TB: Transmission, Pathogenesis, & Classification

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Overview

1. TB Transmission and Pathogenesis
   - Latent TB infection (LTBI)
   - Active TB disease
2. Tuberculosis Classifications
3. Strategies for TB Prevention (& Elimination?)

Poll Question!

What is TB? (choose all that apply)

a) TB = **Tuberculosis**

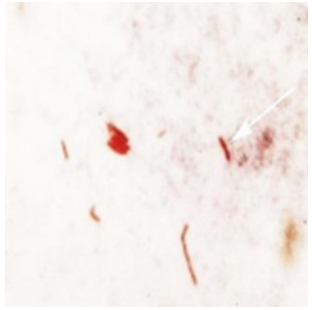
b) An **ancient disease** caused by **mycobacteria**

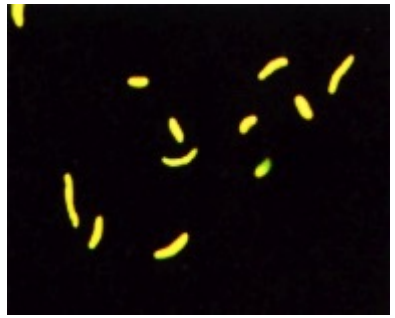
c) An **airborne disease**

d) A **curable** disease

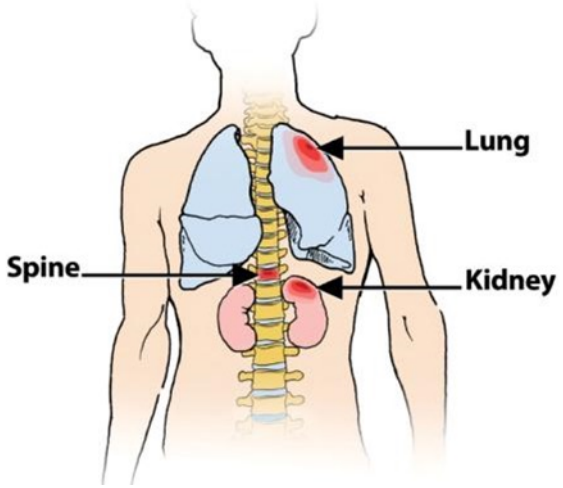
e) A **preventable** disease

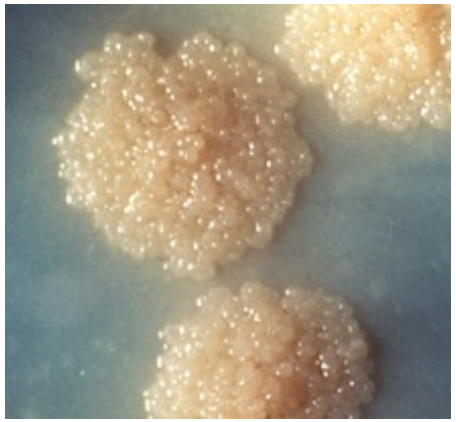
TB = Tuberculosis





Mycobacterium Tuberculosis Complex (**MTBC**)





Poll Question!

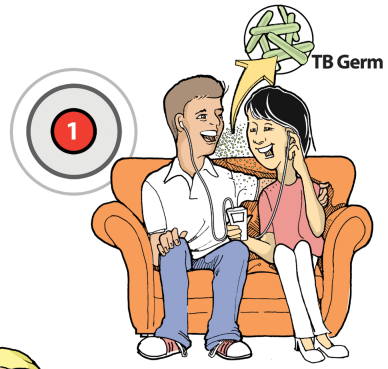
When tubercle bacilli are in the body, but the body's immune system is keeping the bacilli under control and contained, what does the patient have?

a) TB disease

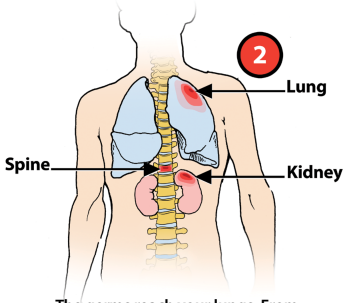
b) Latent TB infection

c) No TB infection or TB disease

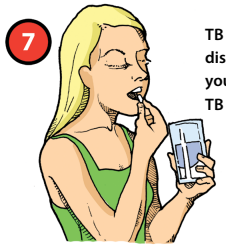
d) Don’t know



TB is spread when a person with TB disease coughs, sings, or speaks and you breathe the air contaminated with TB germs.

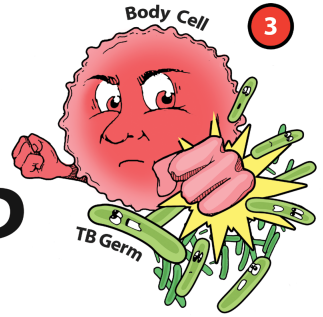


The germs reach your lungs. From there, they can go to other parts of your body.



Taking your TB medicine is very important. You need to take the medicine to help get better and to prevent the spread of TB germs to others.

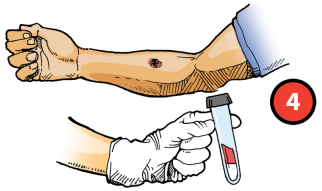
STOP TB



Your body fights the TB germs.

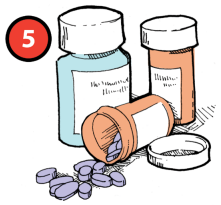
You get TB DISEASE when the TB germs multiply and attack your lungs or other parts of your body. When this happens,

- You have a positive TB skin test or TB blood test.
- You feel sick with cough, fever, weight loss, chest pain, or sweating at night.
- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.



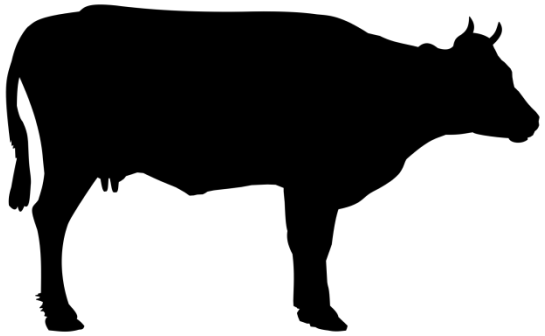
If your body controls the germs, you have LATENT TB INFECTION. When this happens,

- You may have a positive TB skin test or TB blood test.
- You don't feel sick.
- You don't have TB symptoms.
- You can't give TB germs to others.
- You have a normal chest x-ray.



You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE.

