked the development of diagnostic methods**,** such as the skin tests introduced by Pirquet and Mantoux. The BCG vaccine was created by Calmette and Guerin, followed by the discovery of key anti-tubercular drugs like streptomycin and isoniazid. Large-scale public health programs were launched to control TB, though in later years the rise of drug-resistant TB emerged as a major challenge [5].

PATHOPHYSIOLOGY OF TUBERCULOSIS

Tubercle bacilli nuclei that enter the lungs' alveoli during breathing can cause infection in a step known as aerosolization. Once inside, these bacilli Pharmaceuticals 2023, 16, are taken up by alveolar macrophages, but most of them are destroyed or blocked. However, by preventing the fusion of the phagosome with the lysosome, *M. tuberculosis* survives and multiplies inside the macrophages. Asymmetric cell division, a unique type of cell division, is observed in *M. tuberculosis*. If these bacteria remain alive, they may travel through the lymphatic system or bloodstream to the nearby lymph nodes, the upper parts of the lung, kidneys, brain, and bones, where TB disease is more likely to appear. This spread triggers the immune system to mount a stronger defense, and as an analogy, a granuloma acts like a "bacterial prison," surrounding and containing the bacteria with immune cells. The granuloma itself is formed by macrophages and lymphocytes that cluster around *M. tuberculosis*. Various immune cells such as TH1, natural killer (NK) cells, dendritic cells, macrophages, regulatory T cells, foam cells, giant cells, epithelioid macrophages, neutrophils, and B cells are all involved in granuloma formation. Clinically, tuberculosis is classified into primary and secondary forms. In people with weak immune defenses, primary infection develops because the immune system cannot control it. At this stage, the infected person releases aerosols containing *M. tuberculosis* and can spread it to others. When *M. tuberculosis* survives but is not eliminated by the immune system or granuloma, the disease is referred to as latent TB, which has the potential to progress into secondary TB (Table 1 and Figure 1) [6].

IMPORTANCE

Early Screening and Triage

- AI applied to chest X-rays or radiographs can identify signs such as lesions, cavities, and infiltrates that may indicate TB, making it a useful first-line screening tool. This is particularly important in regions where there are not enough radiologists [7–13].
- Newer approaches make use of cough sound analysis (audio biomarkers) to help triage individuals. For instance, a recent study in Zambia applied deep learning models to cough recordings, and when combined with clinical and demographic information, it was able to differentiate TB from other respiratory illnesses or healthy individuals with strong sensitivity and specificity [14].

