# TRANSMISSION AND PATHOGENESIS OF TB

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# Outline

- Historical Aspects of TB
- TB Transmission and Infectiousness
- Pathogenesis (what happens after exposure)
- TB Infection vs TB disease
- Risk factors for progression to disease
- TB Classification system

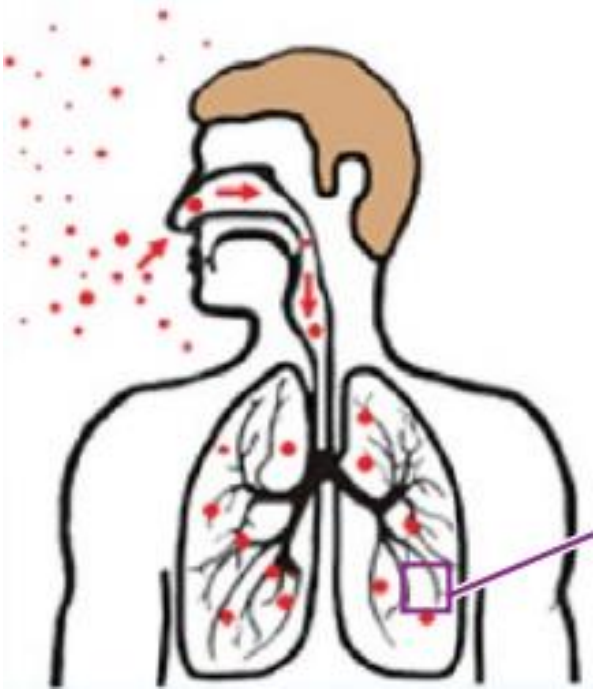
# Historical Background s

- TB has coevolved with its human host: Ancient ancestor of M. tuberculosis is hypothesized to have infected hominids in East Africa 3 million years ago.
- There is evidence of spinal TB in Neolithic, pre-Columbian, and early Egyptian remains.
- Became major problem during the Industrial Revolution due to crowded living conditions.
- In the 17th and 18th centuries, **TB caused one-fourth of all adult deaths in Europe**

Gutierrez MC, Brisse S, Brosch R et al. Ancient origin and gene mosaicism of the progenitor of Mycobacterium tuberculosis. PLoS Pathog. 2005
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases
Bedeir, S.A. (2004). Tuberculosis in Ancient Egypt. In: Madkour, M.M. (eds) Tuberculosis. Springer, Berlin, Heidelberg

# TB Transmission

- Airborne transmission: M. tuberculosis is carried in particles of 1–5 microns in diameter
- Infectious droplet nuclei are generated by coughing, shouting, or singing.
- Particles can remain suspended in the air for several hours.
- Transmission occurs when the droplet nuclei reach the alveoli of the lungs
- No transmission by surface contact.



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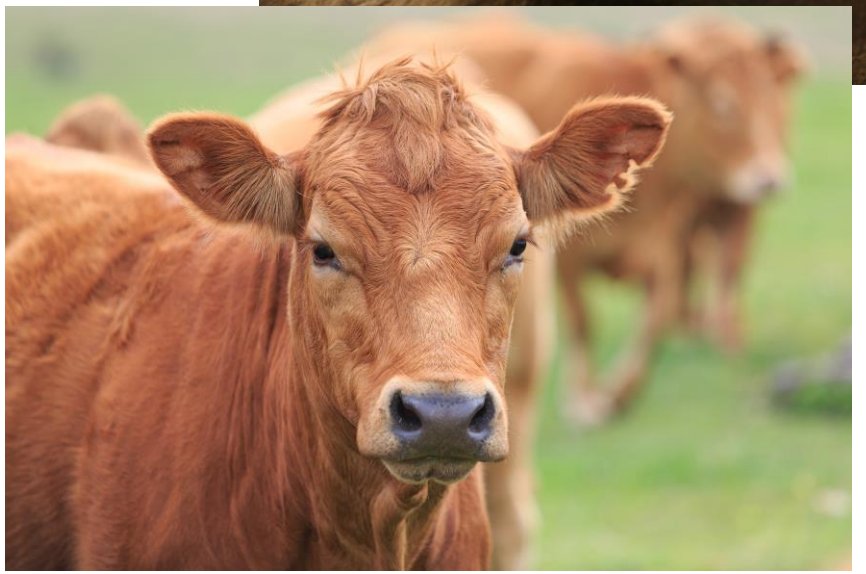
# TB Transmission

