Importance of a TB Medical Assessment

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Think TB

TREATMENT IS PREVENTION – WE DO NOT HAVE AN EFFECTIVE VACCINE – YET

TREATMENT STOPS TRANSMISSION

YOU HAVE TO FIND THEM TO TREAT THEM!

Latent TB Infection (LTBI)

- Persons are **infected** with *Mycobacterium tuberculosis* but:
  - No Active TB Symptoms
  - Chest X-ray may be normal, or show small granuloma, **stable** pleural or parenchymal scarring
  - Positive TST (Tuberculin Skin Test) or IGRA (Blood Test)
  - Not infectious – Do not transmit TB

Active TB Disease

- Persons are **sick** and usually have at least one of the below
    - Abnormal CXR
    - Symptoms and or findings c/w TB disease
    - Specimen which is pcr positive or grows MTB
  - Usually are infectious

LATENT TB INFECTION

- We used to think the bacteria were in a complete resting state or dormant but
  - TB Bacteria **are metabolically active and dividing**, but infection is controlled by the immune system.
- **Current methods of LTBI diagnosis are less than perfect**
- Active TB Disease may develop if immunity wanes.

The Spectrum of Activity of MTB – One Could Think of Popcorn

The Spectrum of TB Disease

Am J Resp and Critical Care Med Vol 203, Jan 15 2021

Classic Conceptualization of TB

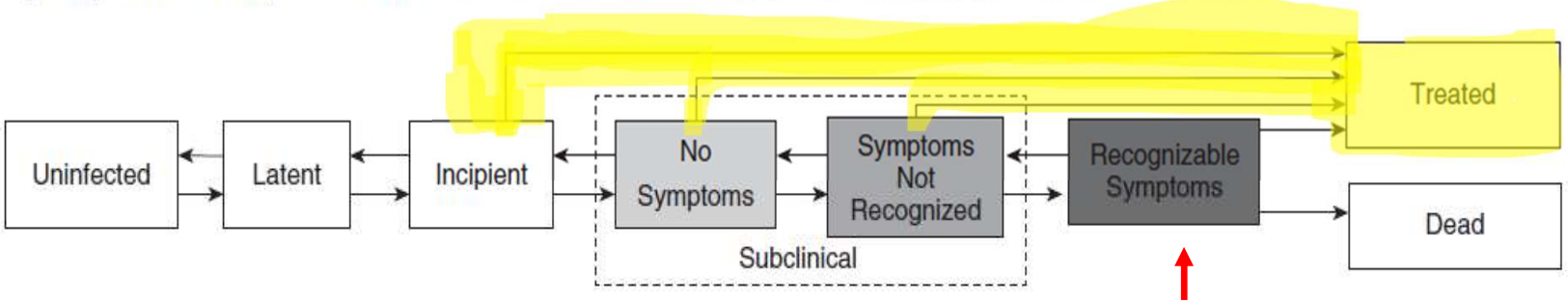
Updated Conceptualization of TB:

Incorporates Three Elements:

1) Subclinical stages from which transmission may occur without recognizable symptoms (extra boxes with grey shading)

2) Regression/resolution to milder disease possible (bidirectional arrows)

3) The potential for diagnosis and treatment before recognizable symptoms develop (upper arrows to "Treated")



Persons at Risk of (**Exposure**) MTB Infection or Disease

- People who have spent time with someone who has TB disease
- People from a country where TB disease is common:
  - most countries in Latin America, the Caribbean, Africa, Asia Eastern Europe, and Russia
    - especially now consider Afghanistan, Iraq, Ukraine
- People who **live or work** in high-risk settings:
  - correctional facilities, long-term care facilities or nursing homes, and homeless shelters
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or TB disease