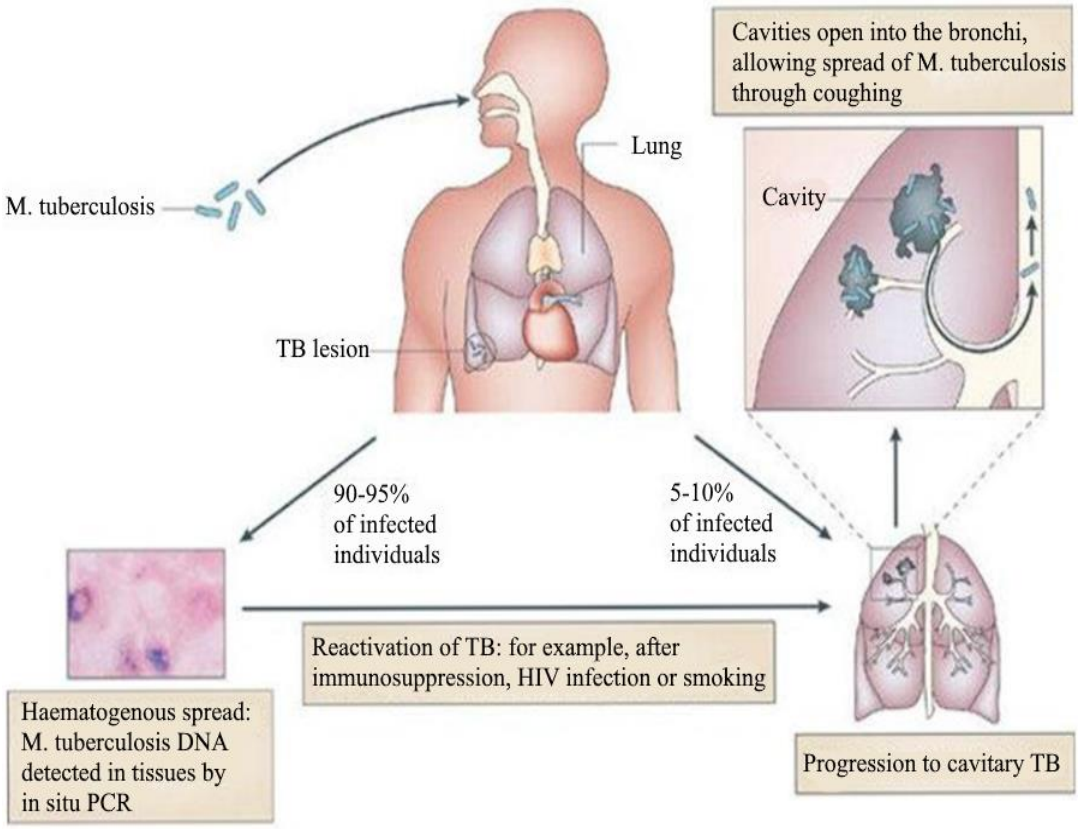

Figure 1. Pathophysiology of tuberculosis.

Table 1. Types of tuberculosis: [7–12].

Types	Description	Common sites	Key features
Latent TB Infection (LTBI)	Infection present but inactive; no symptoms.	Lungs (primary site)	Positive tuberculin skin test/IGRA; not contagious.
Active TB (Pulmonary TB)	Symptomatic disease; bacteria multiply actively.	Lungs	Cough, fever, weight loss; contagious.
Extrapulmonary TB	TB outside the lungs	Lymph nodes, bones, kidneys, meninges, skin	Not usually contagious; site-specific symptoms.
Miliary TB	Disseminated TB via bloodstream	Multiple organs (lungs, liver, spleen)	"Millet seed" appearance on X-ray; high mortality.
TB Meningitis	TB infection of meninges	Brain, spinal cord	Severe neurological symptoms; high fatality if untreated.
Drug-Resistant TB (MDR/XDR-TB)	Resistant to first-line drugs (isoniazid, rifampin; others)	Pulmonary & extrapulmonary	Difficult to treat; major public health concern.
Primary vs. Secondary TB	Primary = first infection; Secondary = reactivation	Lungs, lymph nodes	Lungs, lymph nodes.

Diagnosis Accuracy and Speed

Computer-aided detection/diagnosis (CAD) systems that use deep learning have demonstrated high sensitivity (often ≥ 90%) in identifying pulmonary TB from imaging. These tools can also help shorten the time needed to reach a diagnosis [15].

Public Health Surveillance, Hotspot Mapping, Active Case Finding

AI helps in spotting hidden TB cases, mapping areas with greater risk, assisting in triage, and improving how resources are allocated. This is especially valuable in high-burden regions with limited resources [16].

Novel & Non-Traditional Methods of Detection

Techniques such as analyzing cough sounds with speech foundation models are now being studied as practical and scalable tools for TB screening [17].

CONVENTIONAL METHODS

Sputum Smear Microscopy

SSM is considered the preferred technique for diagnosing pulmonary TB. In fact, in some remote areas of developing countries, it remains the only available diagnostic method (Ben-Selma et al., 2009). The most commonly applied staining methods include Ziehl–Neelsen (ZN) staining and fluorescent staining (Auramine-O / Auramine–rhodamine). SSM is simple to perform and cost-effective, but its sensitivity is limited (requiring $>10^4$ bacilli•mL^{-1} of sputum for a positive result) and it has a high false-negative rate, which may lead to misdiagnosis. In recent years, an operator-independent SSM using the ZEISS Axio Scan has been developed and tested to automatically identify and count acid-fast bacilli, achieving a sensitivity of 97.06% and a specificity of 86.44%. This approach enhances detection efficiency and saves important time for laboratory staff. In addition, specific fluorescent antibody labeling with laser confocal microscopy has been designed to improve the detection of *M. tuberculosis* in lung tissue samples, particularly when the bacteria show weak ZN staining (Erokhina et al., 2019). The Pat–Scan program, developed using digital pathology, has also been introduced to detect and quantify bacilli in paraffin-embedded ZN-stained tissue, thereby helping to reduce diagnostic turnaround time [18].

