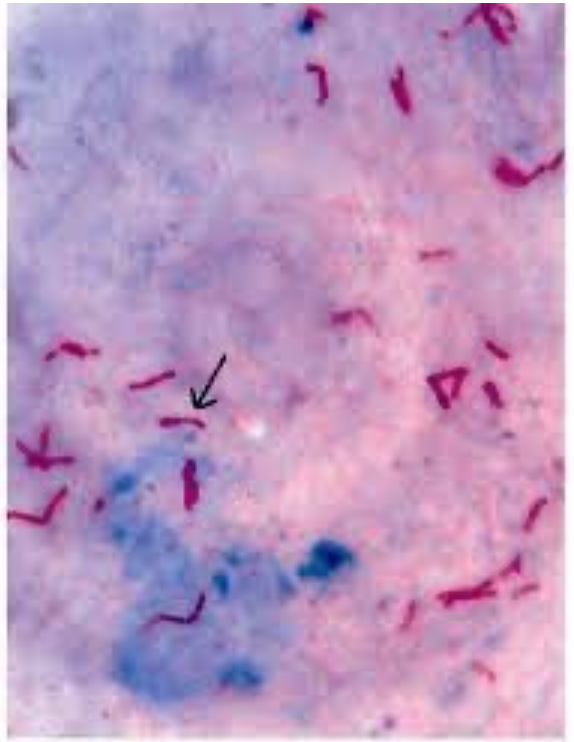
Mycobacterium tuberculosis

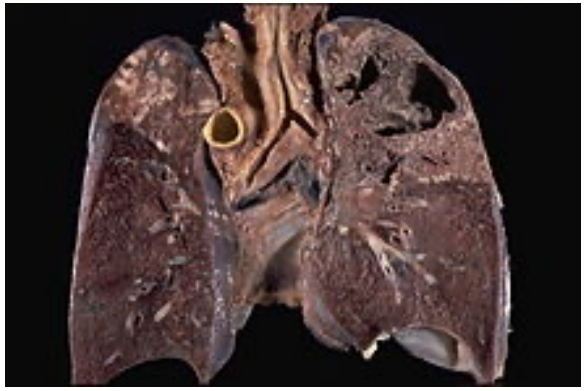
Mycobacterium tuberculosis is a species of pathogenic bacteria in the family Mycobacteriaceae and the causative agent of tuberculosis.

M. tuberculosis has an unusual, waxy coating on its cell surface primarily due to the presence of mycolic acid (Mycolic acids are **long fatty acids found in the cell walls of the bacteria)**

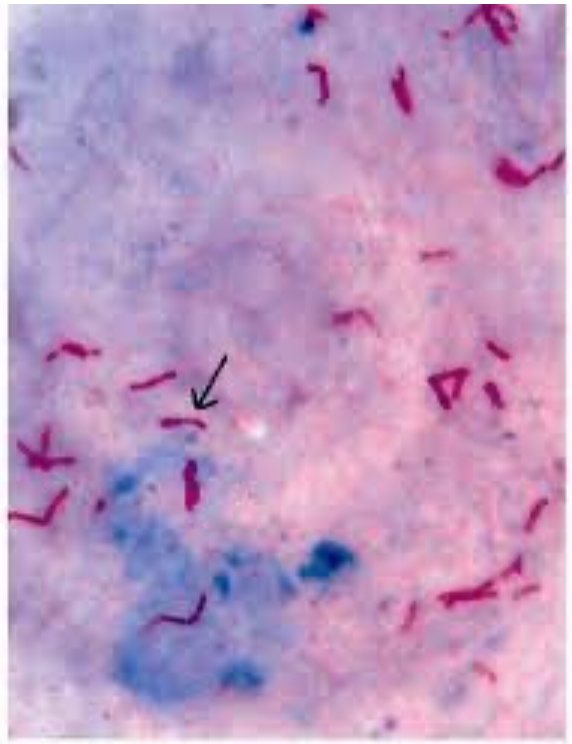
This coating makes the cells impervious to Gram staining, and as a result, *M. tuberculosis* can appear weakly Gram-positive.