Persons at Risk of **Progression** from Latent TB Infection to Active TB Disease

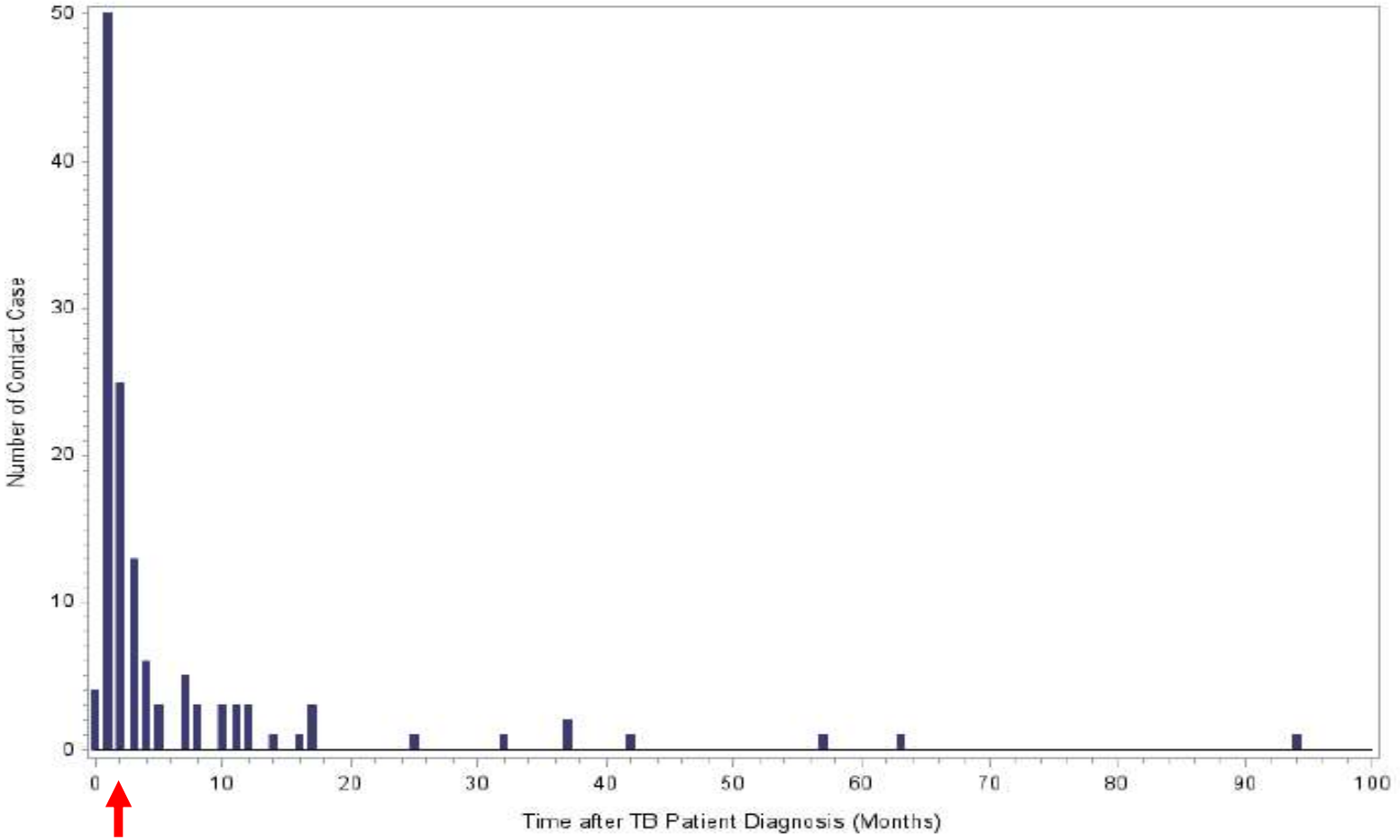
- HIV infection
- Chronic kidney disease
- Silicosis
- **Recent exposure**
- Diabetes
- Chest x-ray abnormality c/w previous inadequately treated TB
- Intravenous drug use
- Smoking – active and passive
- Underweight by >10% (*Maybe*)

ATS-CDC. Am J Respir Crit Care Med 2000;161:S221

Persons at Risk of **Progression** from Latent TB Infection to Active TB Disease

- Immunosuppression
  - Pregnancy and first three months post partum
  - Organ transplant recipients
  - Hematologic cancers and head and neck cancers
  - Medications
    - TNFα inhibitors
    - Prednisone >15 mg, > 4 weeks
    - Chemotherapy
    - Other immunosuppressive drugs

Figure 1. Timing of Tuberculosis Diagnosis among 131 Contacts Diagnosed after the Index Case Diagnosis



