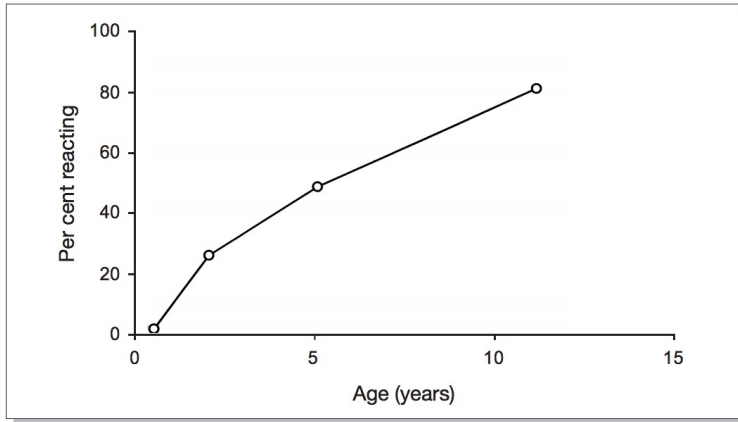


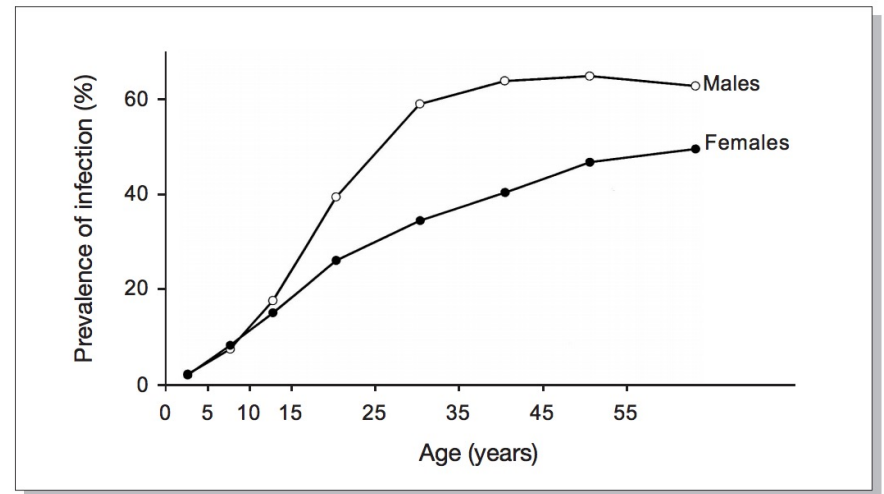
TB in kids

- Age specificity of risk
- Age-specific presentations/clinical features
- Issues with diagnosis/treatment
- Burden and surveillance

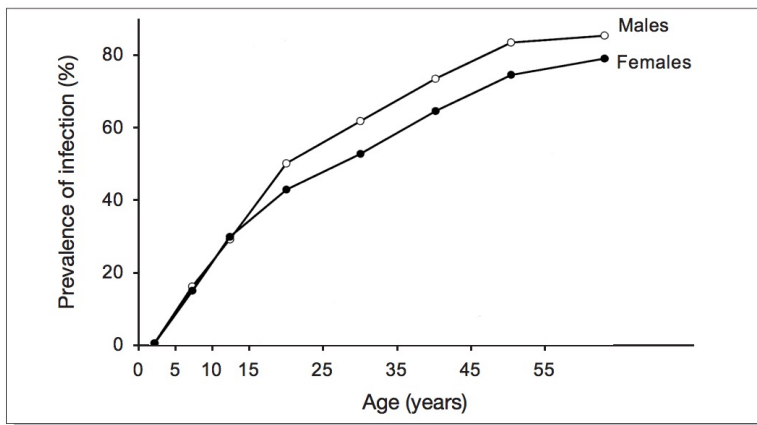
Infection in children



Paris, 1911



India, 1960



Denmark, 1952

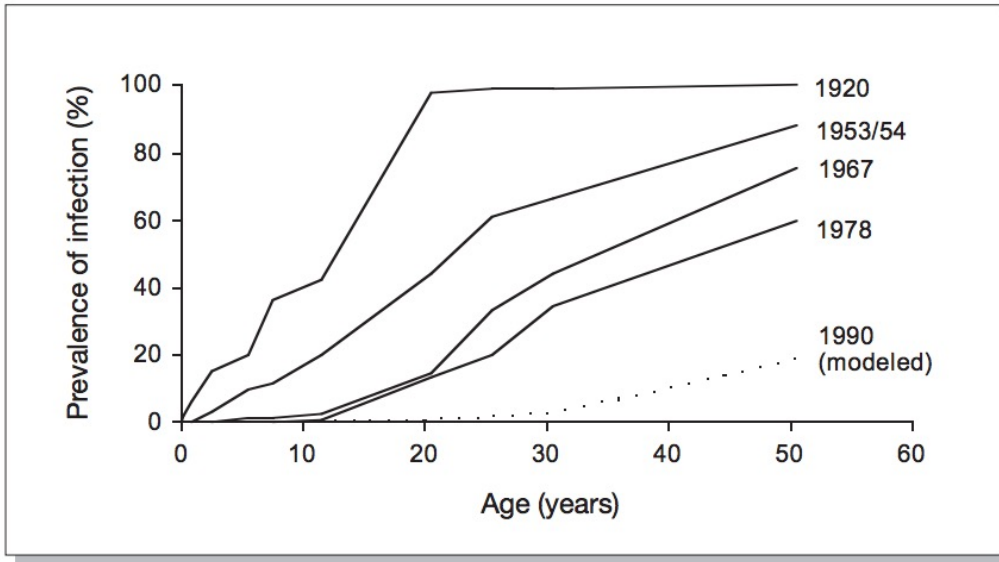


Figure 32. Age-specific prevalence of tuberculous infection in Switzerland from 1920–1990. Data from [104-107].

Decline in TB exposure over time reflected in age distribution.

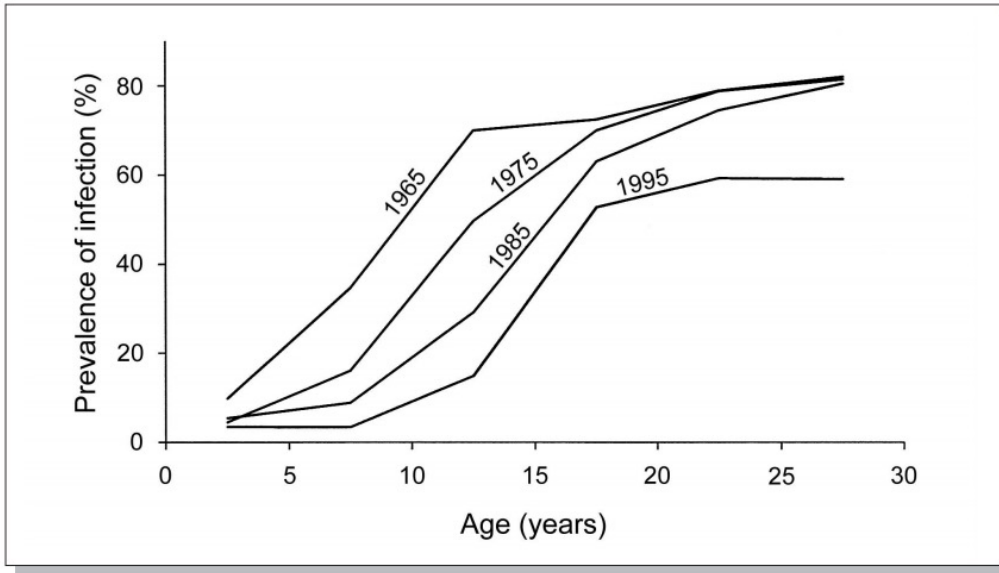


Figure 33. Age-specific prevalence of tuberculous infection, Korea, 1965–1995. Data from [91, 93, 94, 108, 109].

Who infects whom?

- Young children usually infected by HH members while adolescents often infected in community.

Among 60 kids with suspected TB at Houston hospital, 15% of their adult visitors had undetected active TB.