2 Steps to Prevent M. bovis (cow TB)



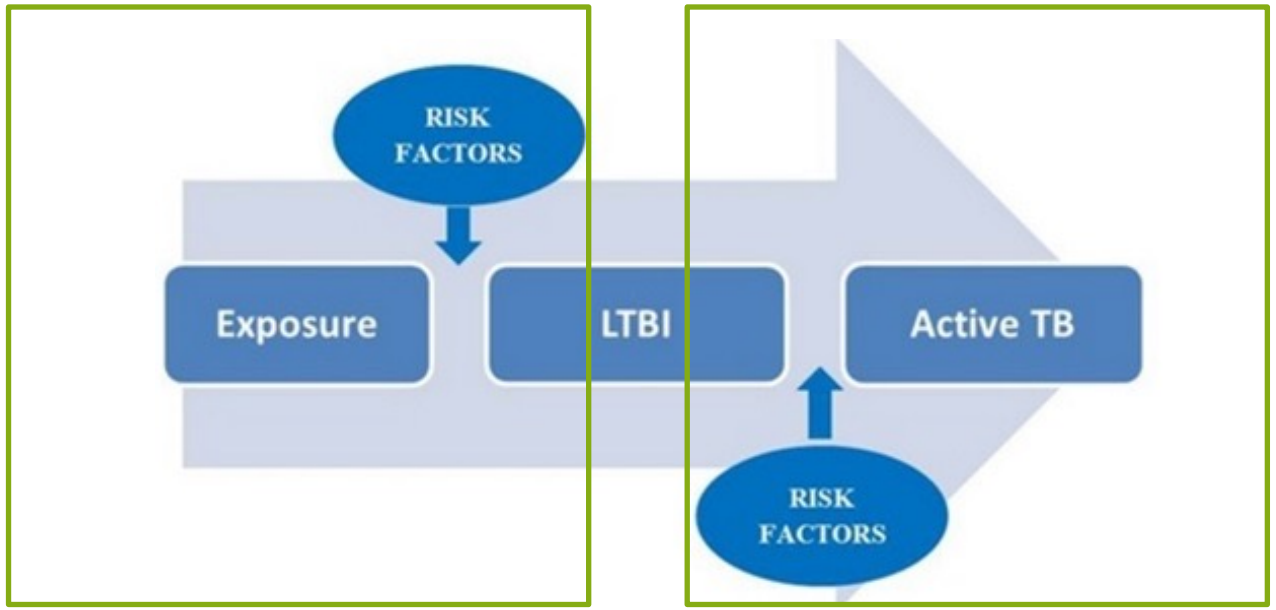
Test cows for TB

Pasteurization

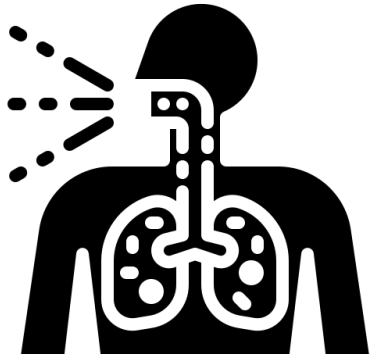
Keep your family safe:
Make sure your Queso Fresco is Pasteurized!

Latent TB infection or active TB disease?

What features distinguish one from the other?



Person/Place/Time

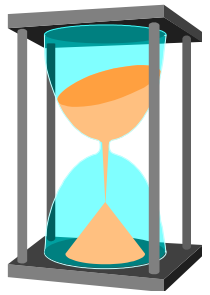


Risk Factors for TB Infection

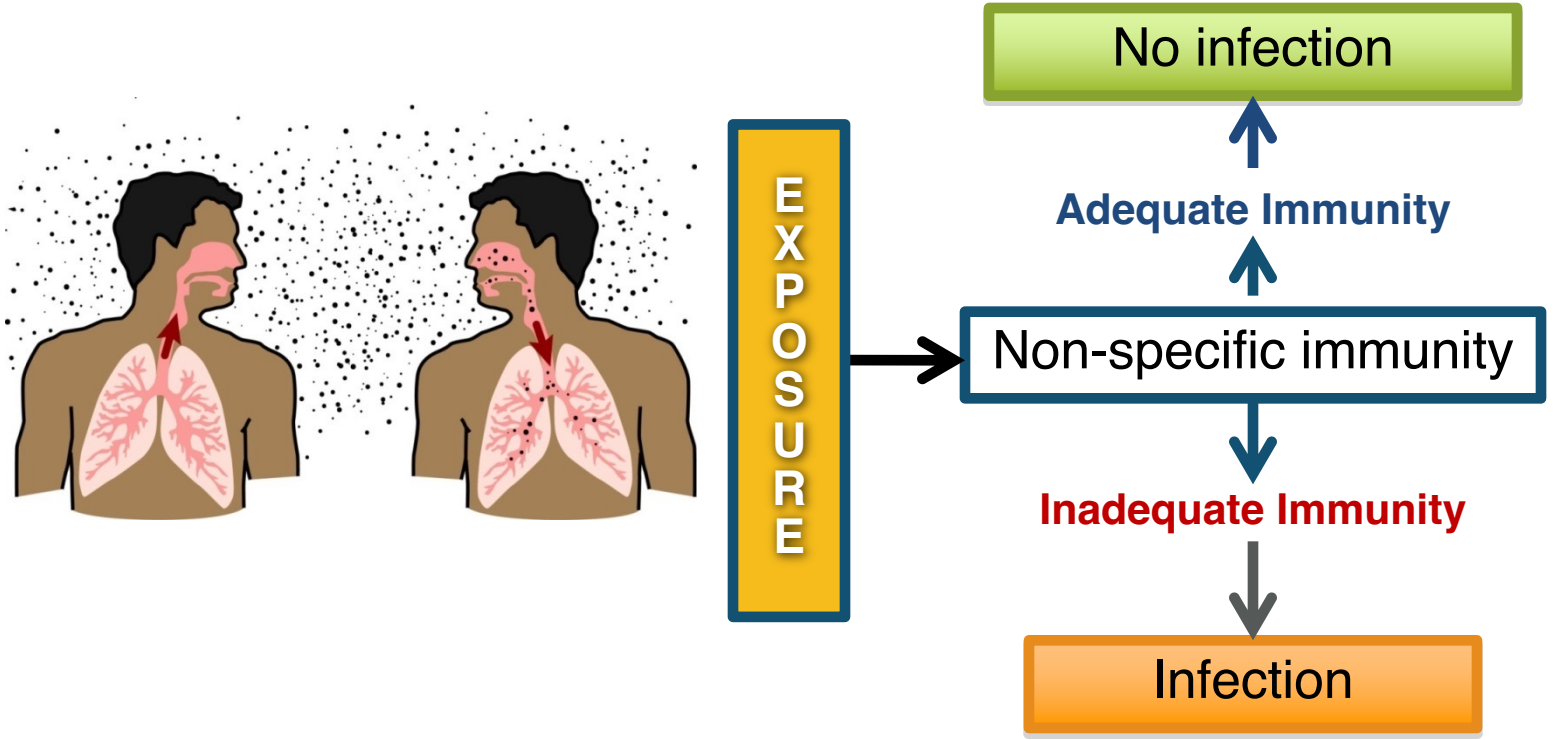
The chance of **INFECTION** increases when…

- The concentration of TB bacteria circulating in the air is greater
  - Coughing; smear-positive; cavitary disease
  - Poor ventilation; small enclosed space

- More time is spent with the infectious person (frequency and duration)
- Exposure occurs in an area where the bacteria can easily survive (no ultra violet light)