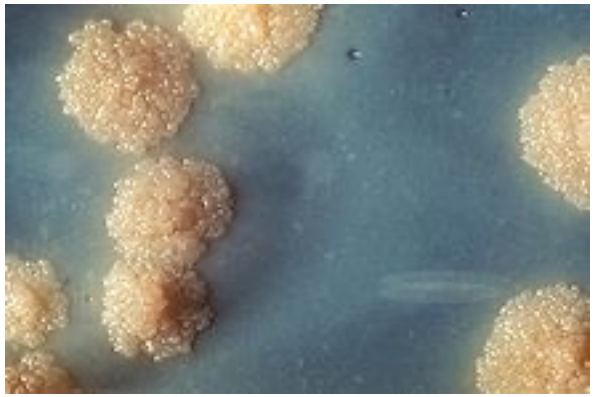
Acid-fast stains such as Ziehl–Neelsen, or fluorescent stains such as auramine are used instead to identify *M. tuberculosis* with a microscope.



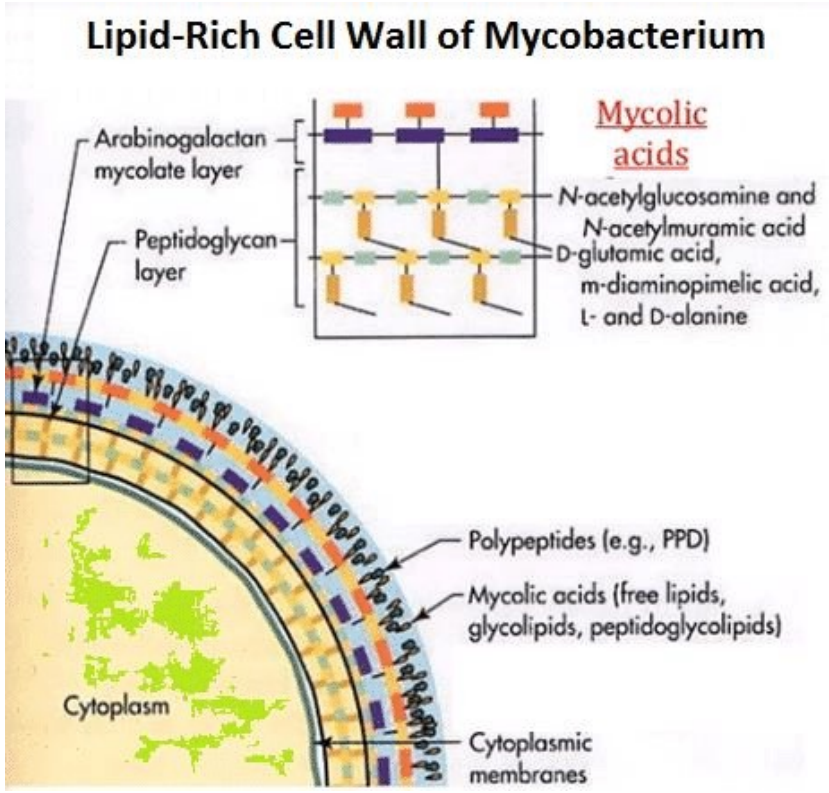


- The physiology of *M. tuberculosis* is highly aerobic and requires high levels of oxygen.
- Primarily a pathogen of the mammalian respiratory system, it infects the lungs.
- The most frequently used diagnostic methods for tuberculosis are the tuberculin skin test, acid-fast stain, culture, and polymerase chain reaction





- *M. tuberculosis* divides every 18–24 hours. This is extremely slow compared with other bacteria, which tend to have division times measured in minutes (*Escherichia coli* can divide roughly every 20 minutes).
- It is a small bacillus that can withstand weak disinfectants and can survive in a dry state for weeks.
- Its unusual cell wall is rich with mycolic acid, is likely responsible for its resistance to desiccation and is a key virulence factor