Volume 23, Issue 10 October 2002 , pp. 568-572

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Tuberculosis Among Adult Visitors of Children With Suspected Tuberculosis and Employees at a Children's Hospital

Flor M. Muñoz ^(a1), Lydia T. Ong ^(a2), Diane Seavy ^(a3), Denise Medina ^(a3), Armando Correa ^{(a2) (a3)} and Jeffrey R. Starke ^{(a2) (a3)} 

(a1) Departments of Molecular Virology and Microbiology and Pediatrics, Baylor College of Medicine, Houston, Texas

(a2) Department of Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, Texas

(a3) Infection Control, Texas Children's Hospital, Houston, Texas

Disease progression

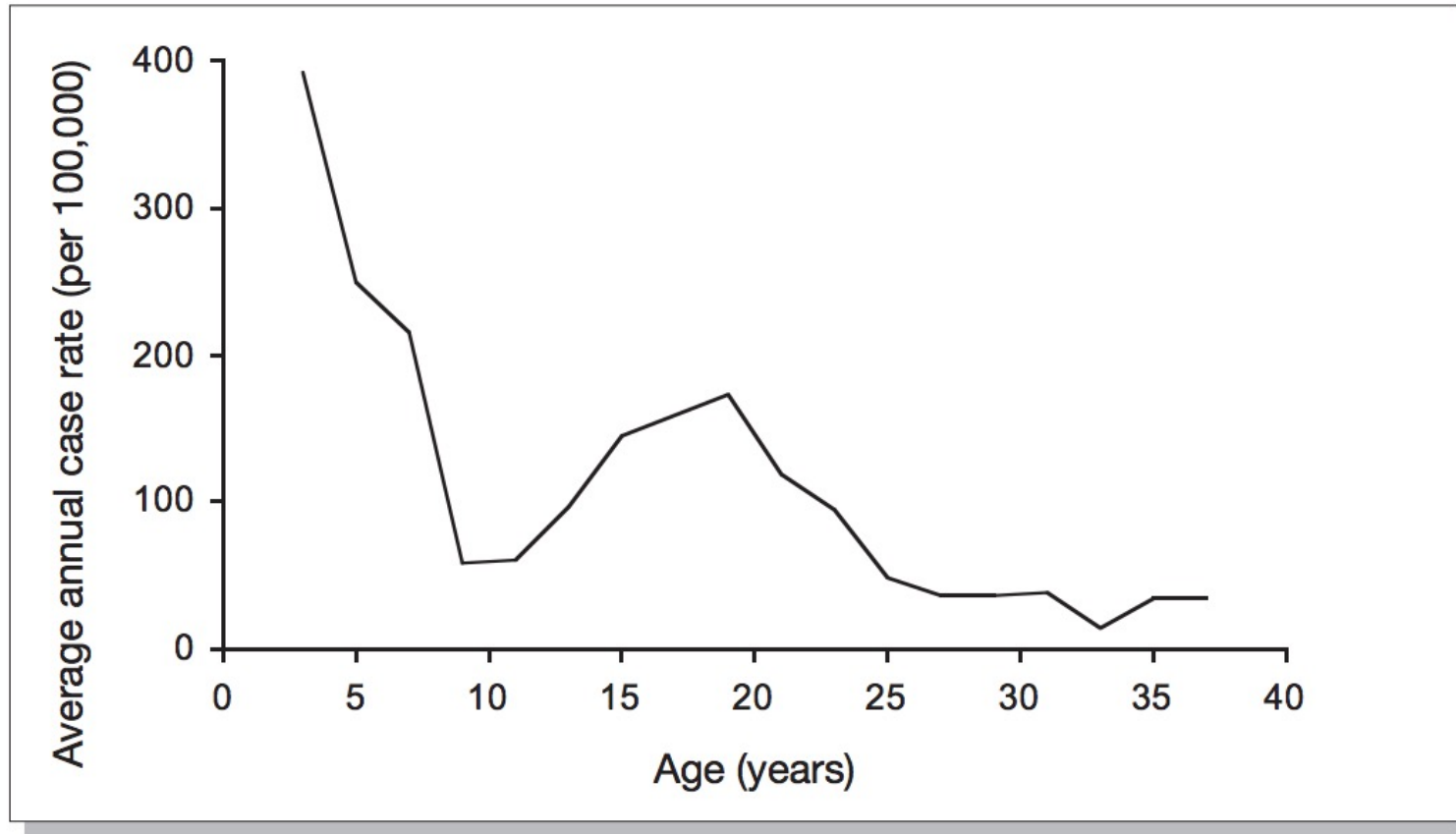


Figure 58. Incidence of tuberculosis among initial reactors to tuberculin by age when tuberculosis was first diagnosed. Figure reproduced with the permission of the American Journal of Epidemiology from [136].

How does that translate into incidence?

N=21,223

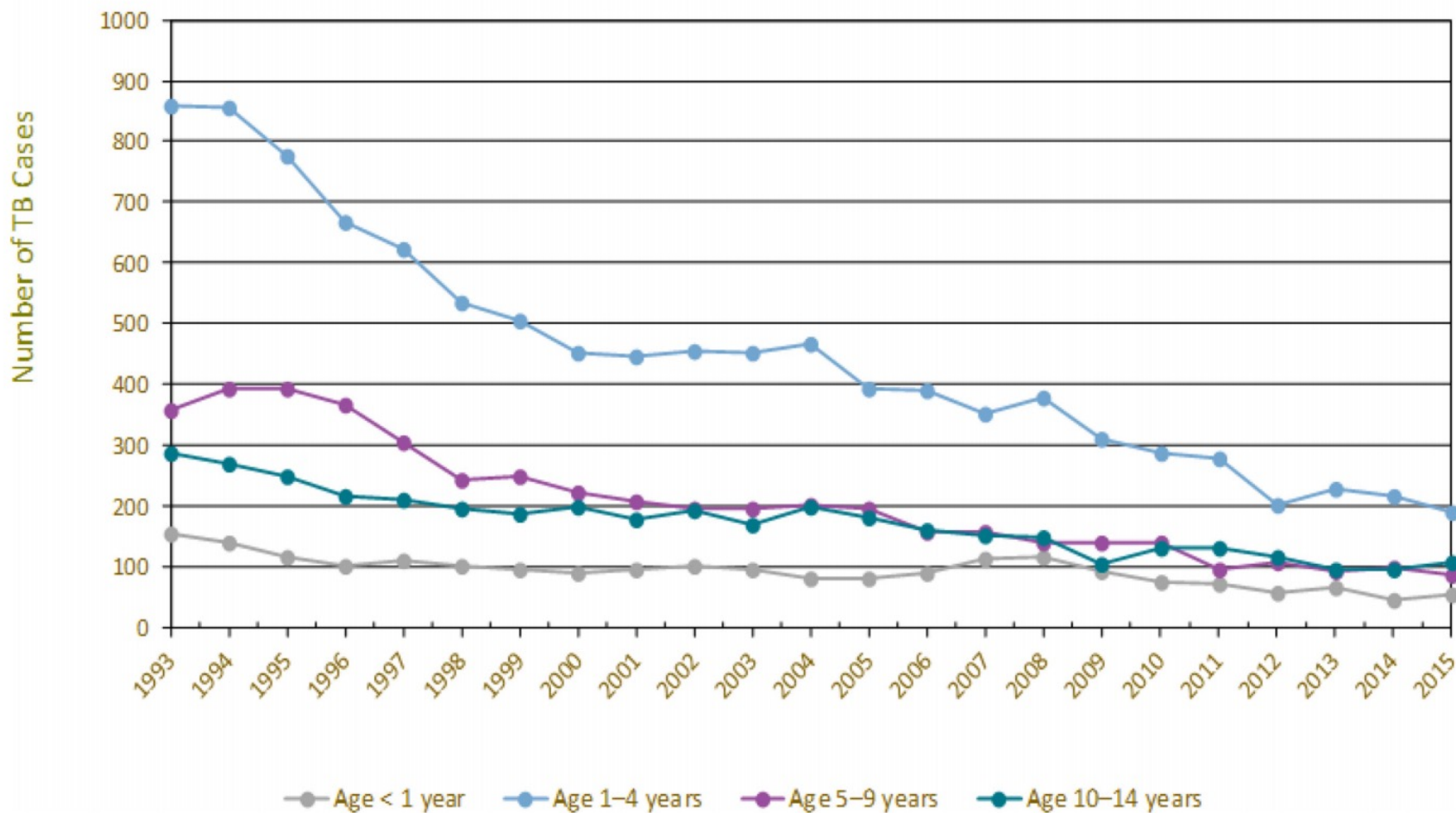
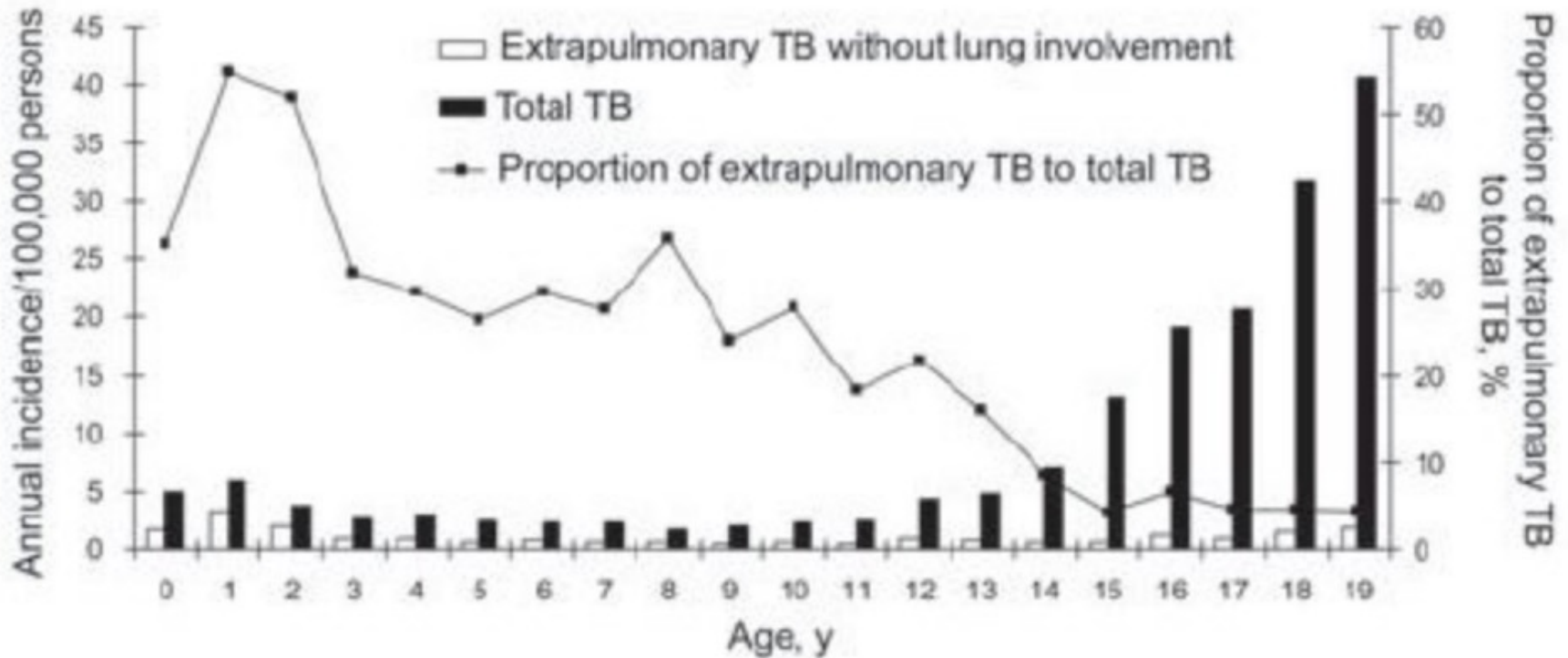


