The Positive Mantoux

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Med/Peds
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Definitions

- Tuberculin
  - Discovered by Robert Koch, a German scientist, in 1890
  - An extract of M. tuberculosis, M. bovis or M. avium
  - Outer membrane protein
- Mantoux
  - Named for Charles Mantoux, French physician
  - Created the test in 1907
  - aka PPD aka purified protein derivative
  - aka TST aka tuberculin skin test

1. http://en.wikipedia.org/wiki/Mantoux_test
2. http://en.wikipedia.org/wiki/Tuberculin

Epidemiology

- 1/3 of the world is infected with TB
- In 2011, 9 million people were sick with active TB disease
- TB is the leading killer of HIV-infected people
- In Minnesota in 2010 there were 135 cases

1. http://www.cdc.gov/tb/statistics/default.htm
2. http://www.health.state.mn.us/tb

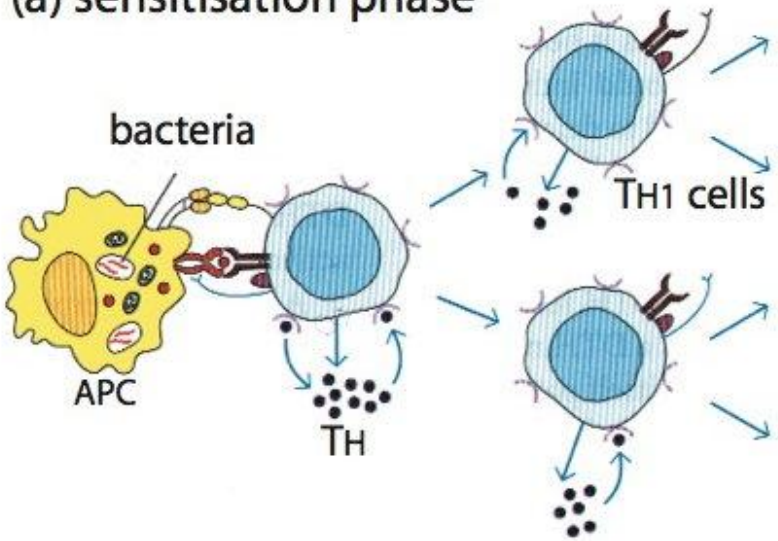
Hypersensitivity Reactions

Type	Prototype	Mechanism	Pathologic Lesion
Type I (immediate)	Anaphylaxis, allergies, asthma	IgE --> mast cells	Vascular dilation, edema, mucus production, inflammation
Type II (antibody mediated)	Autoimmune hemolytic anemia, Goodpasture	IgG or IgM --> binds to antigen on cell	Phagocytosis and lysis of cells
Type III (immune complex mediated)	Lupus, arthus reaction	Deposition of antigen-antibody complexes	Inflammation, necrotrizing vasculitis
Type IV (cell mediated)	Eczema, MS, DM-I, RA, Crohn's, TB	Activated T-lymphocytes release cytokines and cell-mediated cytotoxicity	Perivascular cellular infiltrates, edema, granuloma

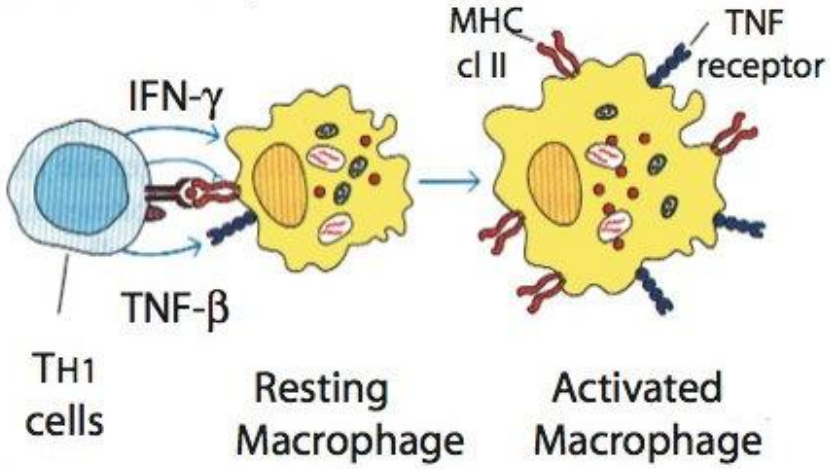
1. Robins and Cotran: Pathologic Basis for Disease.

