Patohisiologi Tuberkulosis Terkini. Perspektif Fisiologi

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Current update & potentials of Tuberculosis Therapy

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01

Introduction & Brief History of Tuberculosis

- In 1882, Robert Koch identified the tubercle bacillus, also known as *Mycobacterium tuberculosis* (*M. tb*), as the etiologic agent of tuberculosis (TB). Since his discovery, the TB epidemic seems to be unabated, spreading in every corner of the globe.
- TB is **highly contagious airborne disease** and one of the top causes of death worldwide.
- **M. tb can stay dormant** for years and persist in the body without any indication of illness, in which many people become asymptomatic carriers.





Alsayed SSR, Gunosewoyo H. Tuberculosis: Pathogenesis, Current Treatment Regimens and New Drug Targets. Int J Mol Sci. 2023;24(6).





02

Epidemiology

Estimated number of incident TB cases in 2023, for countries with at least 100 000 incident cases^a



* The labels show the eight countries that accounted for about two thirds of the global number of people estimated to have developed TB in 2023.

World Health Organization. Global tuberculosis report. 2024.





Epidemiology

Global TB statistics



M. tb infection worldwide

their lifespan



- 2 billion people harbour a dormant form of
- 5 10% of latently infected individuals are predisposed to developing active TB in
- HIV co-infection increases the risk of TB reactivation by 18 times
- around 10 million people fall ill with TB every year at least since 2000
- > 1 million people succumb to death from TB every year at least since 2000



Epidemiology

Global estimates of TB incidence disaggregated by age group and sex (female in purple; male in orange), 2023



Top 15 causes of death worldwide in 2021^{a,b}

Deaths from TB among people with HIV are shown in grey.

- Ischaemic heart disease COVID-19 Stroke Chronic obstructive pulmonary disease Lower respiratory infections Trachea, bronchus, lung cancers Alzheimer disease and other dementias Diabetes mellitus **Kidney diseases** Tuberculosis Hypertensive heart disease Cirrhosis of the liver Diarrhoeal diseases Road injury Colon and rectum cancers
- * This is the latest year for which estimates for all causes are currently available. See WHO estimates, available at https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death.

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^b Deaths from TB among people with HIV are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.





Centers for Disease Control and Prevention National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention



Alsayed SSR, Gunosewoyo H. Tuberculosis: Pathogenesis, Current Treatment Regimens and New Drug Targets. Int J Mol Sci. 2023;24(6). CDC. Module 1-Transmission and Pathogenesis of Tuberculosis. Self-Study Modul Tuberc. 2019;1–32.



Pathophysiology 03



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Innate immune

(Bacterial engulfment in macrophage)

Recruitment of new macrophages and multiplication and spread of the bacteria therein, expanding the infection. More immune cells also arrive (e.g. lymphocytes and neutrophiles) to the infection site.

Innate lymphocytes

(Early stages of granuloma)

Current update & potential of TB Therapy

M.tb induces the macrophage to express and secrete VEGF into the extracelluar space.

Angiogenesis >> Monocytes accumulation

Macrophage recruitment>>

Inflammation >>>

05

Anti-VEGF therapy seems promising as an adjuvant therapy for tuberculosis





Conclusion

- There are many steps in the pathophysiology of tuberculosis.
- Unique character of M. tb are related to the structure of the cell wall and biomolecular mechanism when inside the macrophage
- Anti-VEGF treatments offer an avenue that has only yet seen brief exploration in humans with a drug exclusive to the A isoform of VEGF (bevacizumab).



Reference

1. Alsayed SSR, Gunosewoyo H. Tuberculosis: Pathogenesis, Current Treatment Regimens and New Drug Targets. Int J Mol Sci. 2023;24(6). 2. World Health Organization. 2024 Global tuberculosis report. 2024. 3. Maison DP. Tuberculosis pathophysiology and anti-VEGF intervention. J Clin Tuberc Other Mycobact Dis [Internet]. 2022;28(May):100318. Available from: https://doi.org/10.1016/j.jctube.2022.100318 4. CDC. Module 1-Transmission and Pathogenesis of Tuberculosis. Self-Study Modul Tuberc. 2019;1–32.