2 months

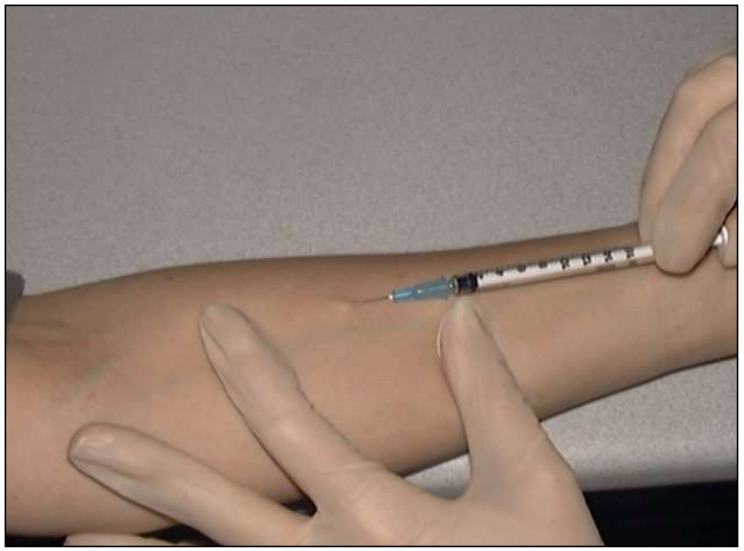
JID
June 2018

Evaluation for TB

- In U.S. usually starts with a screening test to detect evidence of TB infection –
  - Only after the provider considers the Possibility of TB
  - TB Skin Test (**TST**)
  - Interferon Gamma Release Assays (IGRA)

The Tuberculin Skin Test (TST)

- 0.1 ml of 5 TU PPD tuberculin injected intradermally
- **Induration** in millimeters read 48-72 hours after injection



Interferon Gamma Release Assays

- Replacing TST in many jurisdictions
- Blood test
  - measures interferon gamma release in response to stimulation by TB antigens
- More specific
- Equally sensitive
- Do not require a patient to return for reading
- Eliminate false positive TST due to BCG
- Can be used in children down to 2 years of age

Treating TB Infection

Wait –

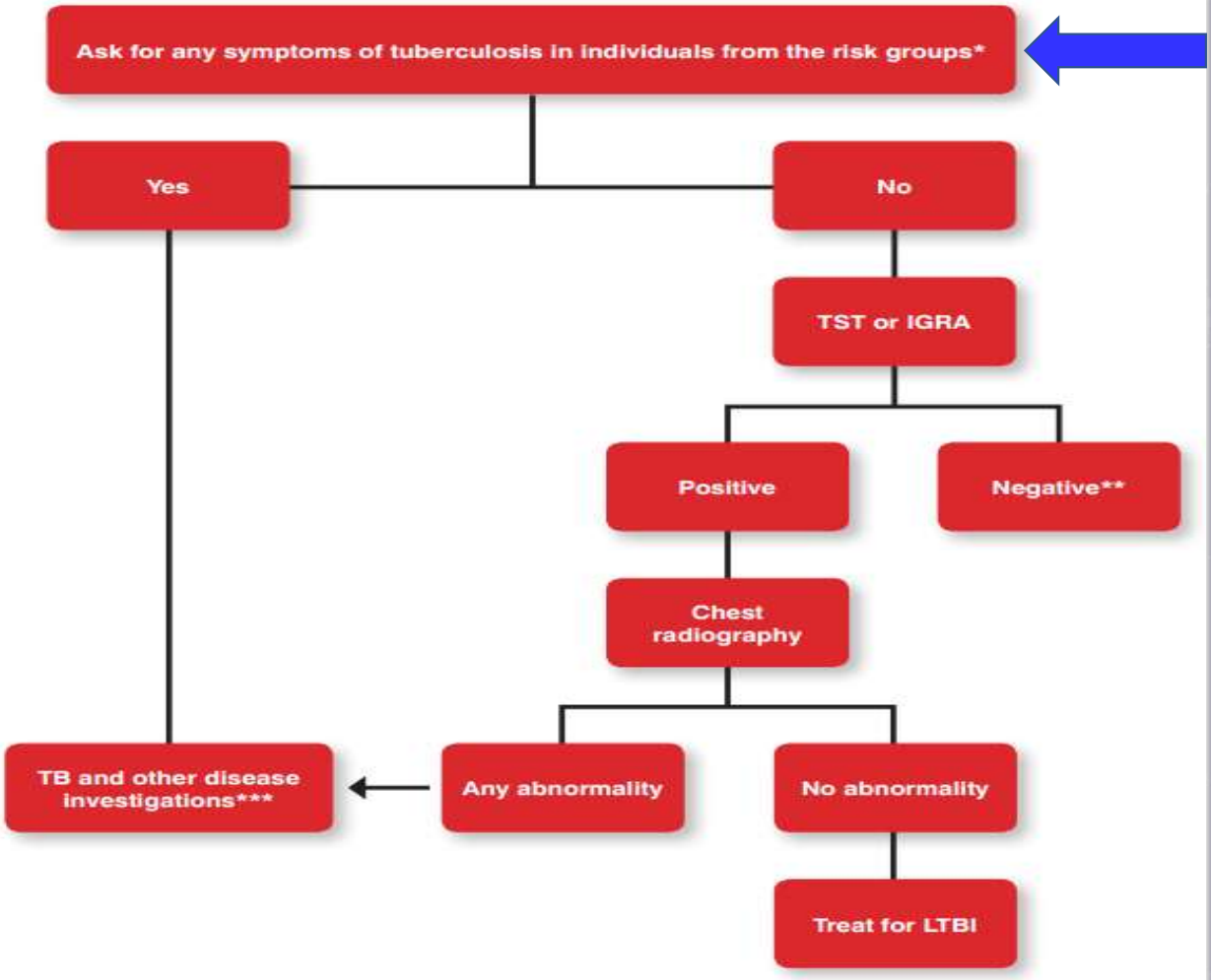
Are We There Yet?