Pathogenesis of type IV hypersensitivity

(a) sensitisation phase



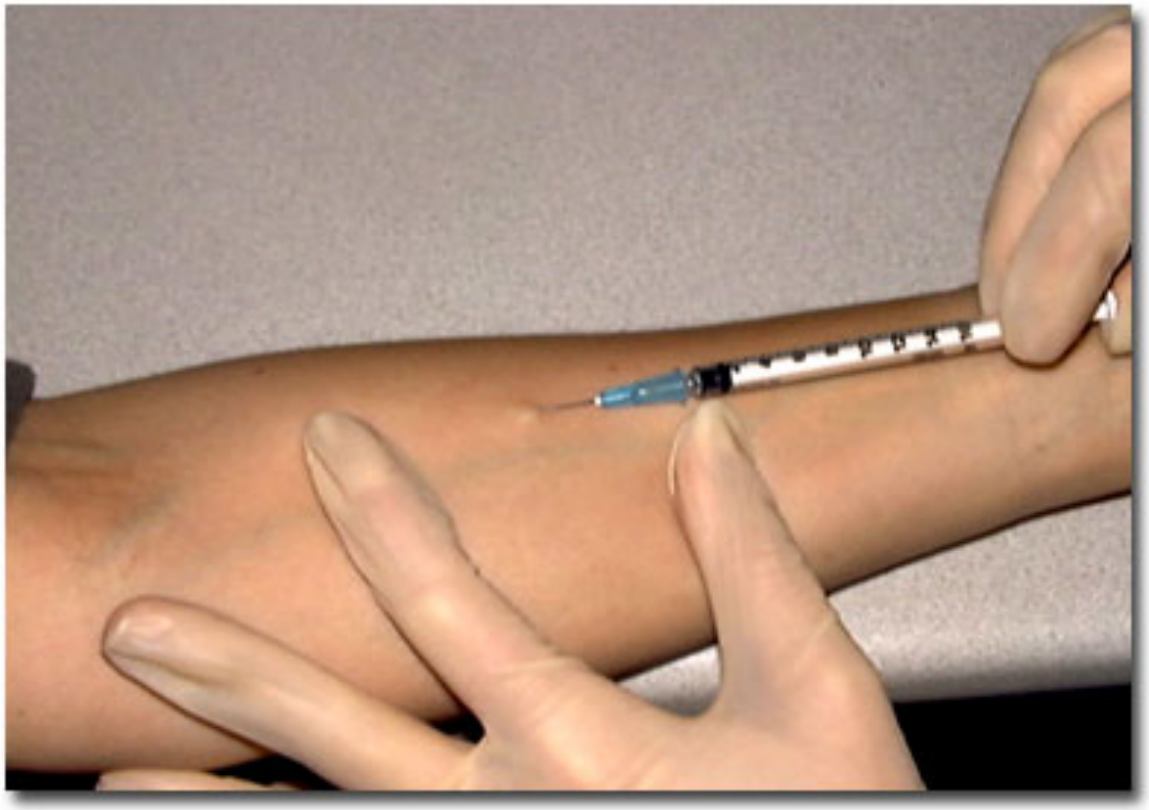
(b) effector phase



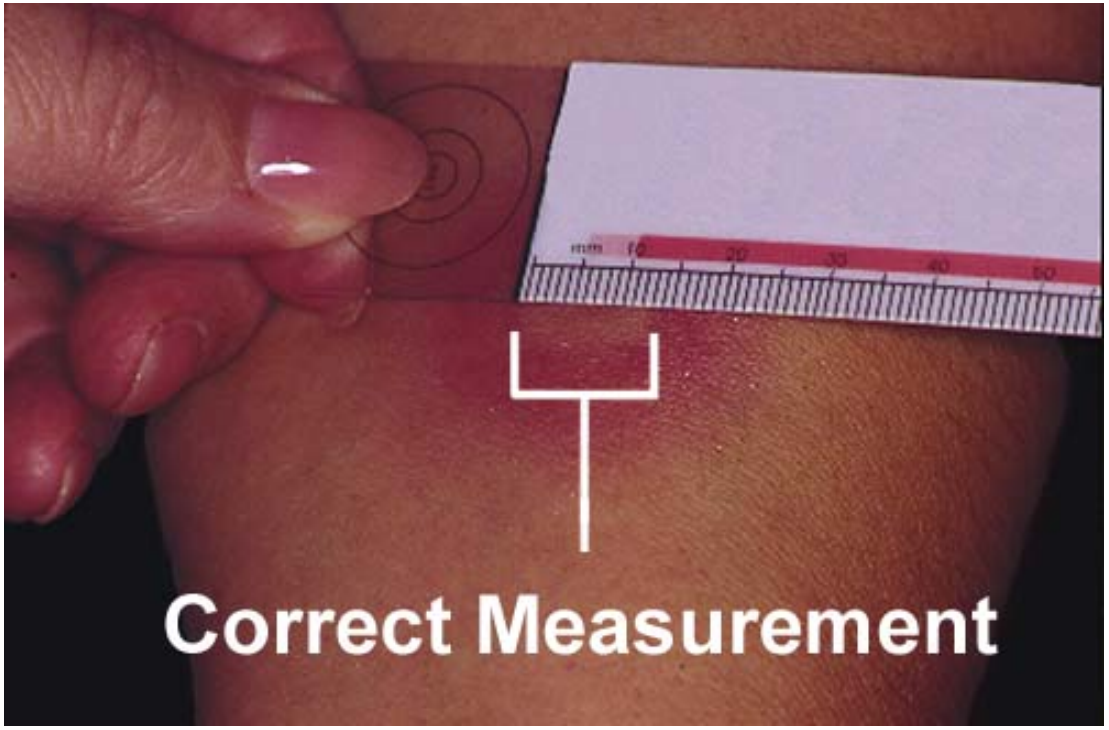
APCs: Macrophages	DTH Cells: TH1