- Rarely:
  - Contact with infected animals/consumption of unpasteurized dairy: M. Bovis
  - Skin inoculation: Laboratory workers
  - Organ transplantation



# Which of the following is the most likely way to acquire TB infection?

- A. Direct contact with surfaces contaminated by TB
- B. Transient contact with an individual with TB disease outdoors
- C. A long period of close contact with a person with TB disease in a poorly ventilated space
- D. Drinking pasteurized milk

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# Which of the following plays a role in TB transmission

- A. AFB sputum smear positivity in an individual with TB disease
- B. The strength of the exposed person's immune system
- C. The space in which the exposure takes place
- D. The duration of the exposure
- E. All of the above

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# Which of the following scenarios is most likely to facilitate TB transmission

- A. A person with non-cavitary, sputum smear-negative TB disease who has not started TB treatment
- B. A person with non-cavitary, sputum smear-positive TB disease who has received 5 days of TB treatment
- C. A person with cavitary, sputum smear-positive TB disease who has received 5 days of TB treatment
- D. A person with cavitary, sputum smear-positive TB disease who has received 2 weeks of TB treatment
- E. Need more information about the exposed individuals and the nature of the exposure

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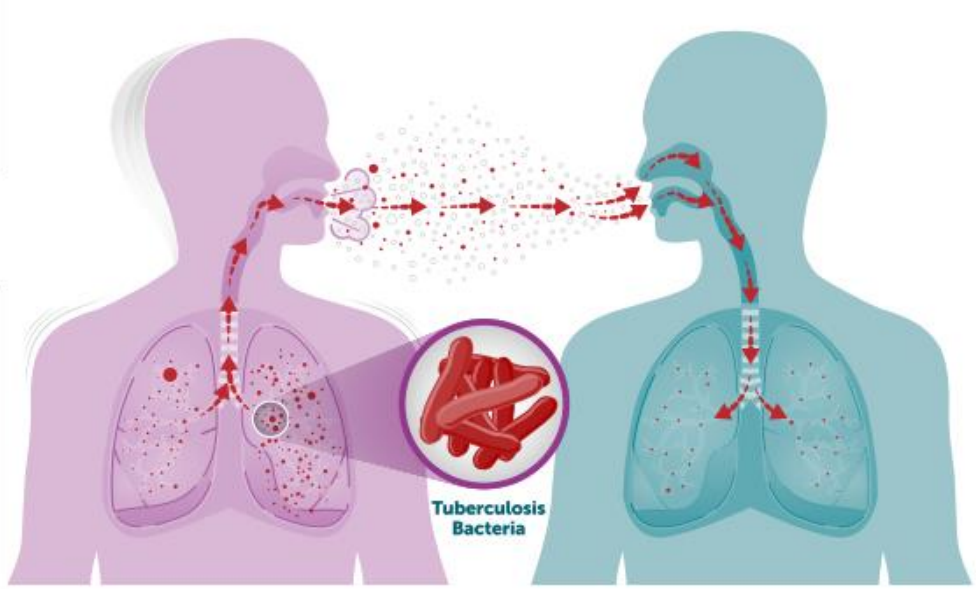
# Likelihood of Transmission:

- The infectiousness of the person with TB
  - Cavitations & smear positivity increase risk
  - Children are typically less infectious
- The susceptibility of the exposed
  - Weakened immune system, younger age (<5 yr)
- The environment where exposure takes place
  - Small/closed/poorly ventilated spaces increase risk
- The nature of the exposure
  - Duration, frequency, and physical proximity