"NO!"

WHO Guidelines on the management of latent tuberculosis infection 2015

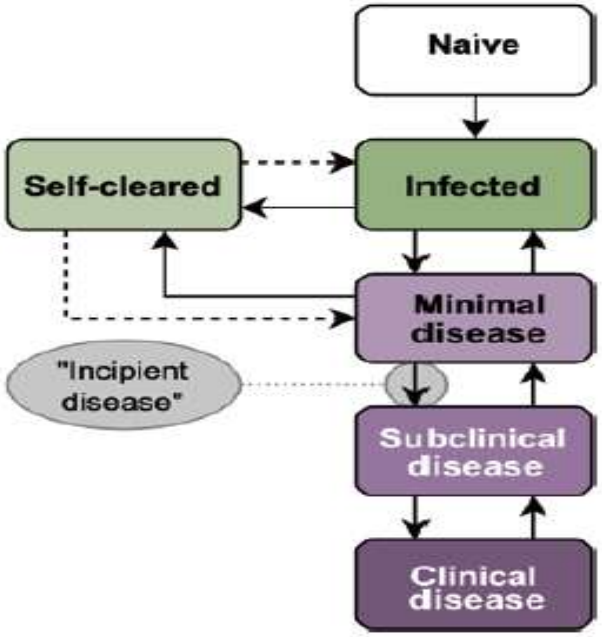
Remember that the TST or IGRA may be negative in those with active TB!

Figure 1. Algorithm for targeted diagnosis and treatment of LTBI in individuals from risk groups



* Any symptoms of TB include any one of: cough, haemoptysis, fever, night sweats, weight loss, chest pain.

Natural History of TB Infection and Disease



Infection

Disease

Clinical Infectious Disease 2021:XX Frascella et al

Active TB Disease or TB Infection? The Clinical Evaluation

The single most important thing prior to starting treatment for TB Infection is to exclude active TB disease.

If in doubt – wait!