FIGURE 1 Tuberculosis (TB) case rates by age group for children, 1993 to 2015. (Data in the public domain, courtesy of the CDC.)

Age 0-4: Extra-pulmonary



Infected through respiratory route

Primary complex at site of initial infection

Hypersensitivity response may include fever, TST or IGRA conversion

Regional LN enlarged

Parenchymal lesion heals (calcification) or expands (pneumonitis)

Hematogenous and lymphatic spread**

Most common sites: apices of lung, liver, spleen, peritoneum, meninges, lymph nodes, bone.

Or disseminated in “miliary pattern.”

LNs may become calcified but viable TB present.

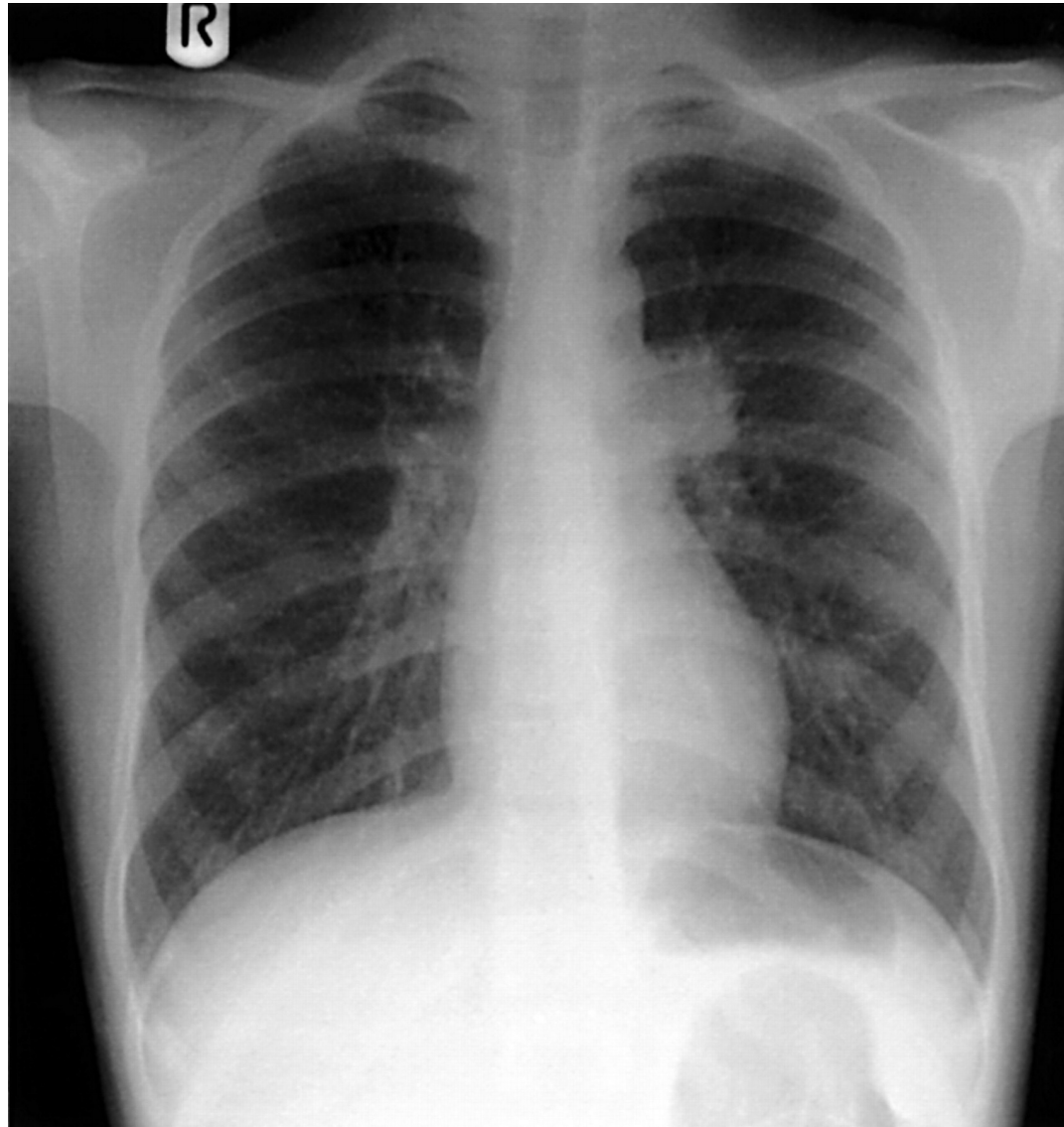
LN enlargement may encroach on bronchi with hyperinflation followed by collapse and consolidation.

Can lead to endobronchial TB or fistula.