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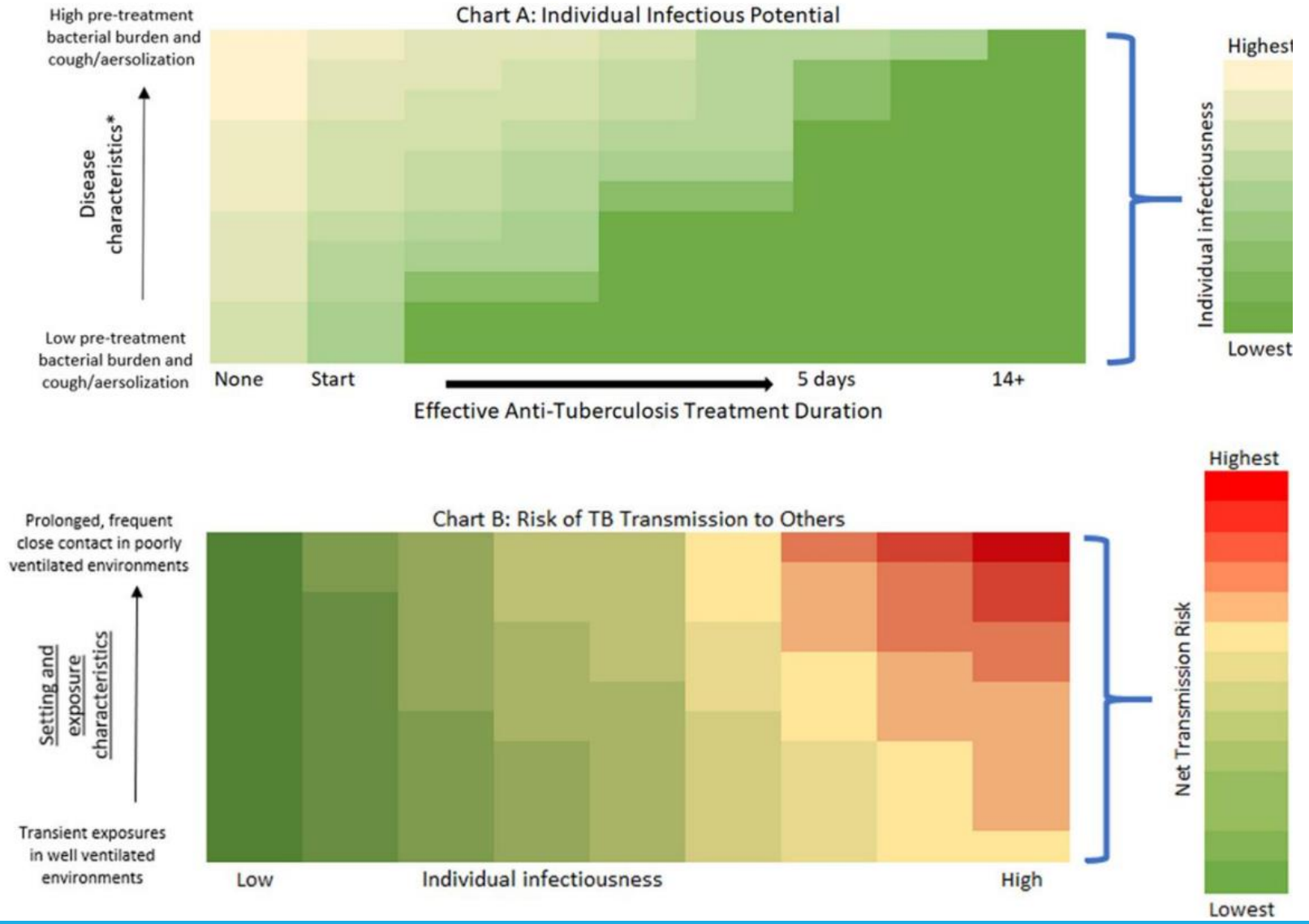
# Infectiousness and Transmission