Evaluate for TB disease

Consider consultation with TB expert

Incipient and Subclinical TB

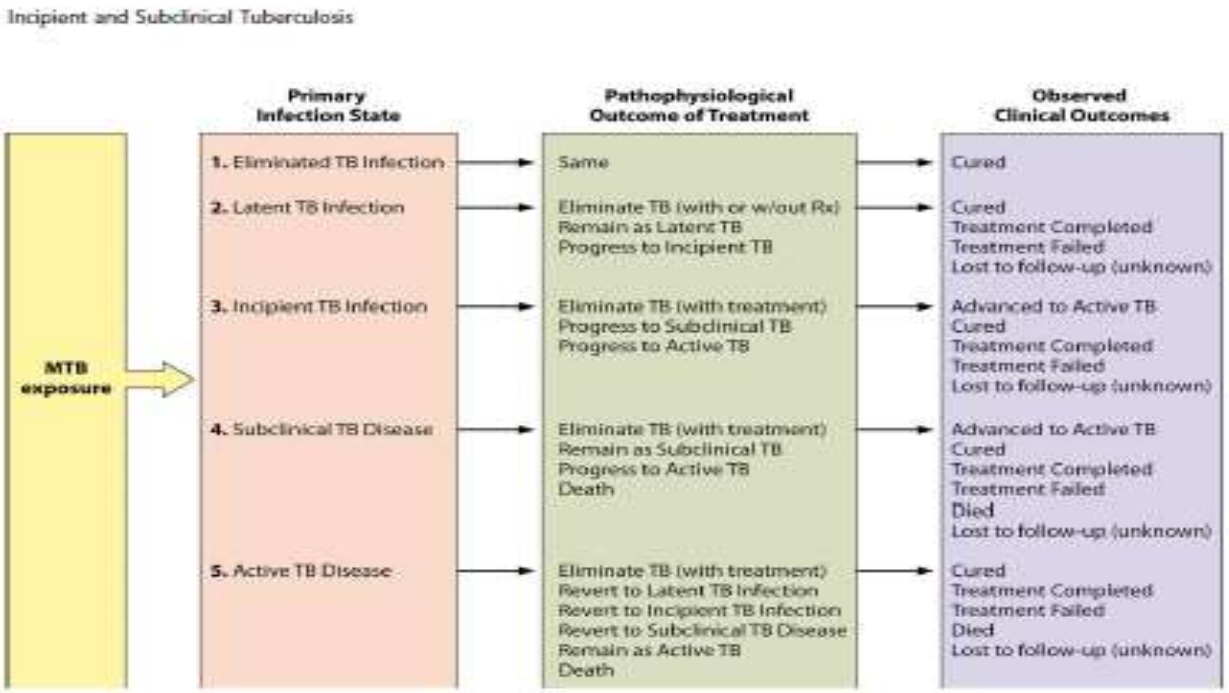


FIG 2 Primary and secondary disease states for the five categorical states of TB. Clinical outcomes following treatment are variable and depend on the respective pathophysiological outcomes. MTB, *M. tuberculosis*.

Evaluate to Exclude Active TB Disease

- If the TST or IGRA is Positive –
  - **OR**
- Child < 5 or immunocompromised person with recent exposure or patient has symptoms –

–even if TST/IGRA negative -

√ History
√ Physical examination
√ Chest X-Ray

How Can TB be “Ruled Out?”

Is There Evidence of Disease?

- Symptoms*
  - Fever
  - Chills
  - Night Sweats
  - Weight Loss
  - Cough (dry/productive)
  - Hemoptysis
  - Fatigue

    * **only one may be present – or patient may deny all**

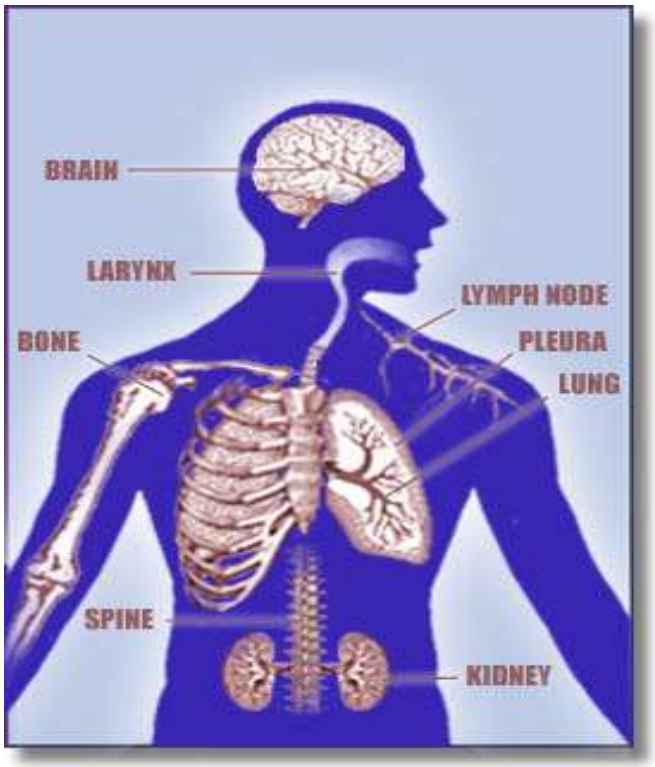
Is Patient at Risk of Progression to Disease?