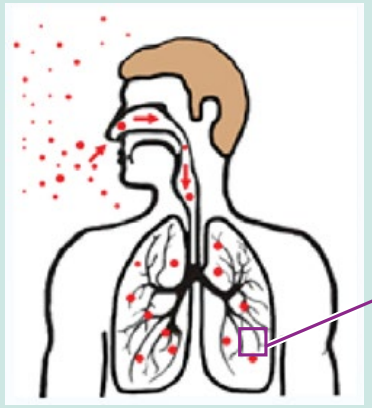
TB Transmission & Pathogenesis



➡ Not everyone who is exposed to TB will become infected

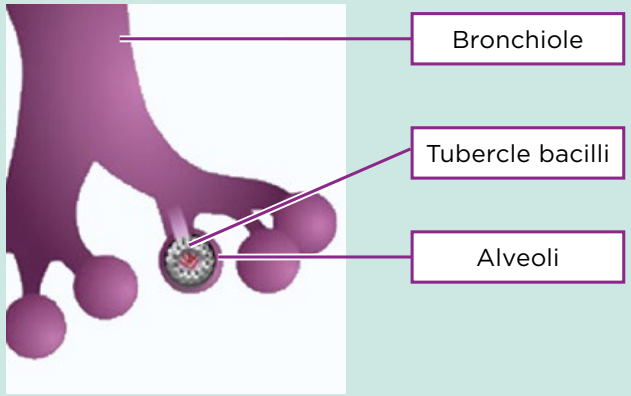
Pathogenesis

1



Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

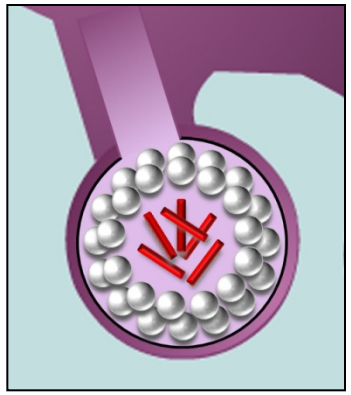
2

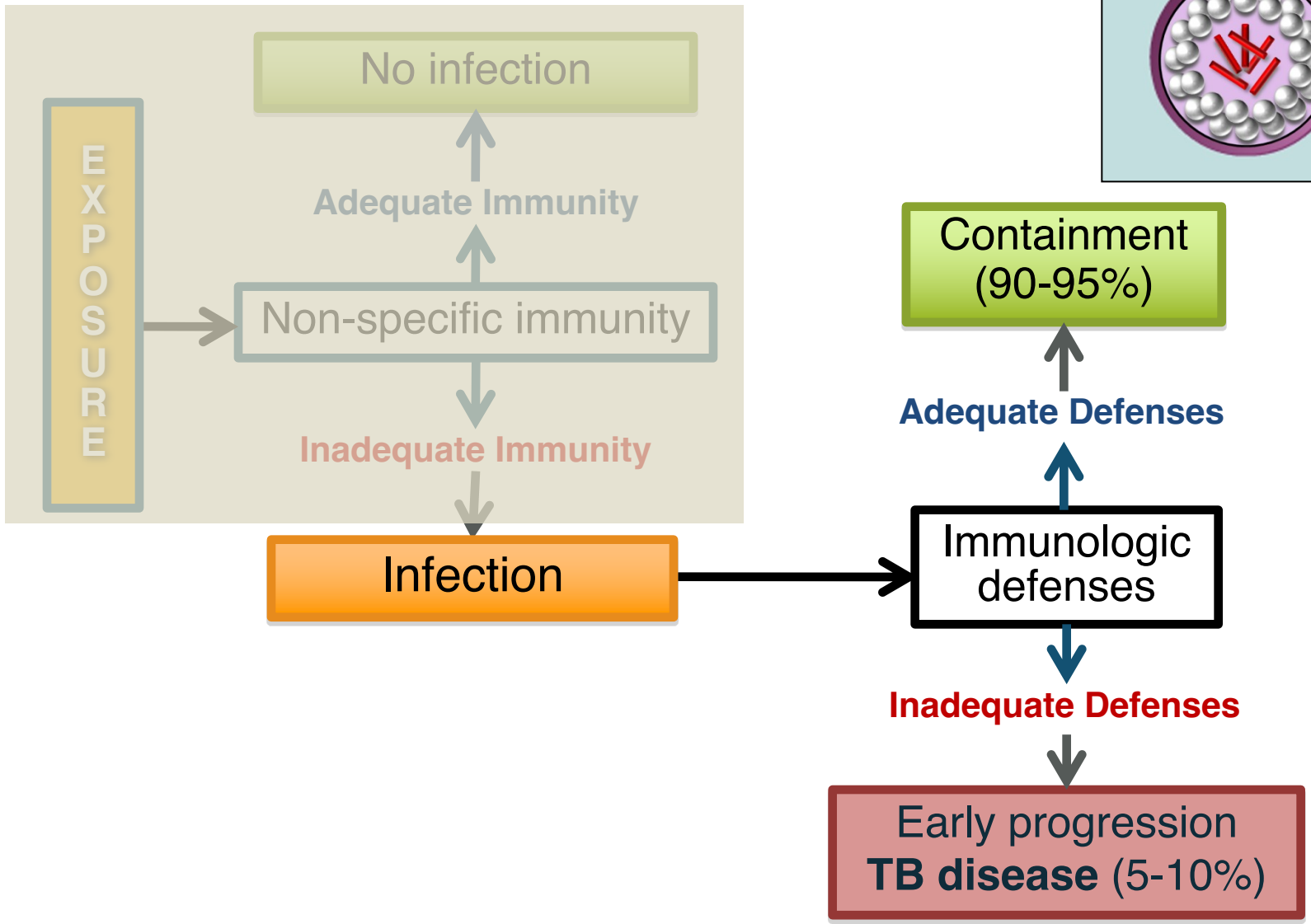


Tubercle bacilli multiply in the alveoli.

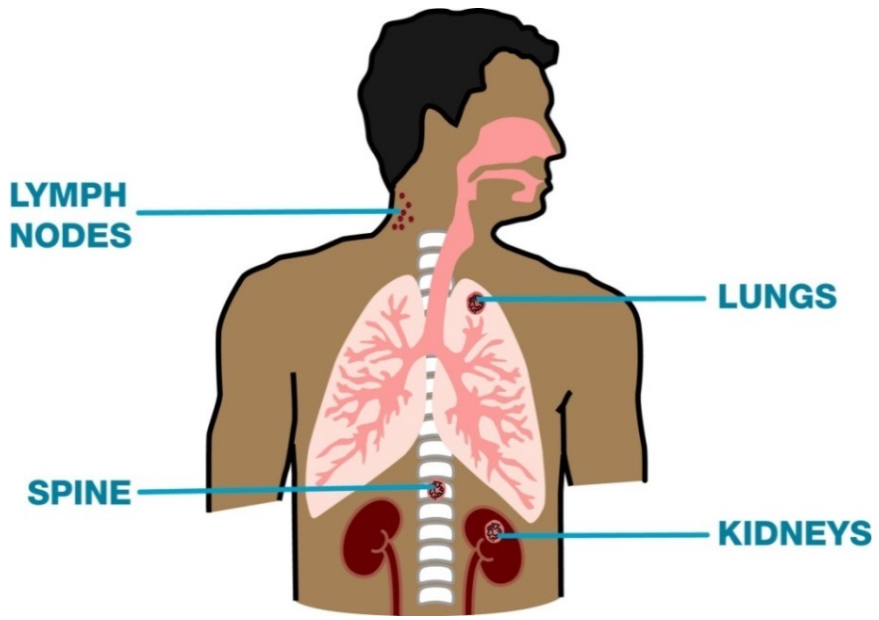
Source: Core Curriculum on Tuberculosis, pages 12 & 13