It is important to note, however, that SSM cannot differentiate between live and dead bacteria, nor can it distinguish *M. tuberculosis* from other nontuberculous mycobacteria. On the other hand, ZN staining provides valuable information on the acid-fastness of bacilli present in patient samples. This detail becomes especially crucial in samples from patients who have already received anti-TB treatment. Moreover, such information can only be obtained through Ziehl–Neelsen staining and not from fluorescent SSM techniques.

Mycobacterial Culture

The clinical samples can be used for mycobacterial culture (10^2 bacilli•mL^{-1} of sputum), which is still considered the gold standard for diagnosing TB. *M. tuberculosis* is commonly cultured on solid media, where it can then be identified and tested for drug sensitivity, giving clinician's reliable guidance for effective antibacterial treatment. Liquid culture systems such as BACTEC MGIT 960, VersaTREK, and MB/BacT Alert 3D make it possible to detect *M. tuberculosis* within just a few days. The BACTEC MGIT 960 automated culture system works by monitoring oxygen quenching fluorescence, and a signal is generated once the mycobacteria begin to grow inside the tube. Studies have shown that MGIT 960 is more effective in the rapid detection of mycobacteria and in enabling earlier TB diagnosis compared with the traditional L–J solid medium. The VersaTREK system functions by sensing pressure variations, detecting the growth of the inoculated specimen through changes in pressure above the broth medium. Similarly, the MB/BacT Alert 3D system identifies the growth of *M. tuberculosis* by using a colorimetric carbon dioxide sensor. Given the naturally slow growth rate of the *M. tuberculosis* complex (MTBC), most positive cultures appear only after at least one week, while negative cultures are generally confirmed after about eight weeks [18].

INNOVATIVE APPLICATIONS

AI-Driven Design & Optimization of Nano Carriers

Machine learning and deep learning can be used to predict which nanoparticle formulations considering factors like size, surface chemistry, polymer or lipid composition, and ligand functionalization–will enhance lung deposition, macrophage uptake, stability, and controlled drug release, significantly reducing the need for empirical trial and error. Several studies and reviews have explored nan carriers for TB and suggest that AI represents the next step for their optimization [6].

AI Applied to

AI applied to PET/CT scans, chest X-rays, and sputum or blood biomarker data can pinpoint the location and activity of lesions. When this information is combined with smart delivery systems such as targeted inhaled particles or localized drug release it allows for spatially focused therapy and real-time monitoring of treatment response. Clinical applications of AI for TB imaging are already showing significant progress [19].

Manufacturing & Quality Optimization (Smart Pharma)

Machine learning can optimize microfluidic synthesis parameters, scale-up procedures, and batch quality assurance for complex nano medicines, reducing variability and accelerating the path to clinical use for AI-designed TB carriers. Regulatory horizon reports have highlighted the application of AI and ML throughout the entire medicine's lifecycle [20].

AI to Select Drug Combinations for Encapsulation / Targeted Release AI and Systems

Biology based machine learning can be used to screen and prioritize multi-drug combinations that act synergistically and are suitable for co-encapsulation, considering factors such as compatible solubilities and release kinetics. This approach is especially important for TB's multi-drug regimens, as it reduces the need for extensive experimental screening and highlights better combination formulations to help minimize drug resistance [21].

ADVANTAGES

Enhanced Targeting & Controlled Release

- AI-assisted modeling of inhaled drug particles can predict lung deposition and optimize controlled release kinetics.
- This approach enhances local drug concentrations in the lungs while minimizing systemic side effects [22].

Better Multi-Drug Regimen Management

AI can identify drug combinations that act synergistically and are suitable for co-encapsulation.

This strategy helps maintain effective plasma drug levels while reducing the risk of drug resistance, including MDR and XDR-TB [23].