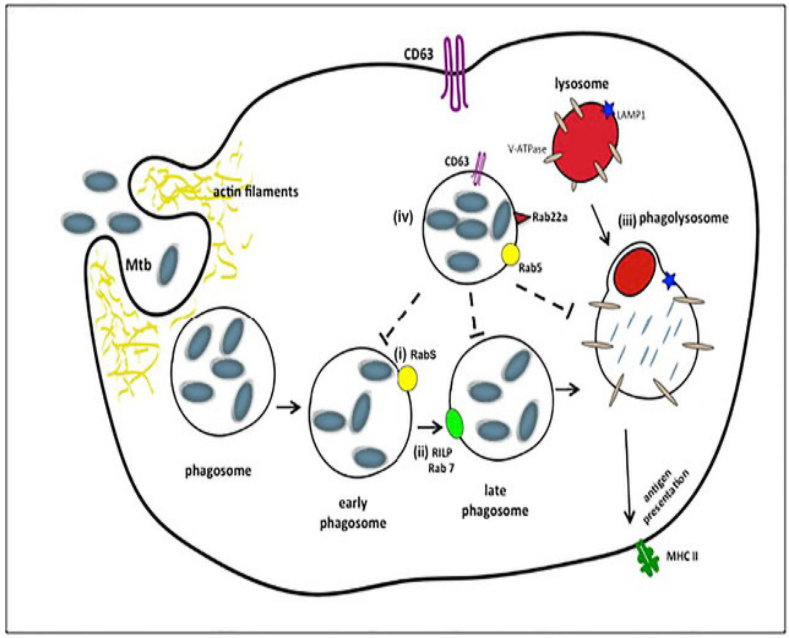


Culture

- *M. tuberculosis* can be grown in the laboratory. Compared to other commonly studied bacteria, *M. tuberculosis* has a remarkably slow growth rate, doubling roughly once per day.
- Commonly used media include liquids such as Middlebrook 7H9 or 7H12, egg-based solid media such as Lowenstein-Jensen, and solid agar-based such as Middlebrook 7H11 or 7H10.
- Visible colonies require several weeks to grow on agar plates. It is distinguished from other mycobacteria by its production of catalase and niacin. Other tests to confirm its identity include PCR or gene probes .

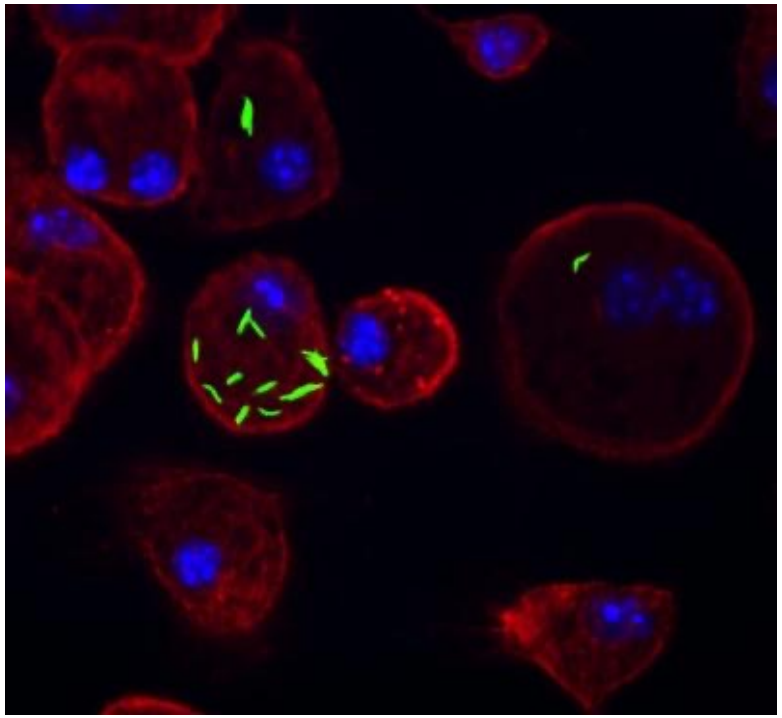
Pathophysiology

- Humans are the only known reservoirs of *M. tuberculosis*.
- major spread is through air droplets from a person who has the disease either coughing, sneezing or speaking.
- When in the lungs, *M. tuberculosis* is phagocytosed by alveolar macrophages, but they are unable to kill and digest the bacterium. Its cell wall inhibits the fusion of the phagosome with the lysosomes.
- In addition, production of the diterpene isotuberculosinol prevents maturation of the phagosome.
- Mutations in genes involved in the specific biosynthetic pathways resulting in normal development of the phagosome and reduction of mycobacterial infection.