TB Pathogenesis



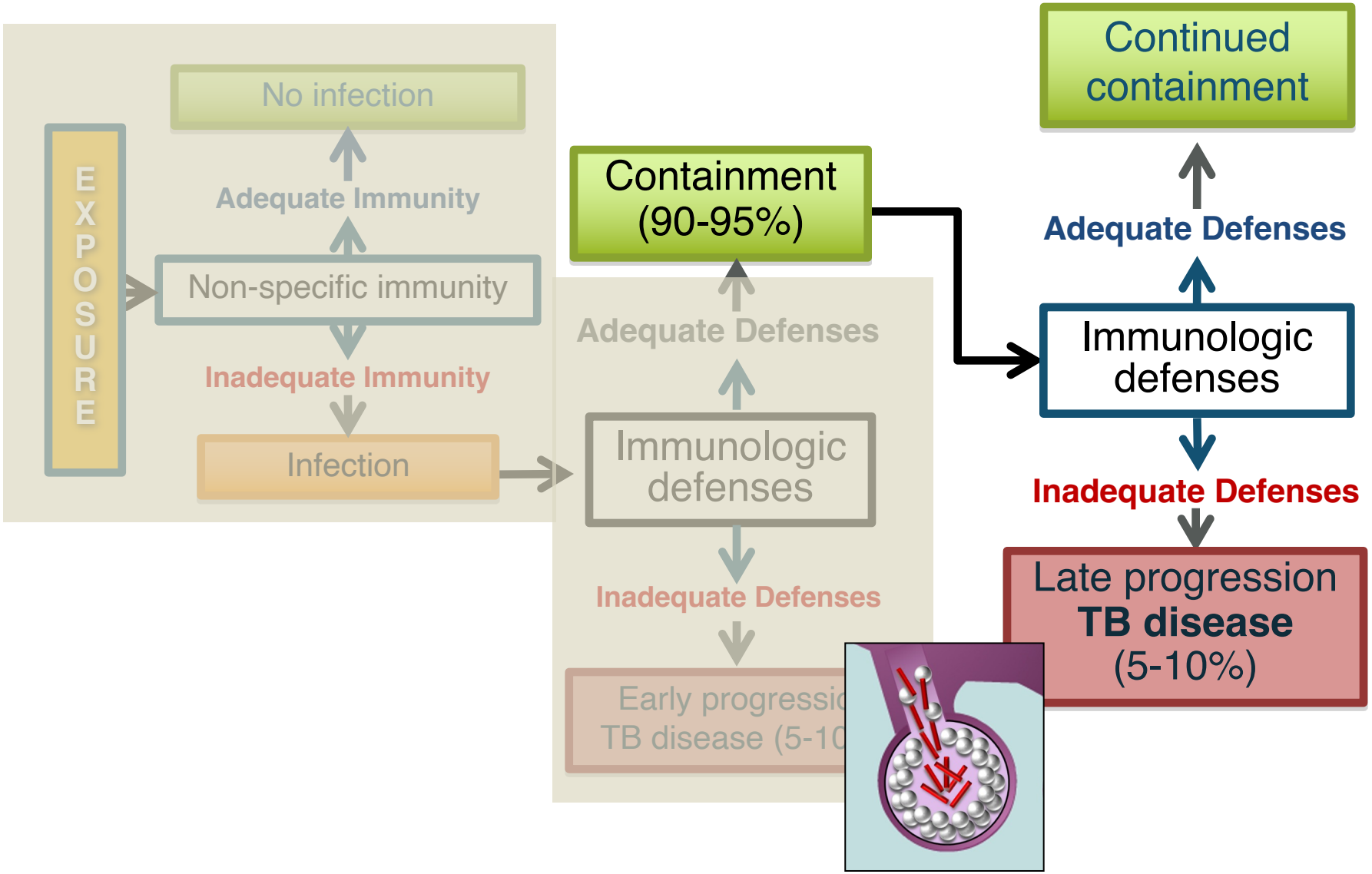


DISSEMINATION:
Spread of TB to Other Parts of the Body



1. Lungs (~85% all cases)
2. Pleura
3. Central nervous system (spine, brain, meninges)
4. Lymph nodes
5. Genitourinary system
6. Bones and joints
7. Disseminated (miliary)

TB Pathogenesis (3)



Risk Factors for Progression of Infection to TB Disease

- 10% of adults infected with TB who have a normal immune systems develop TB at some point in their lifetime
- Highest risk: Recent infection (within 1-2 years of infection)
- Conditions/treatment that impairs immune control of *M.tb*

Condition (partial list)	**TB risk**[a]
HIV/AIDS	10 - 100
Organ-transplant recipients	20 - 70
Chronic renal failure requiring dialysis	6.9 - 52.5
TNF-alpha blockers	1.6 - 25.1
Silicosis	2.8
Fibronodular disease on CXR	6 - 19
Diabetes mellitus	1.6 - 7.83
Smoking	2 – 3.4

[a] Relative risk of TB compared to the general population

Ai J-W, *et al*. *Emerging Microbes and Infections* (2016) 5, e10; doi:10.1038/emi.2016.10

For individualized risk, Online TST/IGRA Interpreter:
http://www.tstin3d.com/en/calc.html

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.

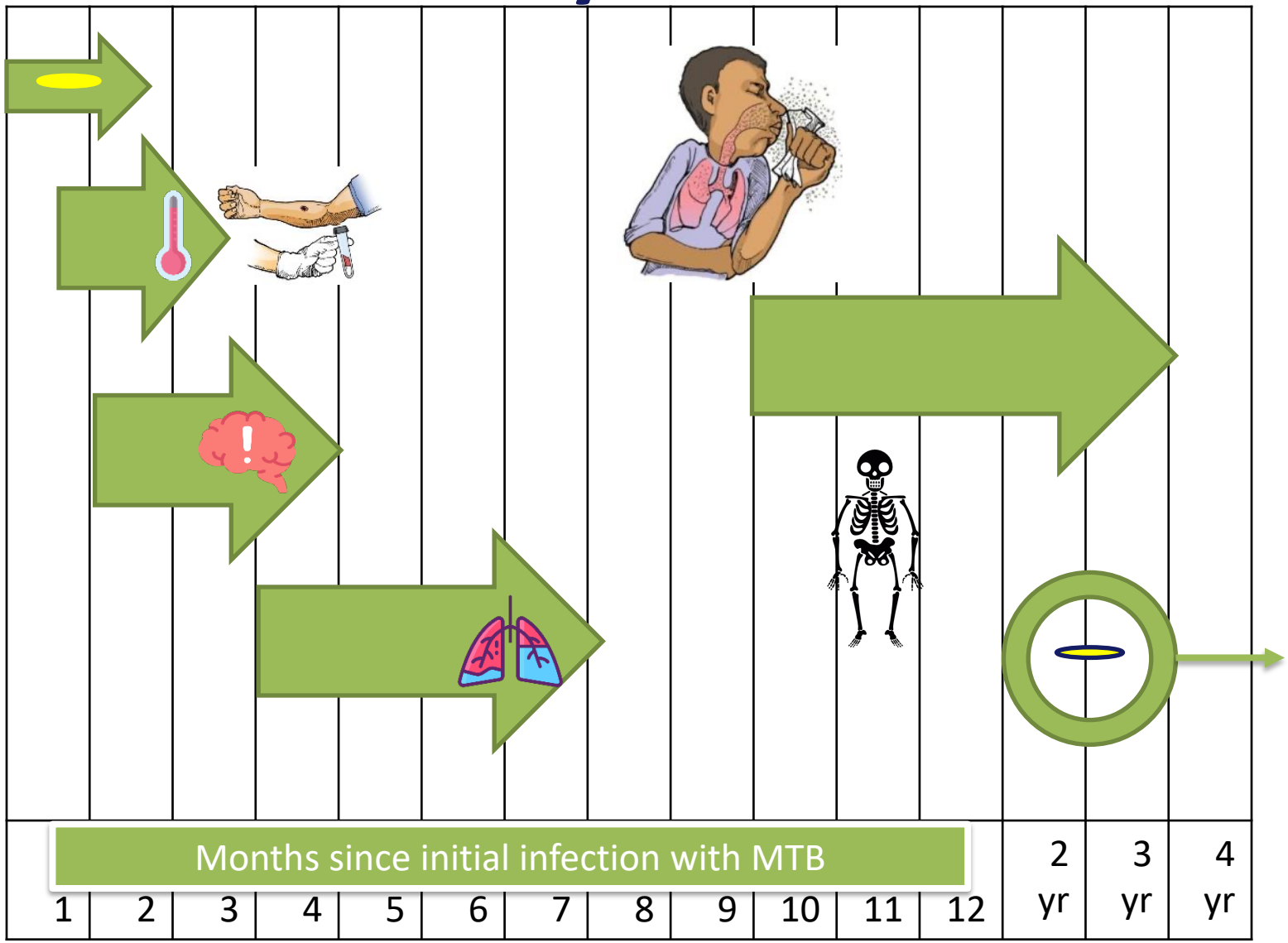
Source: Core Curriculum on Tuberculosis, page 18

Risk of Progression from TB Infection to Disease by Age

Age at Primary Infection	No Disease (%)	Pulmonary TB (%)	Miliary or Central Nervous System TB (%)
Birth -12 months	50	30-40	**10-20**
1-2 years	75-80	10-20	**2-5**
2-5 years	95	5	0.5
5-10 years	98	2	<0.5
>10 years	80-90	10-20	<0.5

Adapted from Marias et al Am J Resp Crit Care 2006;173:1078-1093

Natural History of TB: Timeline



Person with LTBI	Person with TB Disease
Has a small amount of TB bacteria in his/her body that are alive but **inactive**	Has a large amount of **active** TB bacteria in his/her body
Cannot spread TB bacteria to others	May spread TB bacteria to others
Does **not** feel sick, but may become sick if the bacteria in his/her body become active	May feel sick, and may have symptoms such as a cough, fever, and/or weight loss
Usually has a positive TB skin test or TB blood test result indicating TB infection	Usually has a positive TB skin test or TB blood test result indicating TB infection
Chest radiograph is typically **normal**	Chest radiograph may be **abnormal**
Sputum smears and cultures are **negative**	Sputum smears and cultures may be **positive**
Should consider treatment for LTBI to prevent TB disease	Needs treatment for TB disease
Does **not** require respiratory isolation	May require respiratory isolation
Is not a TB case	Is a TB case

Source: Core Curriculum on Tuberculosis, page 15

Imaging Reports & TB

What key words make you "think TB"?