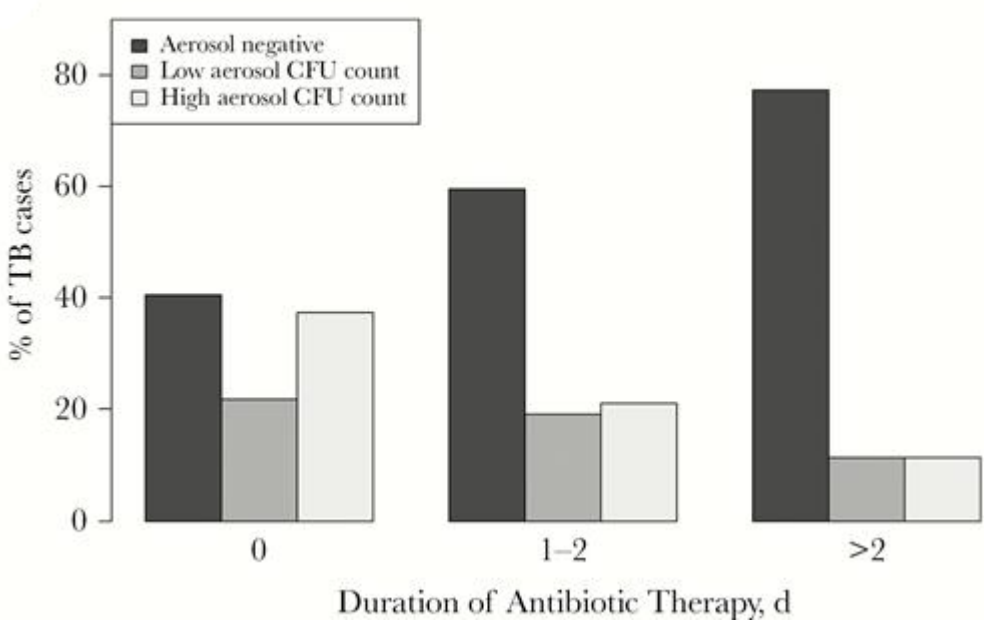



Shah M et al. NTCA Guidelines for Respiratory Isolation and Restrictions to Reduce Transmission of Pulmonary Tuberculosis in Community Settings. CID. 2024

# Impact of TB disease treatment

- Infectiousness declines rapidly within 2-3 days after initiation of anti-TB therapy
- Declines further for every additional day of treatment
- Smear positivity did not correlate with ability to culture M. TB from sputum or with infectiousness
- Odds ratio for aerosol positivity was
  - 2.56 (P = .03) for those with 1–2 days of therapy, and
  - 5.5 (P < .001) for those without treatment

  All compared to those who completed more than 2 days of TB disease treatment




Acuña-Villaorduña C et al. Host Determinants of Infectiousness in Smear-Positive Patients With Pulmonary Tuberculosis. Open Forum Infect Dis. 2019

*Clinical Infectious Diseases*

GUIDELINES

# National Tuberculosis Coalition of America (NTCA) Guidelines for Respiratory Isolation and Restrictions to Reduce Transmission of Pulmonary Tuberculosis in Community Settings

**Maunank Shah,[1] Zoe Dansky,[1] Ruvandhi Nathavitharana,[2] Heidi Behm,[3] Shaka Brown,[4] Lana Dov,[5] Diana Fortune,[6] Nicole Linda Gadon,[4] Katelynne Gardner Toren,[7] Susannah Graves,[8] Connie A. Haley,[9] Olivia Kates,[1,10] Nadya Sabuwala,[11] Donna Wegener,[12] Kathryn Yoo,[13] and Joseph Burzynski[14]; on Behalf of the National TB Coalition of America**