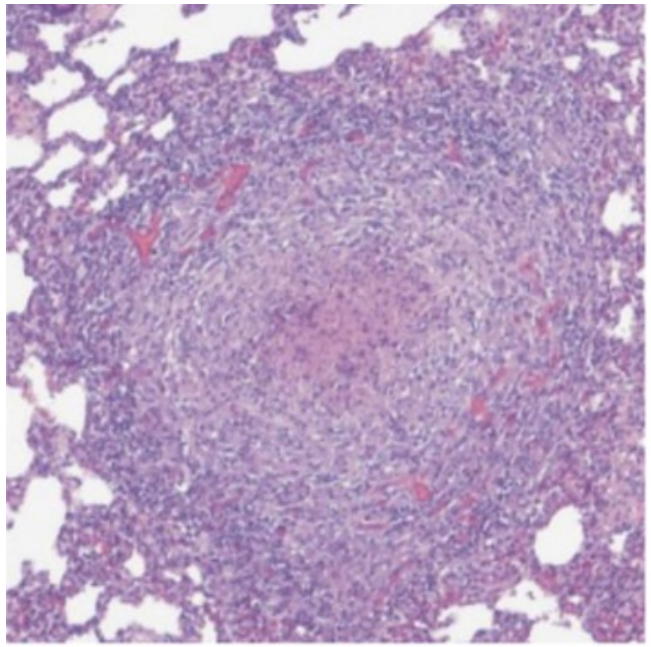


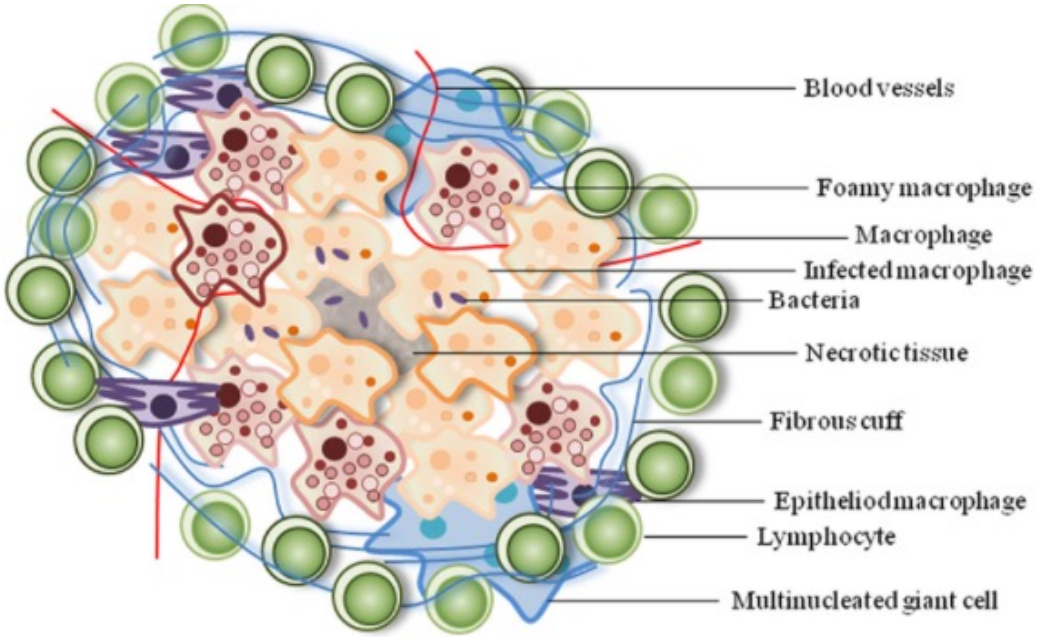
- In M.tuberculosis infection, the PPM1A protein levels were found to be upregulated , as PPM1A inhibits the intrinsic and extrinsic apoptotic pathways.

- As a result of having apoptosis being suppressed, it provides *M. tuberculosis* with a safe replicative niche, and so the bacteria are able to maintain a latent state for a prolonged time.

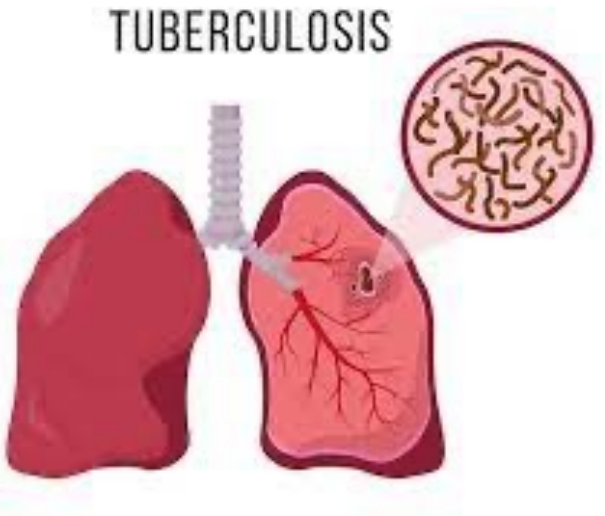


- Granulomas, organized aggregates of immune cells, are a hallmark feature of tuberculosis infection.
- Granulomas play dual roles during infection: they regulate the immune response and minimize tissue damage, but also can aid in the expansion of infection.