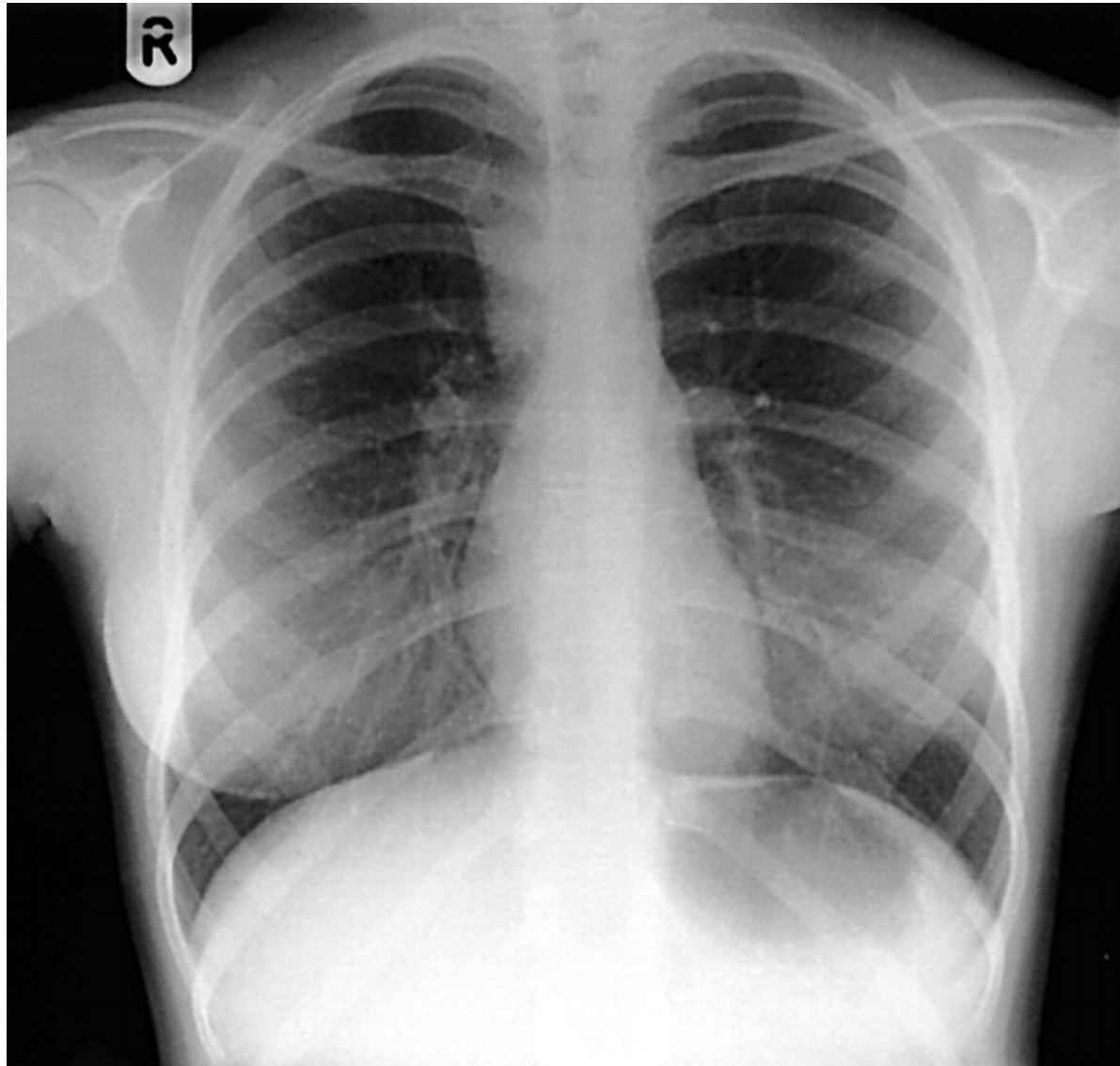


Miliary TB

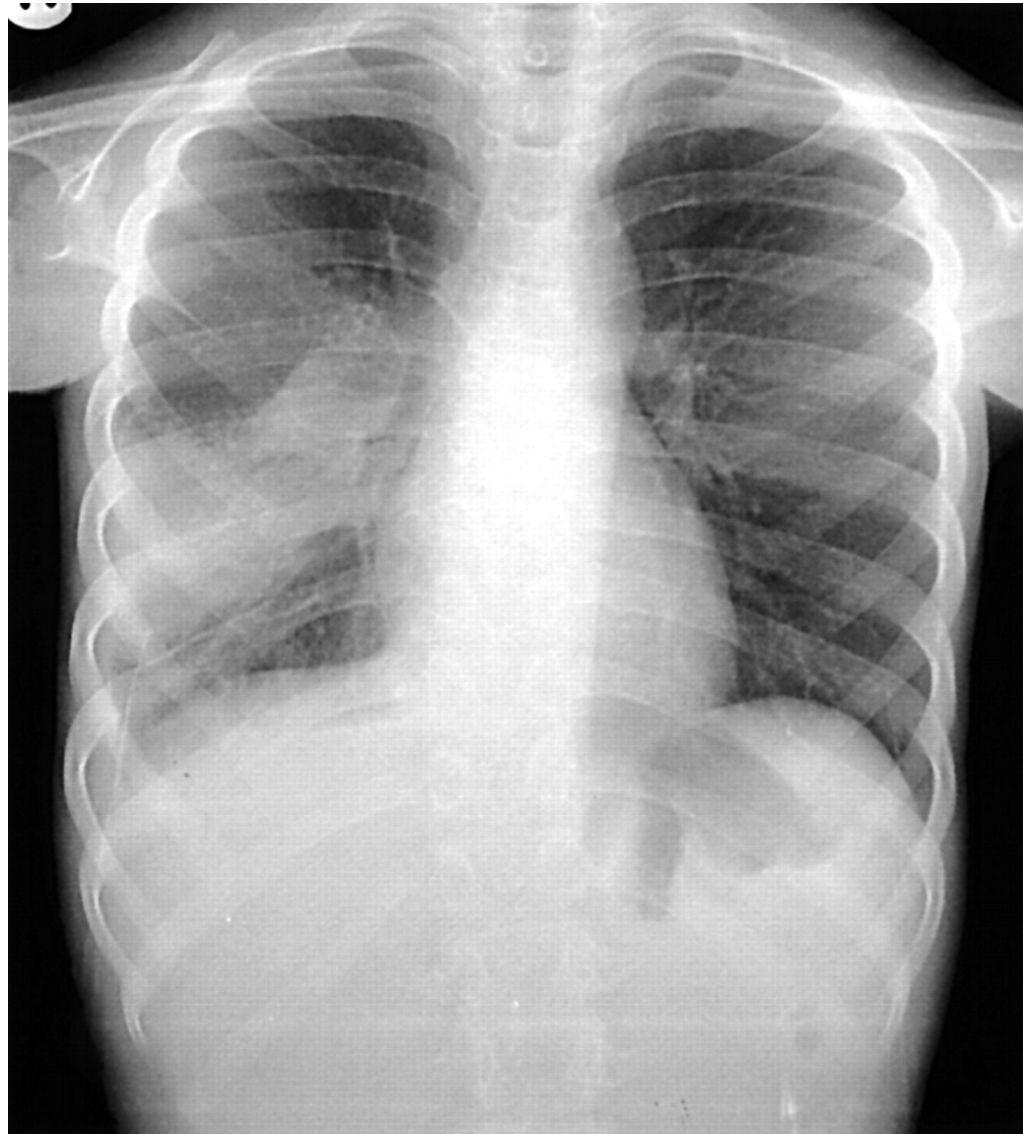
Hilar tuberculosis: there is a prominent node in the left hilum of the lung.



Paratracheal tuberculosis: there is a right paratracheal swelling the normal distance between trachea and the right lung being about 1 cm.



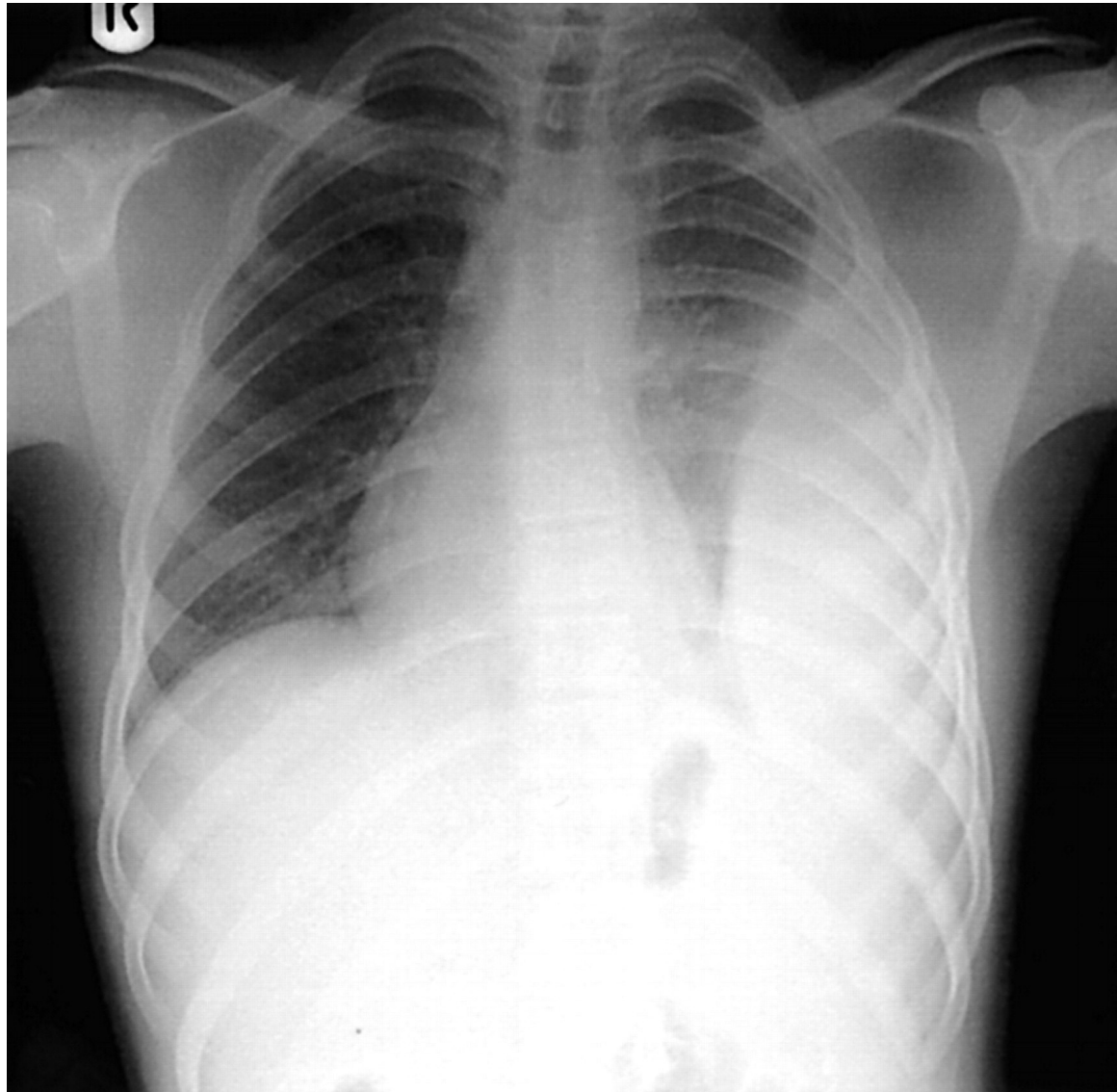
Collapse/consolidation: there is a large right hilar mass with collapse consolidation of the lateral segment of the right middle lobe.