Faster Translation & Manufacturing

- AI can optimize nanoparticle synthesis, scale-up processes, and quality assurance to ensure reproducible formulations.
- This accelerates the development of TB drug delivery systems, moving them more efficiently from the laboratory to clinical application [24].

Optimized Nano Carrier Design

Machine learning can predict key properties of nanoparticles or liposomes such as size, charge, and ligand density to enable targeted delivery to lung macrophages, the primary site where *M. tuberculosis* resides. This approach saves considerable time compared with traditional trial and error formulation methods [19].

DISADVANTAGES

Complexity of TB Pathology

- TB lesions are highly heterogeneous, containing features such as caseous necrosis, fibrotic walls, and intracellular bacilli.
- This heterogeneity can make it challenging for AI to accurately predict drug penetration and release across these diverse microenvironments [22].

High Cost & Technical Barriers

- Creating AI-driven drug delivery systems, such as Nano carriers or inhaled therapies, requires costly infrastructure, advanced computational resources, and interdisciplinary expertise.
- This can be particularly challenging in low and middle-income countries, which often carry the highest TB burden [6].

Regulatory, Ethical & Privacy Concerns

- There is a lack of well-defined regulatory pathways for the use of AI in TB diagnosis and treatment [23].
- Additionally, in resource-limited settings, there are risks of patient data misuse and insufficient privacy protections [24].

FUTURE SCOPE

Enhanced Screening & Early Detection

- AI-powered chest X-ray (CXR) tools are expected to be widely implemented in resource-limited regions to help triage suspected TB cases where radiologists are in short supply [25].
- Future AI models will combine radiology findings, clinical symptoms, and demographic information to minimize misdiagnosis [26].

Treatment Monitoring & Adherence Support

Smartphone-based AI tools, such as video DOT and smart pillboxes, can enhance monitoring of treatment adherence, identify patterns of non-compliance, and enable timely interventions [27].

Outcome Prediction & Prognosis

Deep learning models that track chest X-ray progression during therapy can predict both treatment response and the risk of relapse [28].

Public Health Surveillance & Forecasting

AI can assist national TB programs by analyzing case data, social determinants, and population mobility patterns to predict outbreaks and optimize the allocation of resources [29].

Integration into Clinical Workflows

Future AI systems are expected to be integrated into portable X-ray machines, mobile applications, and national health databases, offering real-time decision support [30].

RESULTS AND DISCUSSION

Artificial intelligence (AI) has transformed tuberculosis (TB) management by boosting early detection, increasing treatment accuracy, and optimizing medication delivery systems. AI-assisted imaging and machine learning approaches allow for speedier identification, more precise monitoring, and the development of enhanced nanocarriers for targeted medication delivery, which improves therapeutic outcomes and reduces adverse effects. Despite limitations such as high implementation costs, limited datasets, and regulatory issues, AI has the potential to revolutionize worldwide tuberculosis management by enabling personalized therapy, improved adherence monitoring, and efficient public health surveillance.

CONCLUSION

Tuberculosis (TB) remains one of the most critical global health challenges, not only because of its high rates of infection and mortality but also due to the increasing burden of multidrug resistant (MDR) and extensively drug-resistant (XDR) forms. While conventional methods of diagnosis and treatment are vital, they often fall short in terms of speed, accuracy, and accessibility, especially in low-resource settings. The use of artificial intelligence (AI) in TB care is opening new possibilities by improving early screening, enhancing diagnostic accuracy, enabling personalized treatment, and advancing drug

delivery systems through nanotechnology and machine learning. AI is also proving valuable in public health by strengthening surveillance, monitoring treatment progress, and offering predictive insights that support global TB control strategies. Still, major challenges such as limited datasets, technical complexities, high costs, and regulatory as well as ethical concerns must be overcome to achieve equitable adoption. Moving forward, consistent investment, collaboration across disciplines and rigorous validation are essential to unlock AI full potential. With proper implementation, AI powered solutions could transform how TB is prevented, diagnosed, and treated, bringing the world significantly closer to the long-term goal of eradicating the disease.

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Conflict of Interest

None.

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Ethics Statement

None.

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