- Medical History:
  - HIV
  - Silicosis
  - Chronic Kidney Disease
  - Diabetes
  - Immunosuppression
  - Drug/alcohol/tobacco
  - TB exposure

TB Exam – Focus on Possible Sites of TB Disease

- Lungs – Pulmonary

- Extrapulmonary
  - Larynx
  - Lymph nodes (cervical inguinal, supraclavicular, mediastinal, abdominal
  - Pleural effusion
  - Genitourinary
  - Bones & joints
  - Miliary (disseminated)



Physical Exam

- General assessment – does person look well?
- Lung exam
- Check for lymph nodes
- Palpate liver
- *In children* look at growth curve/weight/activity
- Look for anything that will complicate therapy!
- Laboratory abnormalities c/w active TB
  - Elevated platelet count, low serum albumin, anemia

Radiologic Exam

- CXR must be done **before treatment of TB Infection**
  - Must be read as normal

    Or
  - IF abnormal:
    - Not consistent with Active TB
    - Stable abnormality confirmed over a 3 - month period

CXR - Can Suggest TB Disease but Does Not Definitely **Diagnose or Exclude** TB Disease

Cavitary lesions
Upper lobe infiltrates
Pleural effusion especially in those with recent exposure
"Tree in bud" findings on CT exam

Common mimics of TB =

- Non-tuberculous mycobacteria (NTM)
- fungal infection
- bacterial abscesses

Usually thin walled cavities

- necrotic neoplasm (especially lung neoplasm)

May be Normal!

CXR – Old Healed TB

- Nodules & fibrotic lesions may contain slowly multiplying bacilli; these persons have a higher risk for progression to active TB disease

Caution: I usually have several patients in the San Antonio TB Clinic with positive cultures for TB and a CXR report that says c/w old healed TB.

If the CXR is "stable" for 2 – 3 months this is an indication that abnormality represents latent TB infection

If the CXR shows calcified nodular lesions (calcified granuloma) there is a very low risk for progression to TB disease

Bacteriologic and Histologic Examinations

When lung or larynx is site of disease and for **every** patient with extrapulmonary TB:

- **3** sputum specimens for
  AFB smear and culture
  Ask for a pcr (GeneXpert) on initial specimen if you suspect TB disease

- Collected 8-24 hours apart
  with at least 1 early morning specimen
  one induced specimen
  one observed specimen

Bacteriologic and Histologic Examinations

Extrapulmonary Specimens

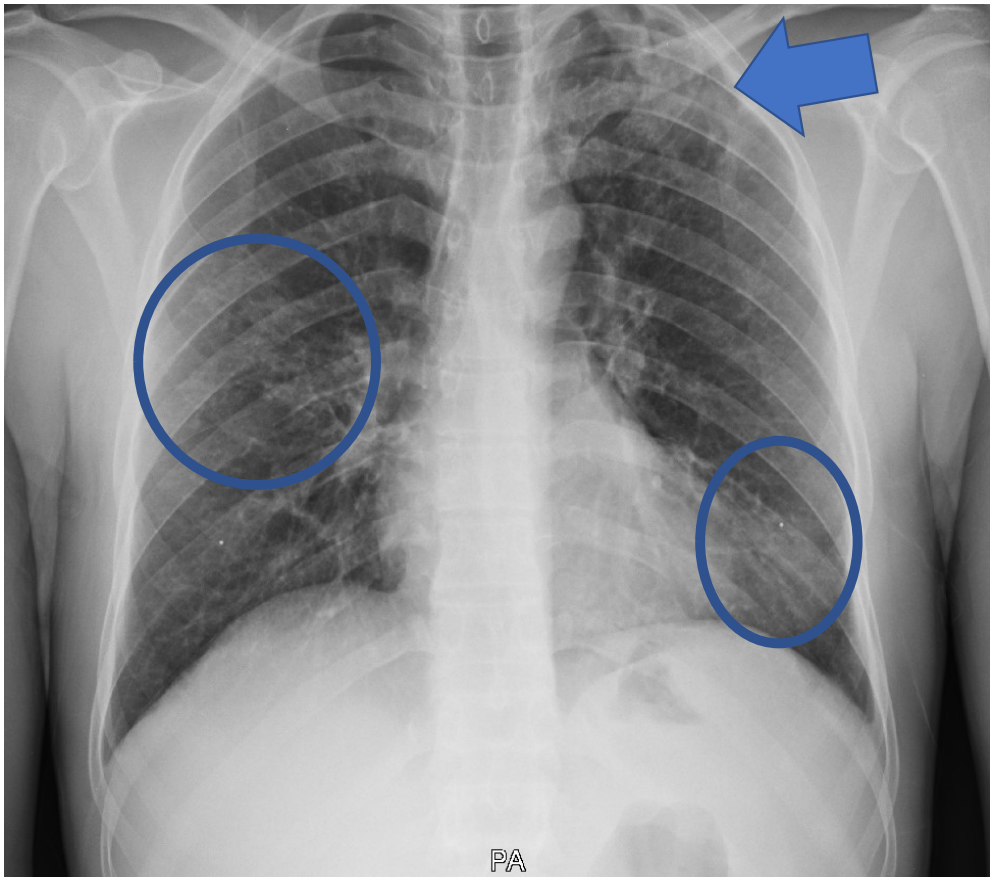
- Urine
- Cerebrospinal fluid *
- Pleural fluid *
- Ascites *
- Pus
- Biopsy specimens