- Cavity
- Miliary pattern
- RUL (upper lobe preference)
- Hilar adenopathy (pediatric)
  - Enlarged lymph nodes

<u>Latent TB</u>:
Calcified granuloma/nodule

What other words *might* indicate (pulmonary) TB?

- Pleural effusion
- Pneumonia
- Infiltrate
- Opacities
- Ground glass
- Tree and bud
- Nodules
- Reticulonodular
- Granulomas
- Necrosis

<u>"Old TB"</u>
Scaring
Fibrosis (can also be present with active TB)
Pleural thickening

Radiographic evidence of surgical interventions? *Ex: plombage or lobectomy*

Key: stable abnormalities
Make sure to get X-ray at end of treatment to know "new normal"

- **Q: Will all TB patients present with a cavity?**
  - A: No. There are a wide range of radiographic presentations with TB disease.
- **Q: Does a cavity automatically mean the patient has TB?**
  - A: No. TB is a possible cause of cavitary disease. Collect sputum to rule out TB.

X-rays are just one tool

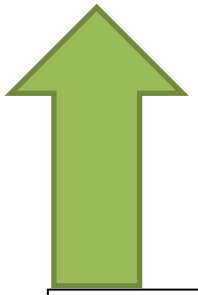
Rule of thumb: If signs/symptoms or abnormal x-ray, collect sputum

Look at whole picture

LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

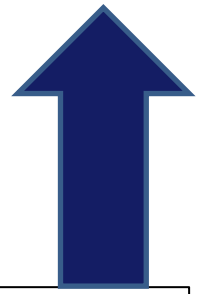


Is not currently sick. Can be treated to prevent future illness

LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

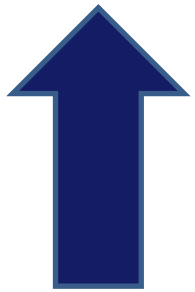


Collected specimens may culture out *M.tb*

LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

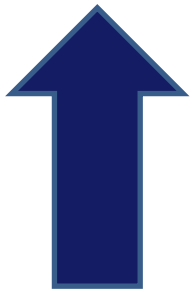


May require respiratory isolation precautions

LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

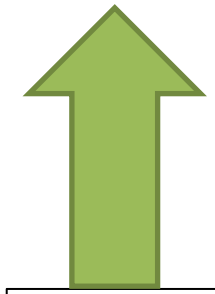


May feel sick and may have symptoms such as a cough, fever, and/or weight loss

LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

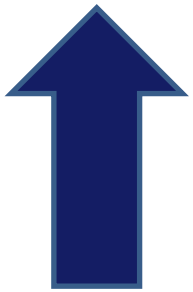


Is not contagious. There is no risk of spreading TB to others at this point in time.

LTBI or TB?

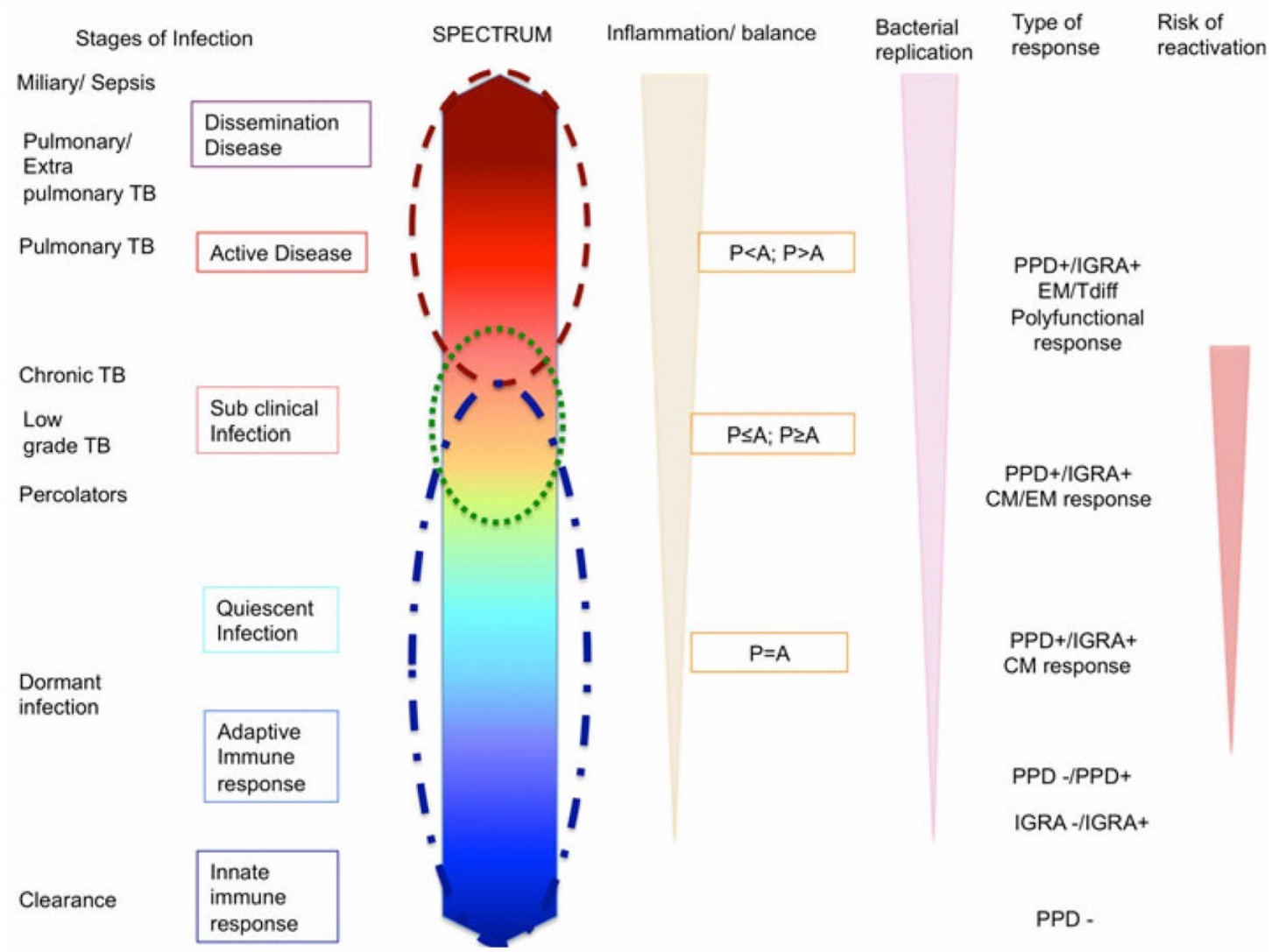
Latent TB Infection

Tuberculosis (TB)



Never treat with a single drug. Standard treatment starts with four drug therapy: (RIPE).