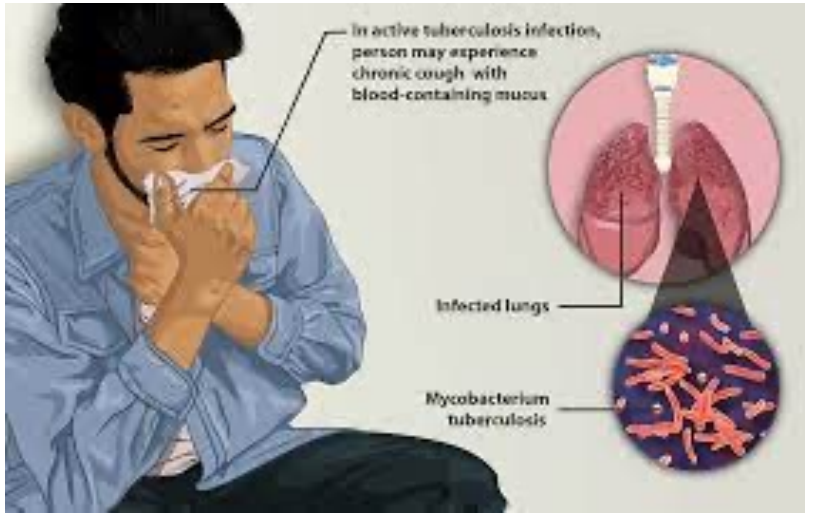


- one of virulence factors is cord factor (is a glycolipid molecule found in the cell wall of *Mycobacterium tuberculosis*), which serves to increase survival within its host.
- In addition, pre-existing first-line TB drugs such as rifampicin and streptomycin have decreased efficiency in clearing intracellular *M. tuberculosis* due to not being able to effectively penetrate the macrophage niche.



Symptoms

- Symptoms of *M. tuberculosis* include coughing that lasts for more than three weeks, hemoptysis (cough with blood or bloody mucus), chest pain when breathing or coughing, weight loss, fatigue, fever, night sweats, chills, and loss of appetite.
- *M. tuberculosis* also has the potential of spreading to other parts of the body.
- This can cause blood in urine if the kidneys are affected, and back pain if the spine is affected



Antibiotic resistance

- *M. tuberculosis* is a clonal organism and does not exchange DNA via horizontal gene transfer
- the emergence and spread of antibiotic resistance in *M. tuberculosis* poses an increasing threat to global public health
- Multidrug-resistant Tuberculosis (MDR-TB) is characterised by resistance to at least the two front-line drugs isoniazid and rifampin
- Isoniazid and rifampin resistance are tightly linked, with 78% of the reported rifampin-resistant TB cases in 2019 being resistant to isoniazid as well
- Rifampin-resistance is primarily due to resistance-conferring mutations in the rifampin-resistance determining region (RRDR) within the rpoB gene

- Isoniazid function occurs through the inhibition of mycolic acid synthesis by its binding to a protein encoded by the *inhA* gene.
- As a result, isoniazid resistance is primarily due to mutations within *inhA* gene.
- MDR in *M. tuberculosis* becomes increasingly common, and led to the emergence of extensively drug resistant (XDR-) TB which considered as a public health crises.
- XDR-TB is characterised by resistance to both rifampin and Isoniazid, as well second-line fluoroquinolones and at least one additional front-line drug.

Treatment

- Person with TB disease will probably be treated with a combination of antibacterial medications for a period of six to 12 months.
- The most common treatment for active TB is isoniazid in combination with three other drugs—rifampin, pyrazinamide and ethambutol.
- Patient may begin to feel better only a few weeks after starting to take the drugs but treating TB takes much longer than other bacterial infections.

- Patient must continue taking his medication as prescribed for the entire time his doctor indicates or he could get sick again, have a harder time fighting the disease in the future and spread the disease to others.
- Not completing the entire course of medication could also contribute to drug-resistant TB which takes much longer, 20 to 30 months to complete.

Vaccine

- The BCG vaccine (bacille Calmette-Guerin), which was derived from *M. bovis,* while effective against childhood and severe forms of tuberculosis.
- However It has limited success in preventing the most common form of the disease today