[1]Division of Infectious Diseases, Department of Medicine, Johns Hopkins University, School of Medicine, Baltimore, Maryland, USA; [2]Division of Infectious Diseases, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, USA; [3]TB Program, Oregon Health Authority, Portland, Oregon, USA; [4]We Are TB, Stop TB USA, Atlanta, Georgia, USA; [5]Washington State Department of Health, Shoreline, Washington, USA; [6]National Tuberculosis Coalition of America, National TB Nurse Coalition, Atlanta, Georgia, USA; [7]Public Health Seattle and King County Tuberculosis Control Program, Seattle, Washington, USA; [8]San Francisco Department of Public Health, San Francisco, California, USA; [9]Division of Infectious Diseases, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA; [10]Berman Institute of Bioethics, Johns Hopkins University, Baltimore, Maryland, USA; [11]Minnesota Department of Health, St. Paul, Minnesota, USA; [12]National TB Coalition of America, Atlanta, Georgia, USA; [13]Texas Department of State Health Services, Tuberculosis and Hansen's Disease Unit (TXDSHS), Society of Epidemiologists in Tuberculosis Control (SETC), Texas, USA; and [14]New York City Department of Health and Mental Hygiene, New York, New York, USA

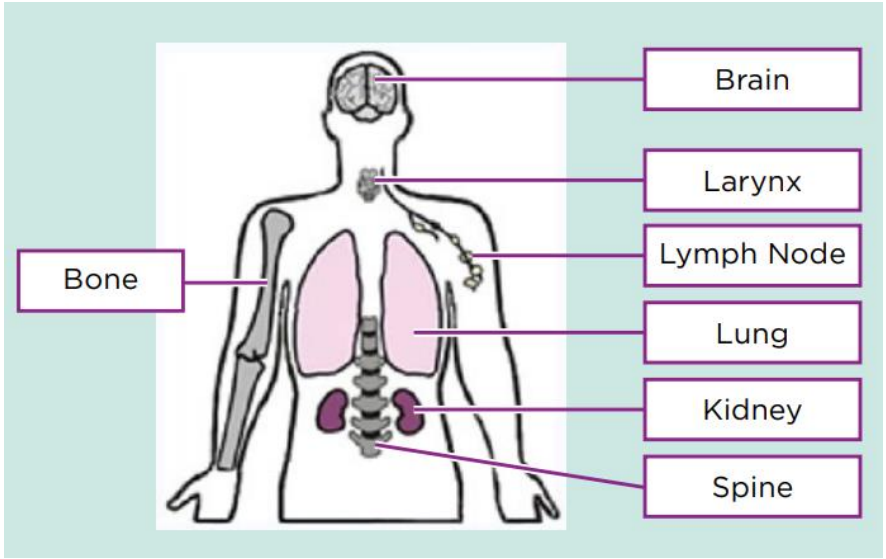
# Isolation recommendations

- Balancing the potential benefits and harm for both the community and people with TB disease
- "PWTB on effective TB disease treatment for at least 5 days should be considered noninfectious or as having a low likelihood of infectiousness, regardless of sputum bacteriologic status, with certain exceptions"
- The 5-day period allows for
  - Assessing adherence and tolerance,
  - Conducting clinical and public health evaluation,
  - Assessing potential exposure to children <5 years and immunosuppressed or other vulnerable populations/high risk environments.

Shah M et al. NTCA Guidelines for Respiratory Isolation and Restrictions to Reduce Transmission of Pulmonary Tuberculosis in Community Settings. CID. 2024

# Pathogenesis

- Once at the alveoli, the M. TB bacilli multiply
- Small number gets into the bloodstream and the lymphatic system, and disseminate to other parts of the lungs and other organs