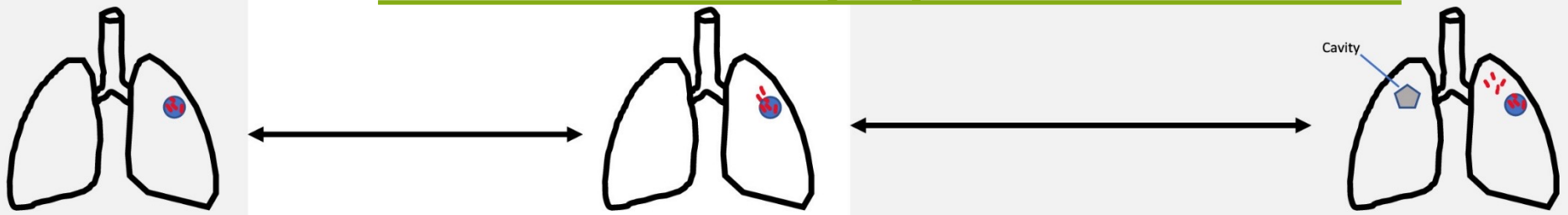
TB Spectrum: Infection to Disease



Gideon and Flynn. *Immunol Res*. 2011 August ; 50(0): 202–212

While the spectrum reflects disease progression, treatment is still for "LTBI" or "TB Disease"

Subclinical = Asymptomatic Disease



TB Spectrum	LTBI	Subclinical TB disease		Active TB disease		
Clinical	Asymptomatic *"Immune sensitized to Mtb" or "latent infection"*	Asymptomatic *"Subclinical, bacteriologically negative" or "incipient disease"*	Asymptomatic *"Subclinical, bacteriologically positive disease"*	Symptomatic *"Clinical bacteriologically negative disease"*	Symptomatic *"Clinical bacteriologically positive disease"*	Symptomatic *"Clinical smear positive/extensive disease"*
Smear	-	-	-/+	-	-	+
Culture	-	-	+	-	+	+
Molecular (Xpert)	-	-	-/+	-	+	+
CXR (Pulmonary TB)	Normal	Minimal abnormalities		Minimal abnormalities		Extensive abnormalities/ cavities
Identification	LTBI screening	Active Case Finding		Passive Case Finding		
Current management approach	1HP, 3HP (weekly), 3HR, 4R, 6H, 9H	Observation or 2HRZ(E)/4HR	2HRZ(E)/4HR	2HRZ(E)/4HR	2HRZ(E)/4HR	2HRZE/4HR

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00112-8/fulltext

What are the classifications for TB?

Poll Question!

TB5 is the American Thoracic Society classification given to a confirmed case of tuberculosis.

a) True

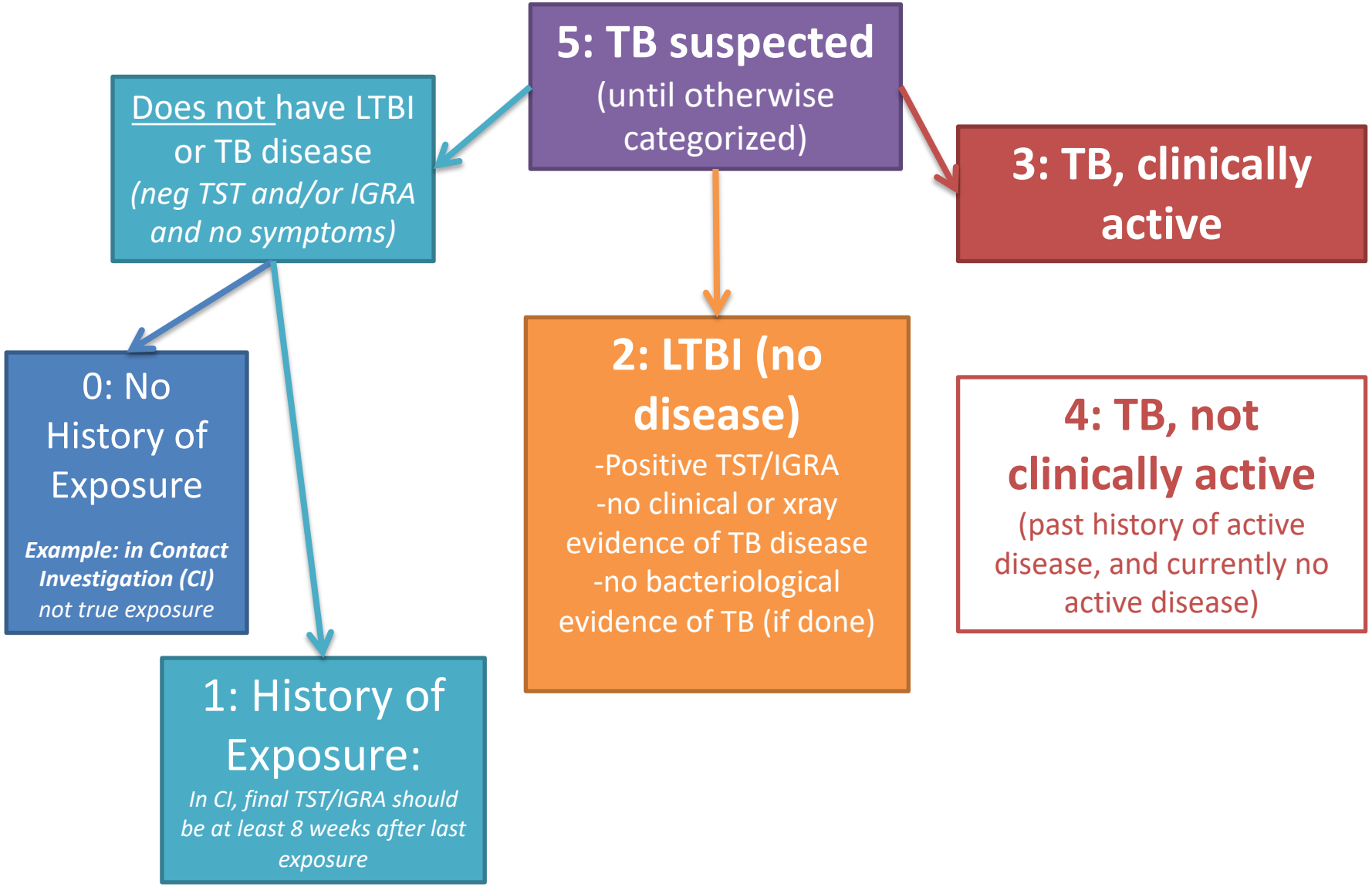
b) False

c) Don’t know

TB Classification Scheme & Definitions

Class	Stage of Disease	Description
0	**No TB exposure, Not infected**	No history of TB exposure. Negative tuberculin skin test (or IGRA)
1	**Exposure, no evidence of infection**	History of TB exposure. Negative tuberculin skin test (or IGRA) test performed at least 8-10 weeks after exposure.
2	**Latent TB infection, no disease**	Positive tuberculin skin test (or IGRA). No clinical, bacteriologic, or radiographic evidence of TB
3	**TB disease, clinically active**	*M. tuberculosis* cultured **OR** clinical, bacteriologic, or radiographic evidence of current TB disease that responds to treatment
4	**Previous TB Disease, not clinically active**	History of episode(s) of TB **OR** Abnormal but stable radiographic findings , positive tuberculin skin test, negative bacteriologic studies (if done) **AND** no clinical or radiographic evidence of current disease
5	**TB suspect** **(TB disease suspected)**	Diagnosis pending. TB disease should be ruled in or out within 3 months

Adapted from: ATS/CDC. Diagnostic Standards and Classification of Tuberculosis in Adults and Children (2000). http://www.atsjournals.org/doi/full/10.1164/ajrccm.161.4.16141#.WA0Auk0zXIU