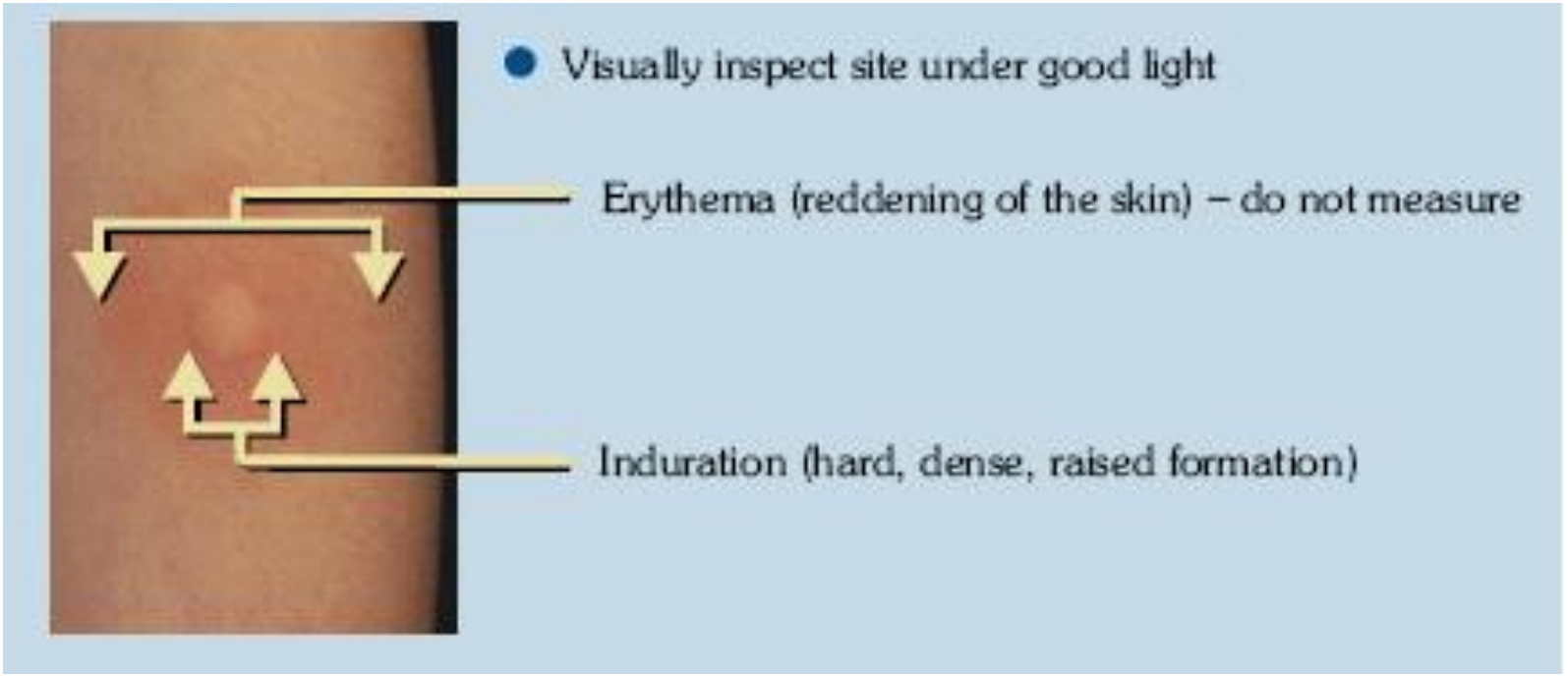
TH1 products: IFN-γ, TNF-β, IL-2, IL-3, IL-8, MCAF, MIF	Macrophage activation: MHC cl II, TNF receptor, oxygen radicals, nitric oxide