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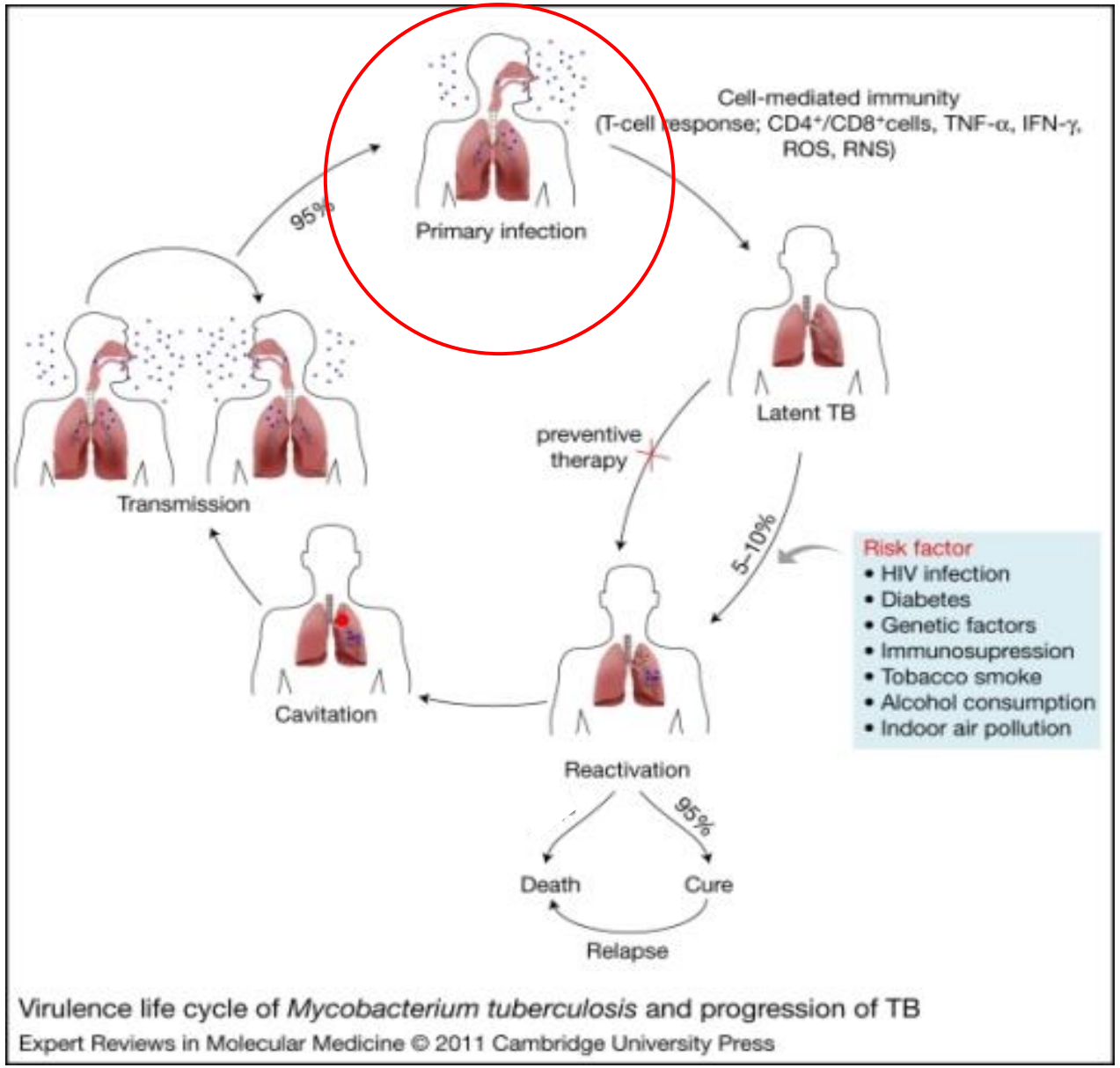
# Pathogenesis

- Primary infection: The Ghon focus and Ranke complex
- lymphohematogenous dissemination
- Bronchial spread
- Within 2-8 weeks, a cell-mediated immune response forms a barrier to lock-in the bacilli (granulomas): (Latent) TB infection
- If that immune response wanes, the bacilli can escape its hold and begin to multiply rapidly: (Active) TB Disease