*recovery poor

Case Study - Immigrant Evaluation For TB Spring 2018

- 13-year-old immigrated from Northeastern African country within last year
- Thin but otherwise well
- Positive T-Spot
- Normal CXR

Latent TB Infection



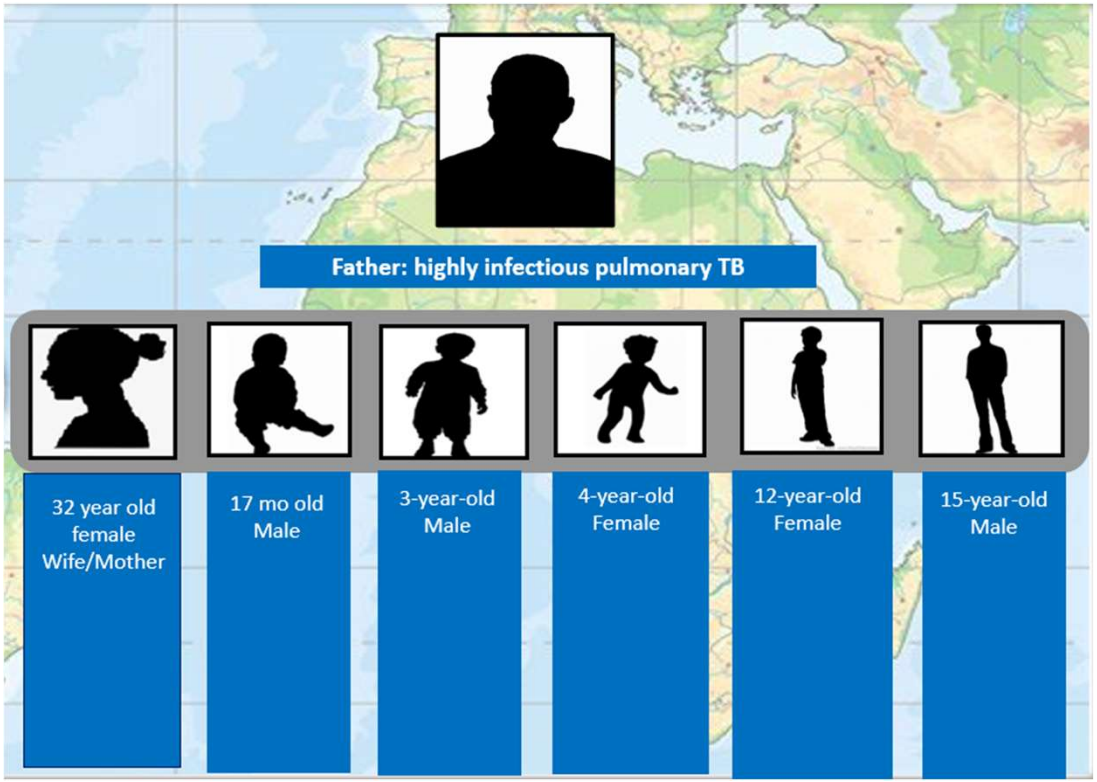
May 2019

37 year old African man
4 months of cough, weight loss, and poor energy
6 weeks after starting TB treatment remains strongly AFB smear positive

AFB – Acid Fast Bacilli

ACTIVE TB DISEASE

Family of Newly Diagnosed Patient Comes to Clinic – **What Now?**



1
2
3
4
5

Public Health's responsibility is to:
Find and treat disease if it is there
Find and treat LTBI if it is there
Protect the vulnerable contacts even if all tests are negative