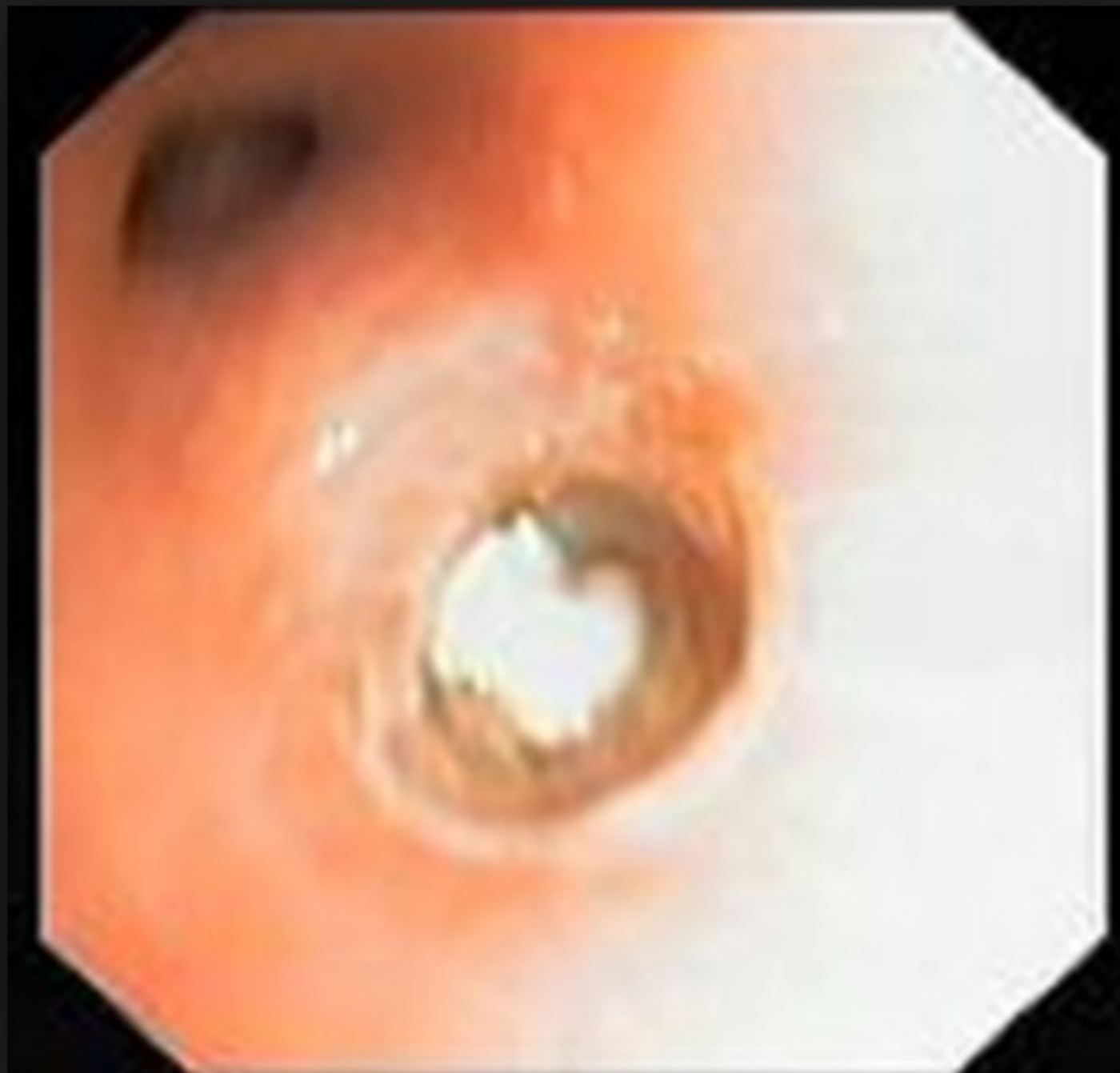


Partial bronchial obstruction: there is a large right hilar and superior mediastinal mass with shadowing in the right upper zone.



Pleural tuberculosis: there is a large left pleural effusion with some mediastinal shift.





Main sites of Extrapulmonary tuberculosis

Central nervous system

- Meningitis

Lymphatics

- Scrofula (of the neck)