Goldsy RA et al. Immunology 5th Ed, 2003, p 384



Wait 48 - 72 hours...


Correct Measurement


Visually inspect site under good light
Erythema (reddening of the skin) – do not measure
Induration (hard, dense, raised formation)

Positive tests

Induration of **5 mm** or more	Induration of **10 mm** or more	Induration of **15 mm** or more
• HIV infected persons • Recent contact with a person with active TB disease • Fibrotic changes on CXR consistent with previous disease • Organ transplants • Immunosuppressed	• Recent immigrants (< 5 years) • IV drug users • Residents and employees of high risk settings • Mycobacteria lab personnel • Clinical condition places you at high risk • Children < 4 years old • Infants, children and adolescents exposed to high-risk adults	• Everyone else

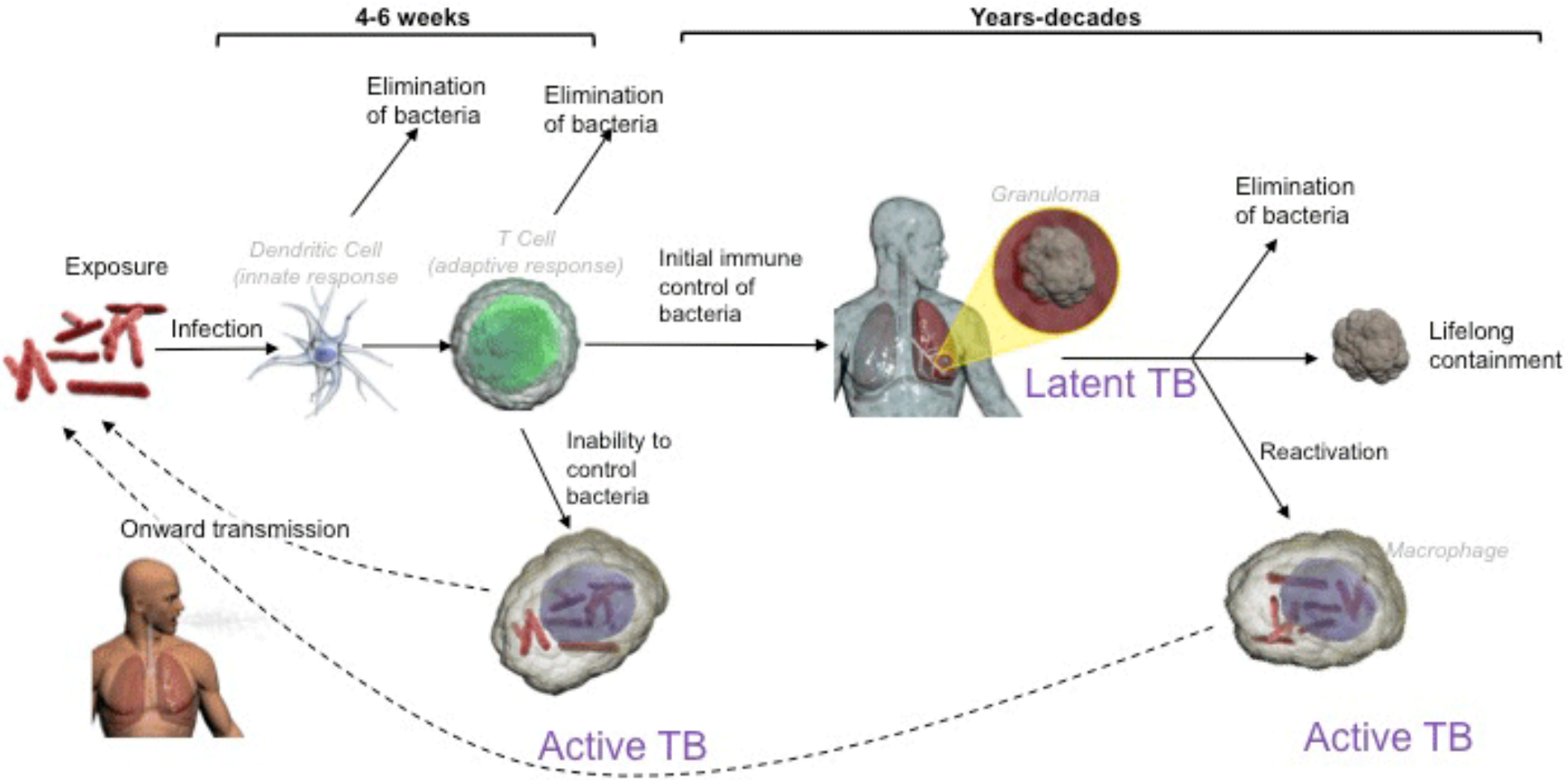
1. http://www.cdc.gov/tb/publications/factsheets/testing/skintesting.htm