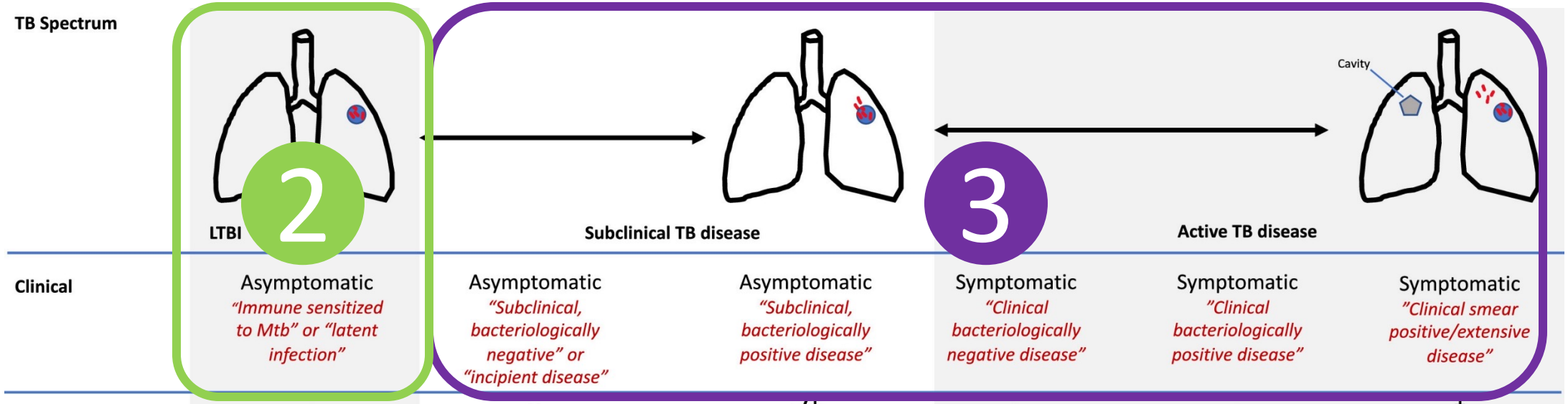

5: TB suspected
(until otherwise categorized)
Does not have LTBI or TB disease
(neg TST and/or IGRA and no symptoms)
3: TB, clinically active
0: No History of Exposure
Example: in Contact Investigation (CI)
not true exposure
2: LTBI (no disease)
-Positive TST/IGRA
-no clinical or xray evidence of TB disease
-no bacteriological evidence of TB (if done)
4: TB, not clinically active
(past history of active disease, and currently no active disease)
1: History of Exposure:
In CI, final TST/IGRA should be at least 8 weeks after last exposure

CDC TB Classifications: Immigrants and Refugees

Classification	Description
No TB	Normal TB screening examinations
Class A TB with waiver	[Active] TB disease and have been granted a waiver
Class B0 TB, Pulmonary	Diagnosed with TB and completed directly observed therapy prior to immigration.
Class B1 TB, Pulmonary (PTB)	Applicants who have signs or symptoms, physical exam, or chest x-ray findings suggestive of tuberculosis disease, or have known HIV infection, but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis disease.
Class B1 TB, Extra-pulmonary (EPTB)	Evidence of EPTB without pulmonary involvement. The anatomic site of infection should be documented.
Class B2 TB, LTBI Evaluation	Applicants who have a positive IGRA or TST but otherwise have a negative evaluation for tuberculosis.
Class B3 TB, Contact Evaluation	Recent contact of a known TB case.

https://www.cdc.gov/immigrant-refugee-health/hcp/panel-physicians/tuberculosis.html
Adapted from above website

How does the classification match up?



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Culture	-	-	+	-	+	+
Molecular (Xpert)	-	-	-/+	-	+	+
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https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00112-8/fulltext

Real Question: “Is this a class 5 or class 3?”

Scenario: Professor X is moving out of state. They are on treatment and cultures just came back confirming pulmonary TB. You are transferring their care and the receiving jurisdiction asks “Is this a class 5 or class 3?” (polling question):

a) Class 5

b) Class 3

c) ????

What public health strategies can prevent & (eventually) eliminate TB disease?

Priority Strategies for TB Prevention & Control

1. Early and accurate detection, diagnosis, and reporting of **TB cases** leading to initiation and completion of treatment

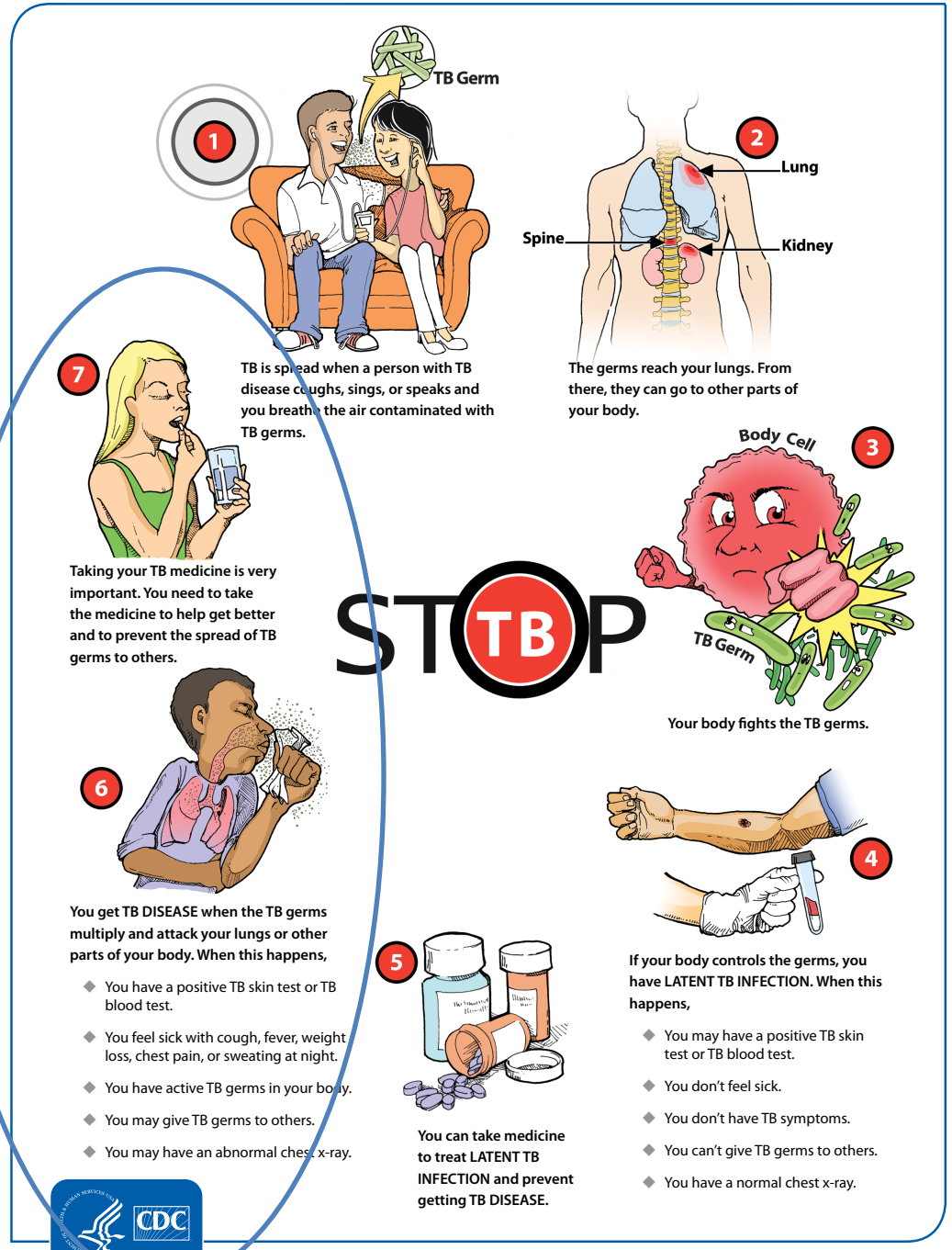
2. Identification of **contacts** of patients with infectious TB and treatment of those at risk with an effective drug regimen

3. Identification of other persons with **latent TB infection** at risk for progression to TB disease and treatment of those persons with an effective drug regimen

4. Identification of settings in which a high risk exists for transmission of *Mycobacterium tuberculosis and application* of effective **infection-control measures**