Pleura

- Tuberculosis
pleurisy

Disseminated

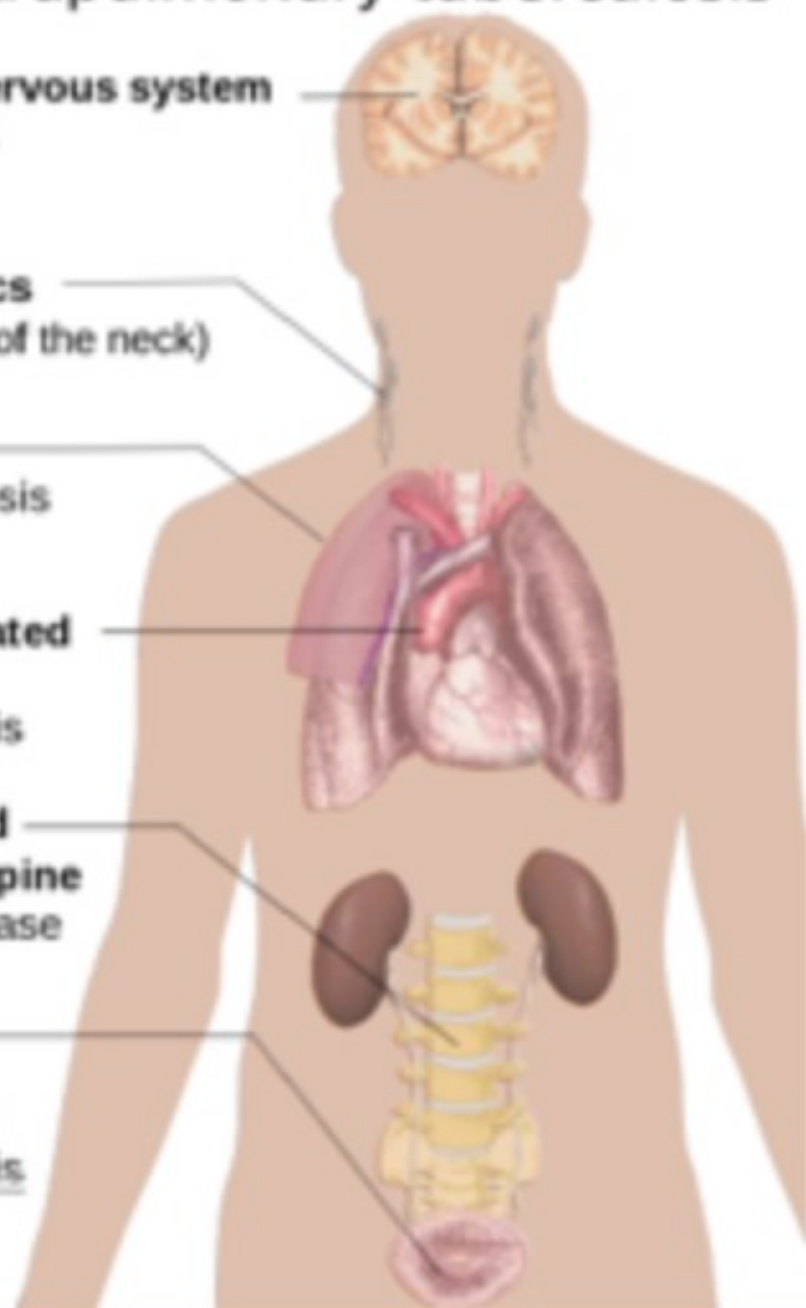
- Miliary
tuberculosis

**Bones and
joints of spine**

- Pott's disease

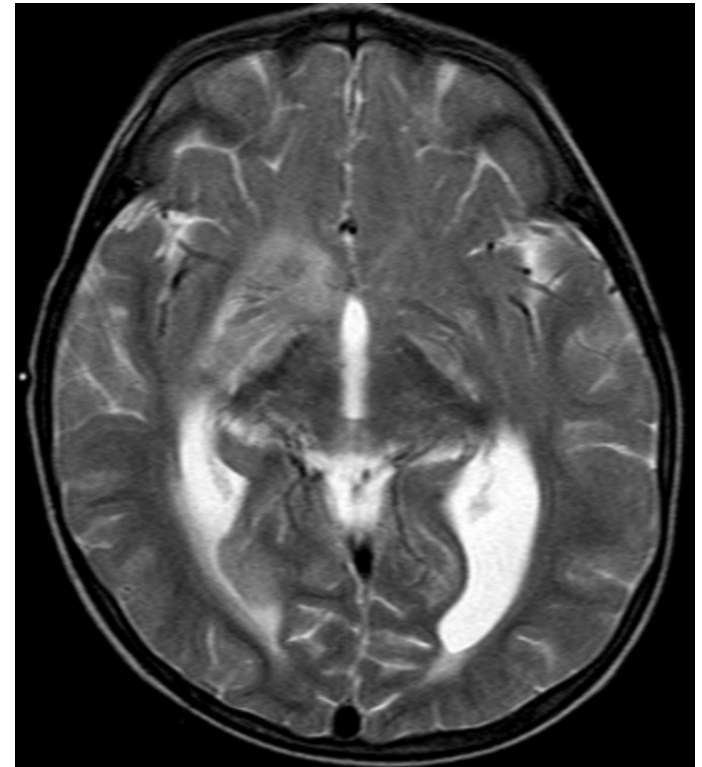
**Genito-
urinary**

- Urogenital
tuberculosis



TB meningitis

- Challenging to diagnose as non-specific: AFB and GE negative, many TST and IGRA neg.
- Similar to other meningitides
 - CN involvement
 - Infarcts
 - Peak age 2-4
- High mortality (50%)
- High rates long term sequelae (75%)
- Can be followed by tuberculoma



Lymphadenitis

Very common presentation in India and other high burden countries. Immigrants from S. Asia 11X increased rate.

Usually painless swelling that ultimately drains. Some fever and weight loss.

Diagnosed by Excisional biopsy or FNA (less accurate) with micro confirmation.

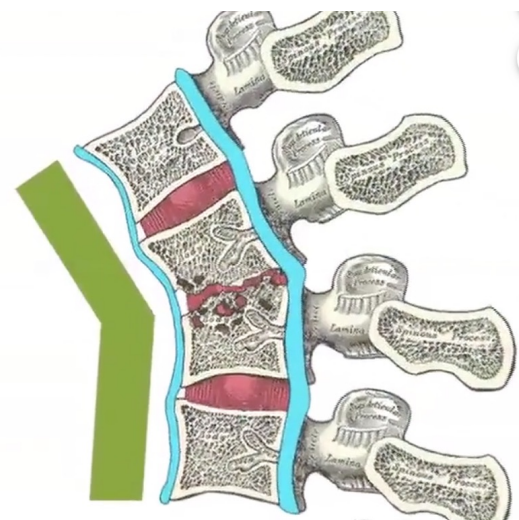
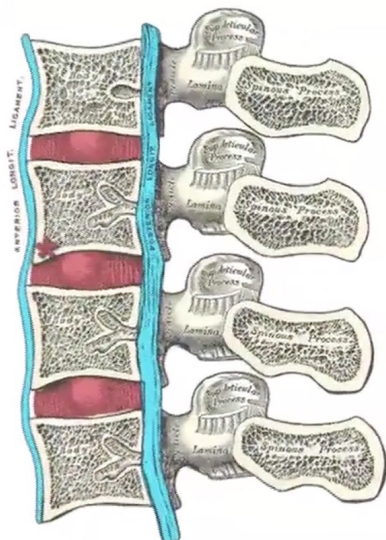
Treatment followed by PUR (paradoxical upgrading reaction) in up to 23%.



Pleural TB

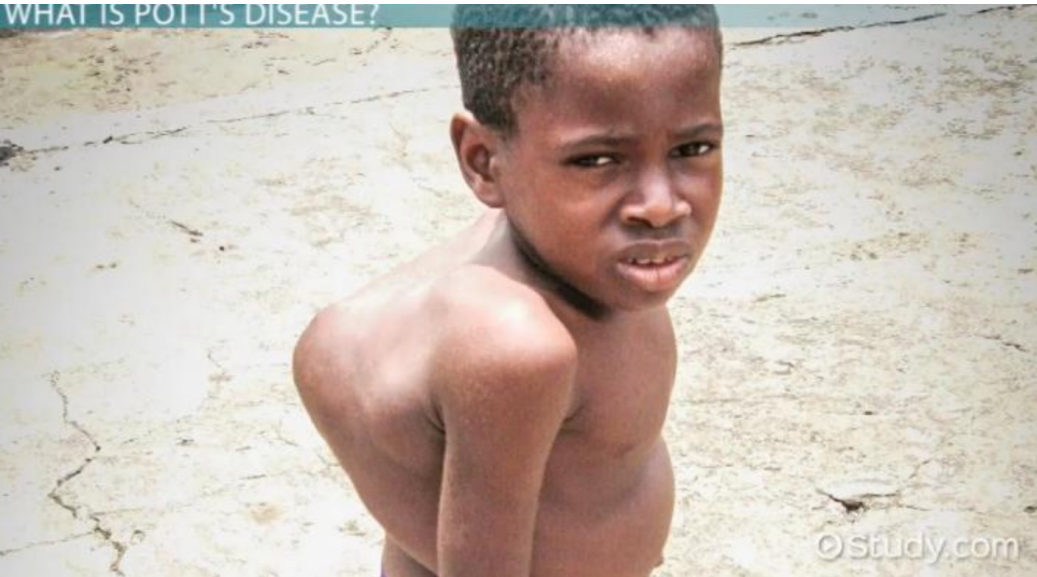
- Sub-pleural focus ruptures into pleural space and elicits a hypersensitivity reaction.
- Common in age 12-17.
- Few bacilli in lesion.
- Pleural fluid high protein, lymphocyte, ADA?
- Micro usually negative but IGRA on pleural fluid promising.
- 70-80% + TST.

Pott's disease

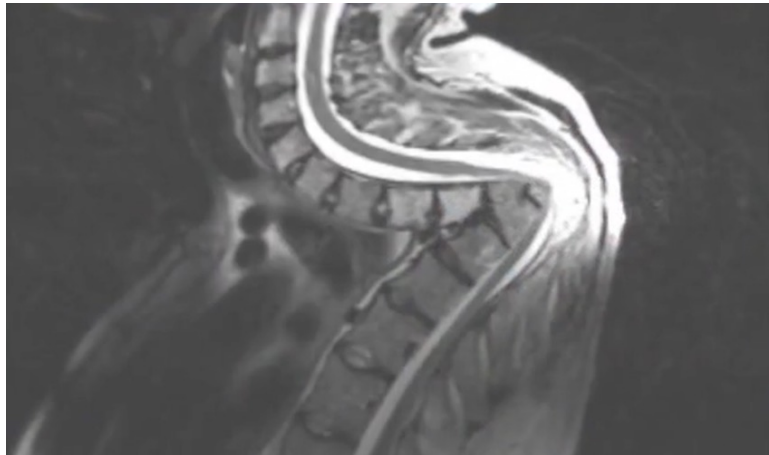


© Study.com

WHAT IS POTT'S DISEASE?



© Study.com



Diagnosis

- Challenges
 - Kids don't produce sputum.
 - Sputum is usually "paucibacillary."
 - Clinical signs and symptoms non-specific and often much less significant than radiology.
 - Extra-pulmonary TB hard to access, often smear and culture negative.