False Positives

- Nontuberculous mycobacteria
- BCG vaccination
  - aka bacille-Calmette-Guérin
  - Used in countries with high risk for TB
  - Thought to wane over 6-10 years
  - QFG/T-spot/etc can be used

1. http://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm

Natural history of TB infection



It's positive, now what?

- History and Physical
  - Coughing > 3 weeks
  - Hemoptysis
  - Chest pain
  - Fevers
  - Night sweats
  - Fatigue
  - Unexpected weight loss
- Chest x-ray
- Consider HIV test

1. http://www.cdc.gov/tb/publications/factsheets/testing/diagnosis.htm

Active disease

Sick

Latent disease

Not sick

Treatment of Latent TB

Table 2. Latent TB Infection Treatment Regimens

Drugs	Duration	Interval	Minimum doses
Isoniazid	9 months	Daily	270
		Twice weekly*	76
Isoniazid	6 months	Daily	180
		Twice weekly*	52
Isoniazid and Rifapentine	3 months	Once weekly*	12
Rifampin	4 months	Daily	120

*Use Directly Observed Therapy (DOT)

- INH 9 months is standard regimen
  also preferred for HIV+ and children 2-11 years
- INH + RPT for age > 12, with higher risk for developing active TB disease
- Consider baseline LFTs and follow-up (every 3 months)

1. http://www.cdc.gov/tb/publications/factsheets/treatment/LTBItreatmentoptions.htm

Mantoux

- Sensitivity
  - 77 – 95%[1,2]
- Specificity
  - Depends on whether or not there are other *mycobacterial agents* active in the area and/or an area where *BCG* is used. In these areas it's 35 - 95%, else 93 - 99%.[1,3]

Quantiferon

Sensitivity: 93-99%

Specificity: 98%

1. Systematic Review: T-Cell–based Assays for the Diagnosis of Latent Tuberculosis Infection: An Update M. Pai, A. Zwerling and D. Menzies Full Text *Ann Intern Med* 2008; 177-184.
2. *How good is the tuberculin skin test?* Bass JB. *Infect Control Hosp Epidemiol.* 2003 Nov;24(11):797-8
3. American Thoracic Society and CDC. Diagnostic standards and classification of tuberculosis in adults and children . (PDF) *Am J Respir Crit Care Med 2000*; 161.

Mantoux vs Quantiferon

- Felt to be interchangable
- Should not use Quantiferon to "confirm" TB after positive Mantoux
- Cost of Quantiferon is comparable to less

	Medicare Reimbursement	Private Insurance Reimbursement	Cost	Potential Profit (using Medicare reimbursement)
PPD	$6.59 (includes nurse placement and read)	$23 (includes nurse placement and read)	$2.90 (Syringe $.30 + $2.60 for Tuberculin) ($26 for 10 test vial)	$3.69
QFG	$90.49 + $24 lab fee = $114.49	$176 (includes lab draw fee)	$30 (Unsure, this is an estimate)	$84.49

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