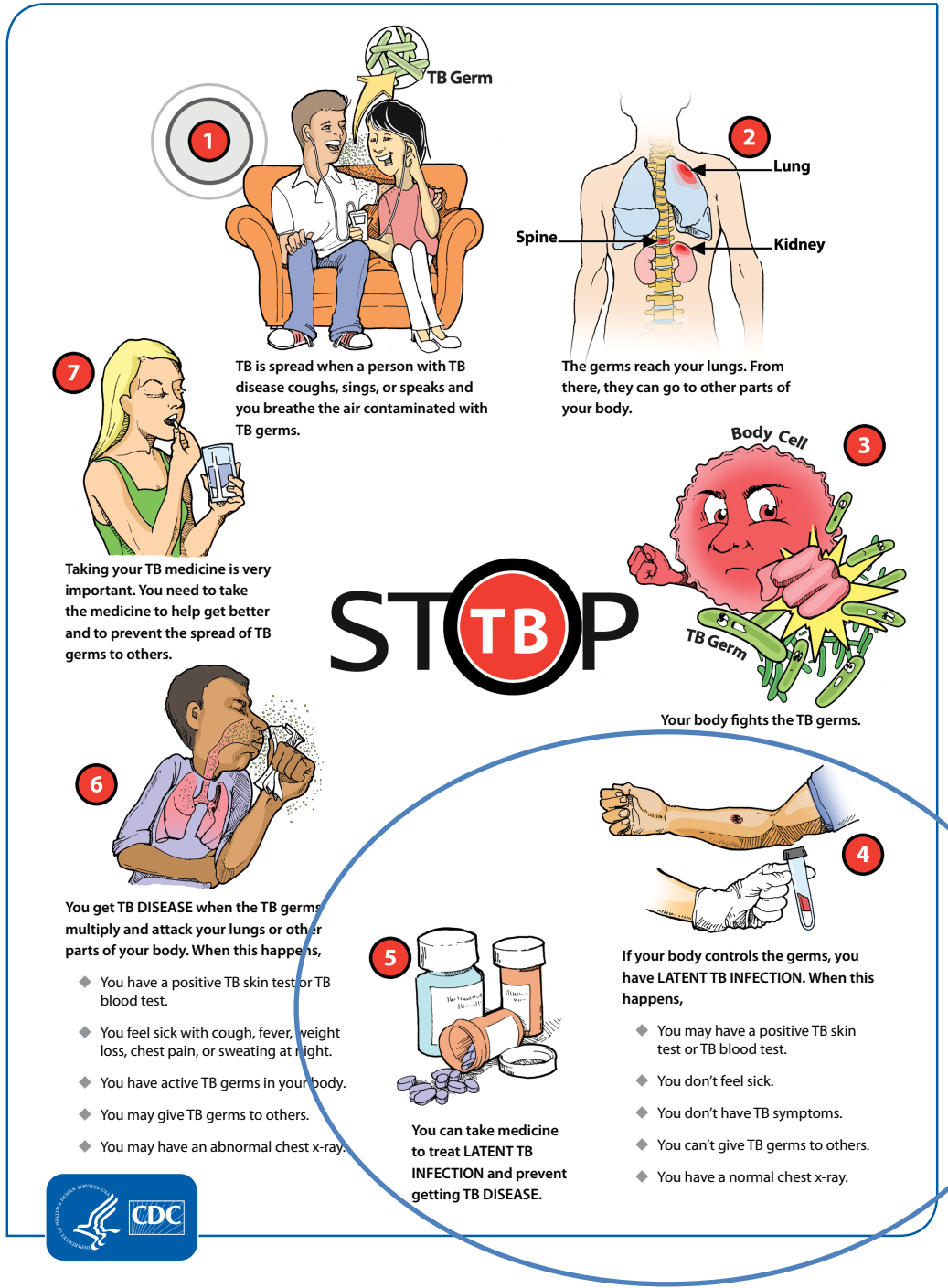
Source: ATS/CDC/IDSA. Controlling Tuberculosis in the United States Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR 2005; 54 (No. RR-12):15.

Active versus Passive Case Finding



TB is Curable

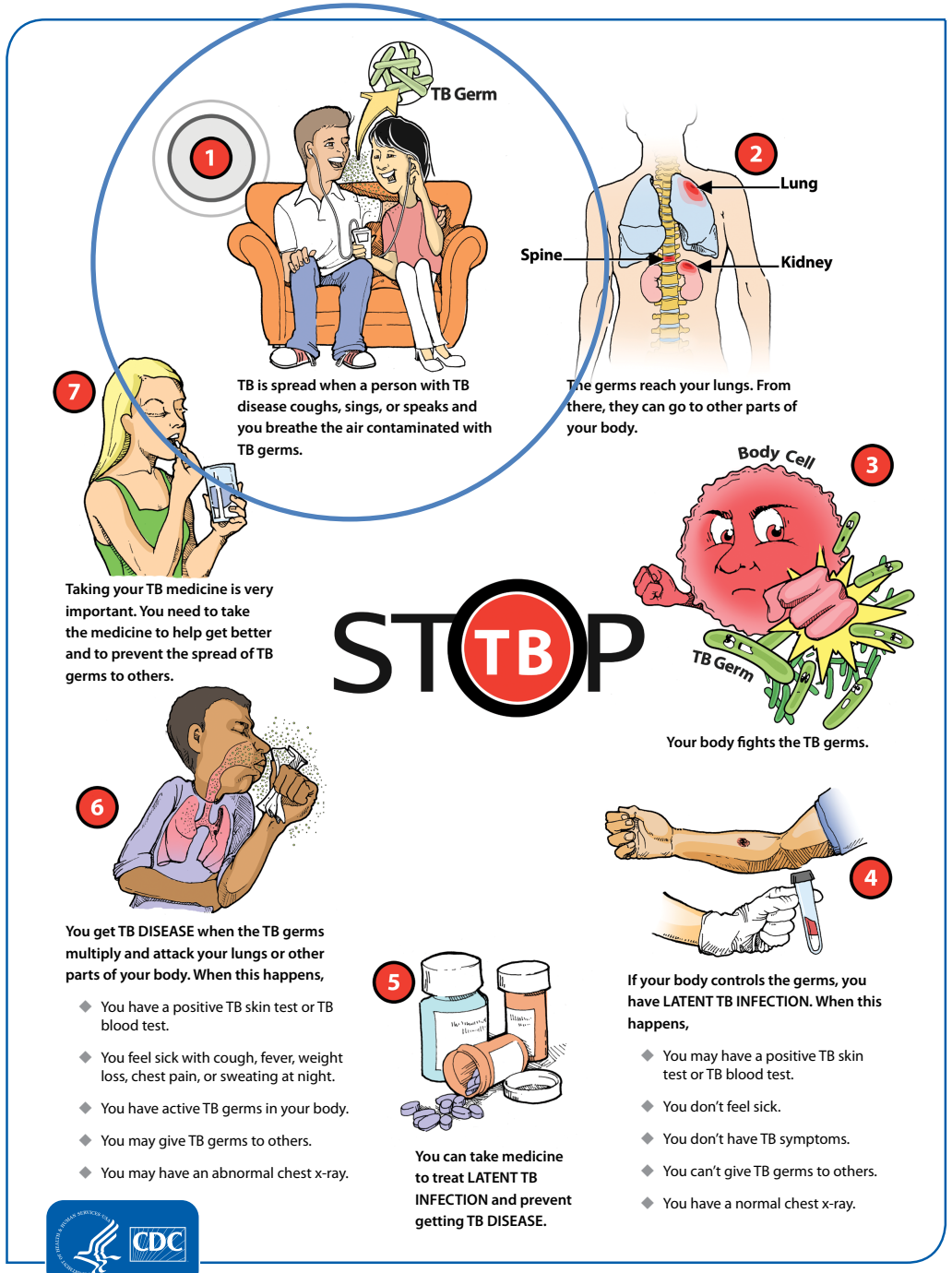
- **Early detection**: If diagnosed & treated early, it decreases risk of becoming infectious
- TB is **reportable** to public health
- **Appropriate treatment** is part of infection control
- **Case management** includes following criteria for release from Airborne Isolation
- **Public health rules** vary by state/jurisdiction



TB is Preventable

- **Contact Investigations** help to find the most vulnerable to developing TB (recently infected), but it only works if treatment is taken.

- **Targeted testing** followed by treatment of LTBI can prevent someone from developing TB disease and passing it onto friends and family (and coworkers and patients!)



Interventions to Decrease Risk of Spreading TB

- **Cough policy**
- **Environmental** controls
- **Administrative** controls
- **Public health rules** vary by state/jurisdiction

Note: this is the old Stop TB Poster
New Stop TB Poster: https://www.cdc.gov/tb/communication-resources/stop-tb-poster.html

Who are your partners?


GIANT microbes
by Drew Oliver
Tuberculosis
TB
NIH/NIAID Image of M. tuberculosis

Final Polling Question!

What is your personal experience with TB? Do you know someone who had TB? (select all that apply)

a) A patient

b) A friend

c) A family member

d) No one I know personally