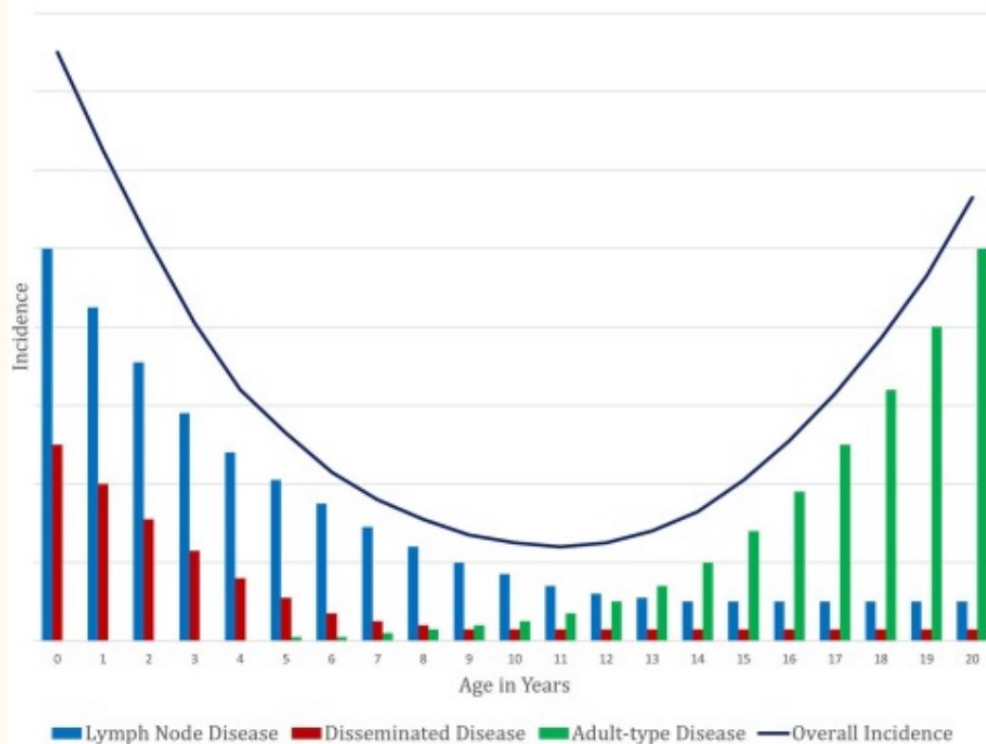
Approaches

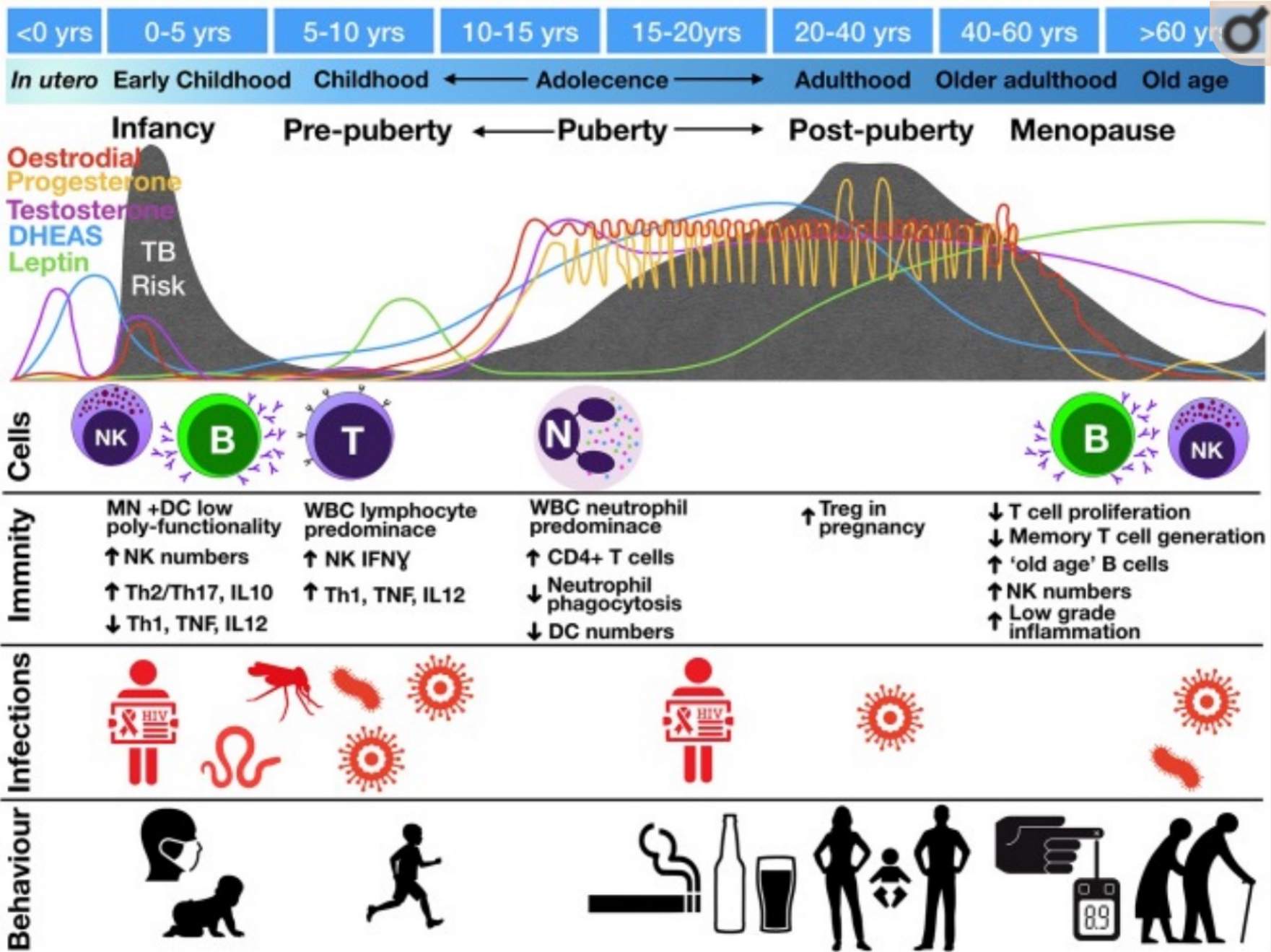
- Induced sputum
- Gastric aspirate
- String test
- Nasopharyngeal swab
- Blood/urine
- Stool

The Wonder Years: What Can Primary School Children Teach Us About Immunity to *Mycobacterium tuberculosis*?

[James A. Seddon](#),^{1,2,*} [Silvia S. Chiang](#),^{3,4} [Hanif Esmail](#),^{5,6} and [Anna K. Coussens](#)^{6,7,8,9}

Click on image to zoom





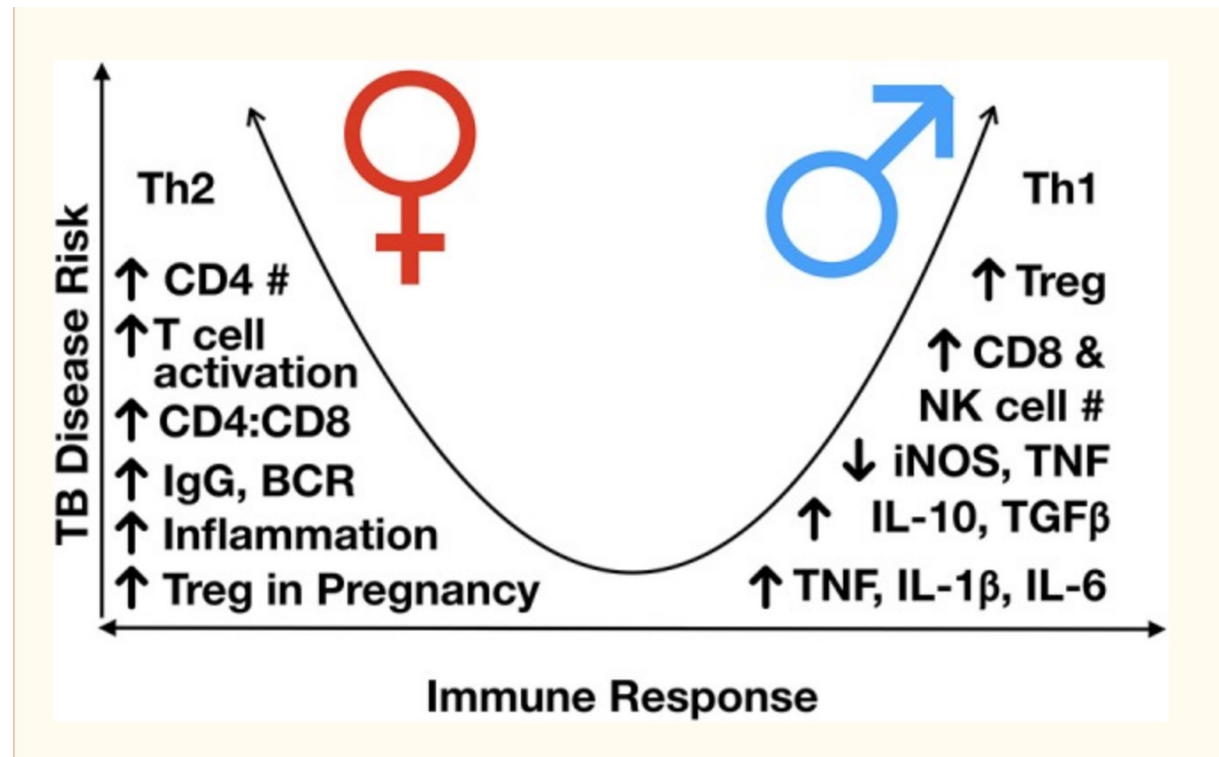
Infants

- “impaired” Th1 and type 1 interferon responses
- Higher Th2/Th17 and Il10 responses
- Early monocytes and DC less polyfunctionality in cytokine response.