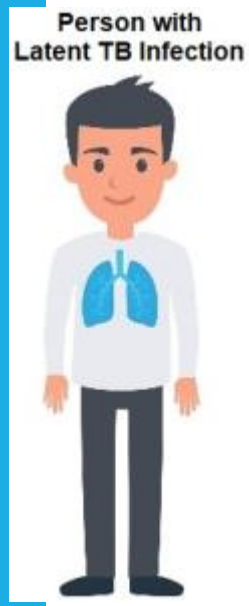


Virulence life cycle of *Mycobacterium tuberculosis* and progression of TB



Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases

# Infection vs Disease

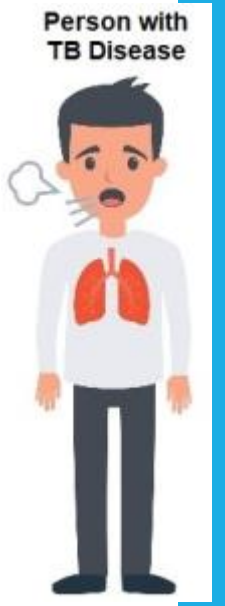



## Persons with TB Infection (LTBI)

- Do not feel sick, no symptoms
- Cannot spread TB to others
- Can have latent TB infection for years
- Have a small amount of TB mycobacteria in their body that are alive but inactive
- Usually have a positive TB blood or skin test
- Should consider treatment for LTBI to prevent TB disease

## Persons with TB Disease

- Usually feel sick, report symptoms
- May be able to spread TB to others
- Have a large amount of active TB mycobacteria in their body
- Usually have a positive TB skin test or TB blood test result indicating TB infection
- Need treatment for TB disease




CDC. TB 101 for Health Care Workers. Lesson 2.

# Which of the following conditions have the highest risk of progression to TB disease

- A. Living with HIV
- B. Diabetes
- C. Cigarette smoking
- D. The first year following infection with M. TB with no history of HIV

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# Risk for Progression to TB Disease

- Living with HIV
- Children younger than 5 years of age
- Recent infection with M. TB (within 2 years)
- Receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids
- History of untreated or inadequately treated TB disease
- Diabetes mellitus
- Weigh less than 90% of their ideal body weight
- Silicosis; chronic renal failure; leukemia; or cancer of the head, neck, or lung
- Prior gastrectomy or jejunoileal bypass
- Cigarette smoking and/or alcohol or drug use

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# Risk for Progression to TB Disease

| Risk Factor | Risk of Developing TB Disease | Description |
|---|---|---|
| **TB infection and no risk factors** | About 10% over a lifetime  | For people with TB infection, **no risk factors**, and no treatment, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime. |
| **TB infection and diabetes** | About 30% over a lifetime  | For people with TB infection, **diabetes**, and no LTBI treatment, the risk is about 30% over a lifetime (3 times as high as those with no risk factors). |
| **TB infection and HIV infection** | About 7% to 10% PER YEAR  | For people with TB infection, **untreated HIV infection** and with no LTBI treatment, the risk is about 7% to 10% PER YEAR, a very high risk over a lifetime. |

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# TB Classification system

| Class | Type | Description |
|---|---|---|
| 0 | No TB exposure— Not infected | •No history of TB exposure and no evidence of M. tuberculosis infection or disease<br>•Negative reaction to TST or IGRA |
| 1 | TB exposure— No evidence of infection | • History of exposure to M. tuberculosis<br>• Negative reaction to TST or IGRA (test given at least 8 to 10 weeks after exposure) |
| 2 | TB infection— No TB disease | • Positive reaction to TST or IGRA<br>• Negative bacteriological studies (smear and cultures)<br>• No clinical or radiographic evidence of active TB disease |
| 3 | TB disease clinically active | • Positive culture for M. tuberculosis **OR**<br>• Positive reaction to TST or IGRA, plus clinical, bacteriological, or radiographic evidence of current active TB disease |
| 4 | Previous TB disease (not clinically active) | • May have past medical history of TB disease<br>• Abnormal but stable radiographic findings<br>• Positive reaction to the TST or IGRA<br>• Negative bacteriologic studies (smear and cultures)<br>• No clinical or radiographic evidence of current active TB disease |
| 5 | TB disease suspected | Signs and symptoms of active TB disease, but medical evaluation **not** complete |

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# THANK YOU!