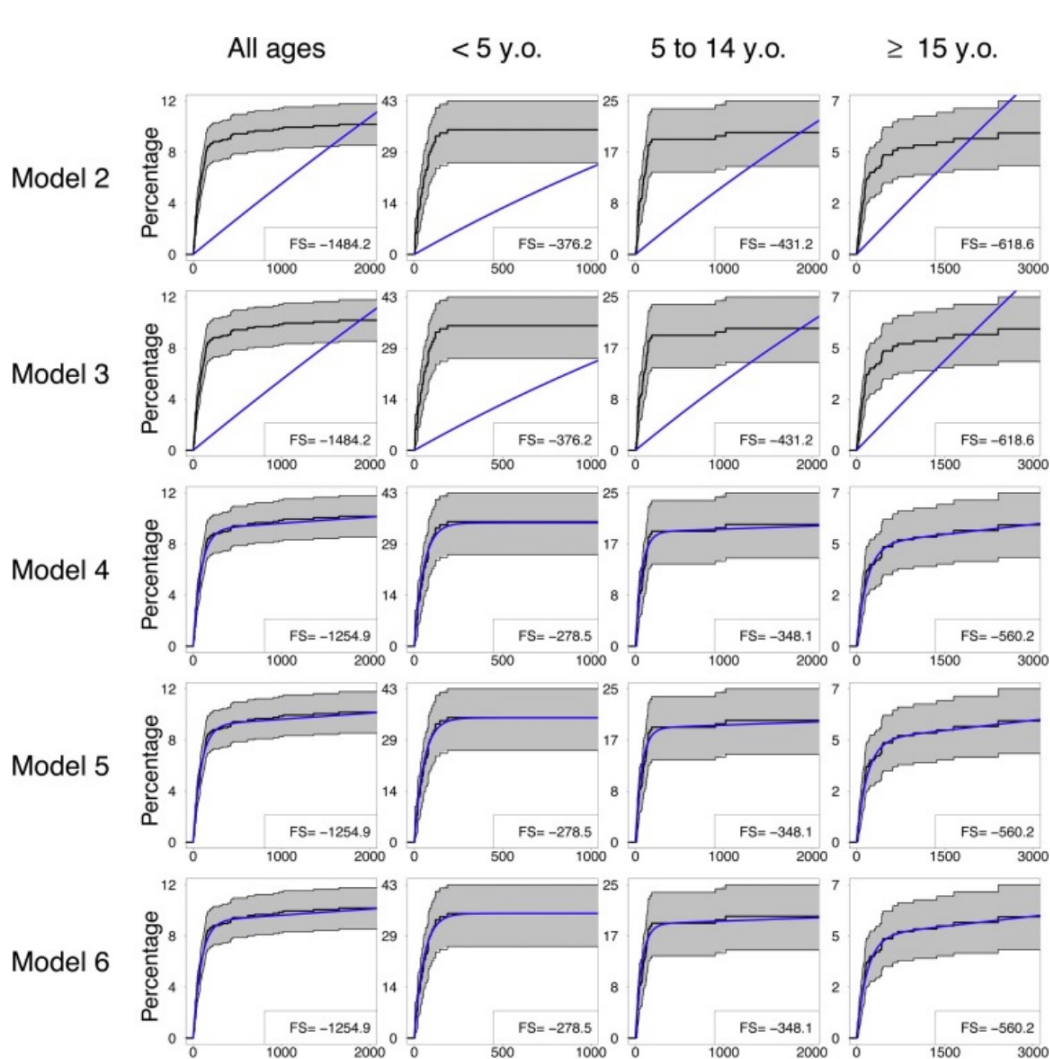
- These responses may allow tolerance to maternal antigens and colonization with commensal bacteria.

Sex differences in TB susceptibility in adolescence

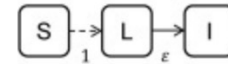
- Incidence in adolescent girls double that in boys among 400k children in Mass.
- Among children with TB, pulmonary infiltrates more common on adolescent girls than boys.



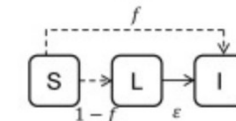
Do kids reactivate?



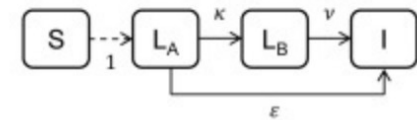
Model 2



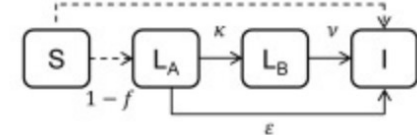
Model 3



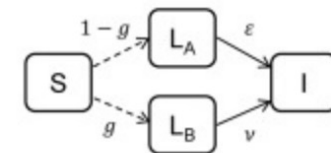
Model 4



Model 5

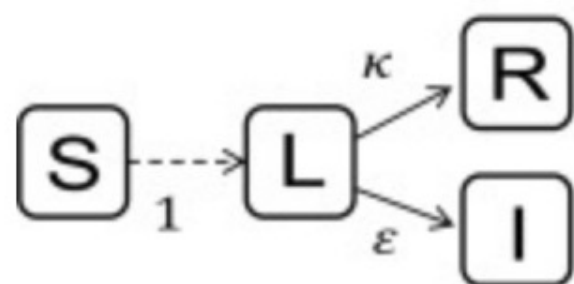


Model 6

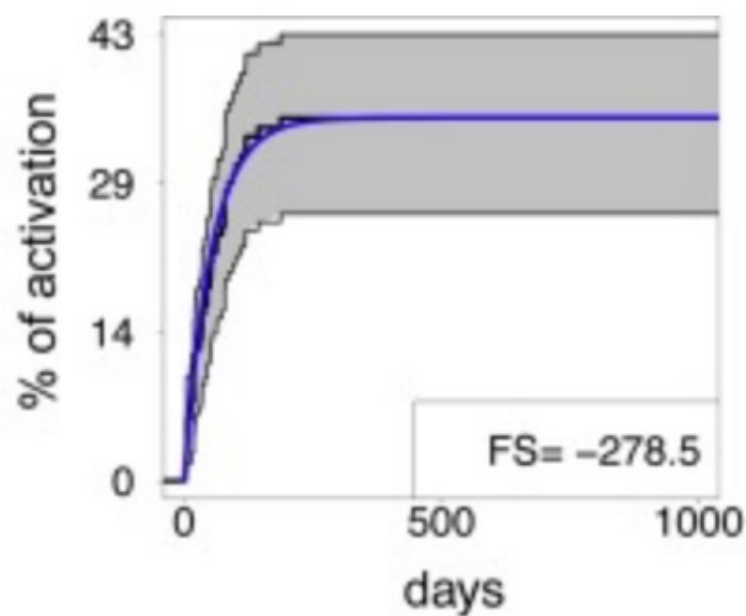


Model 4

(no reactivation)

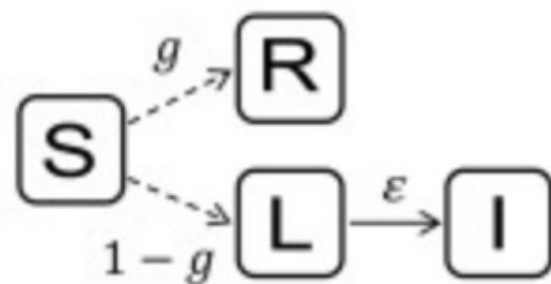


$$\varepsilon = 6.7e^{-3} \quad \kappa = 1.2e^{-2}$$

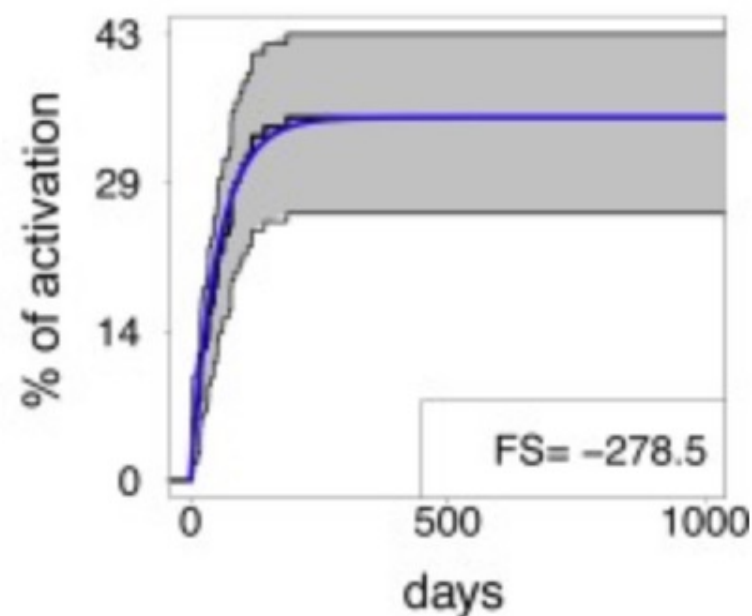


Model 6

(no reactivation)



$$g = 0.65 \quad \varepsilon = 1.9e^{-2}$$



Open research areas

- Role of viral co-infection (CMV)
- Role of increased exposure
- Does early TB infection clear?
- How to diagnose?