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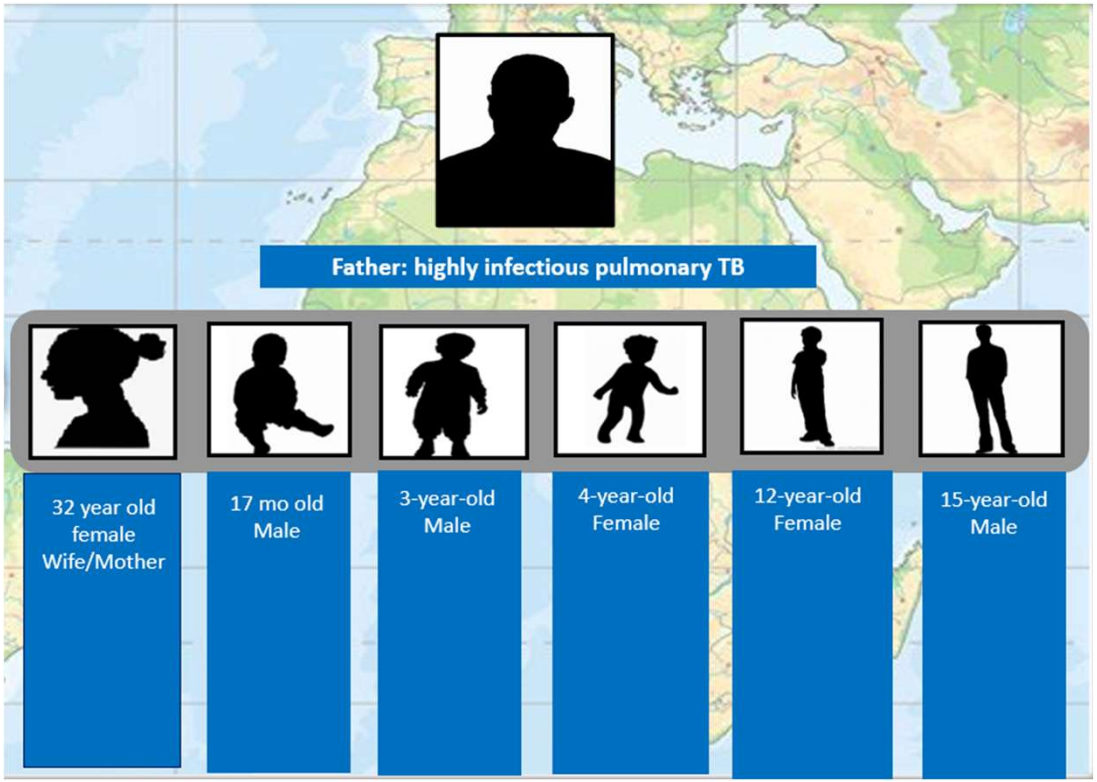

- 1 IGRA-except 17-month-old
  - BCG vaccinated
  - TST for children <2
- 2 Evaluate for symptoms of TB; generally, do they look well? Kids playful? Alert?
- 3 Medical Assessment
  - Weight, BMI, Growth curve for kids
  - Targeted exam – lungs, lymph nodes
- 4 CXR
- 5 Sputum if any signs or symptoms

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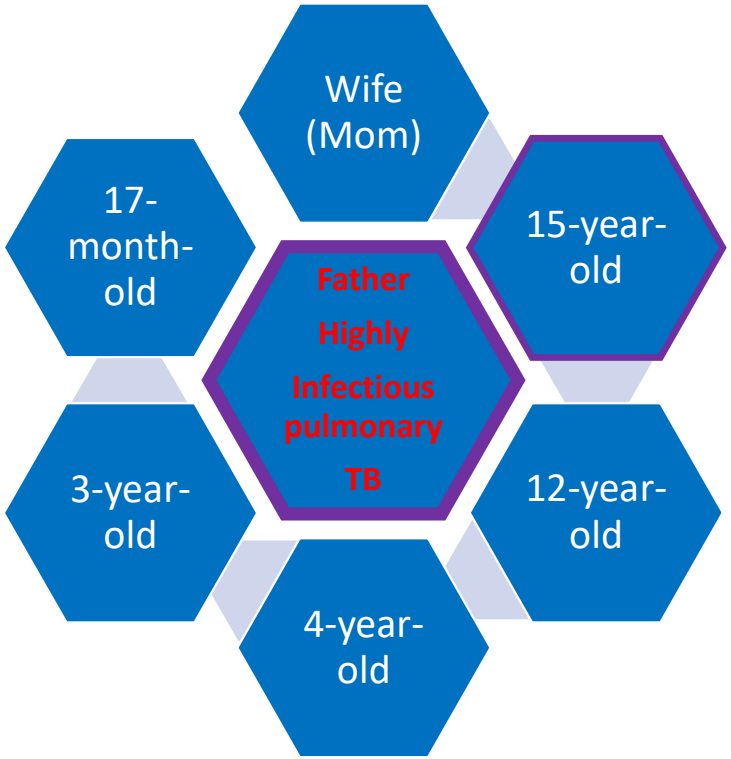

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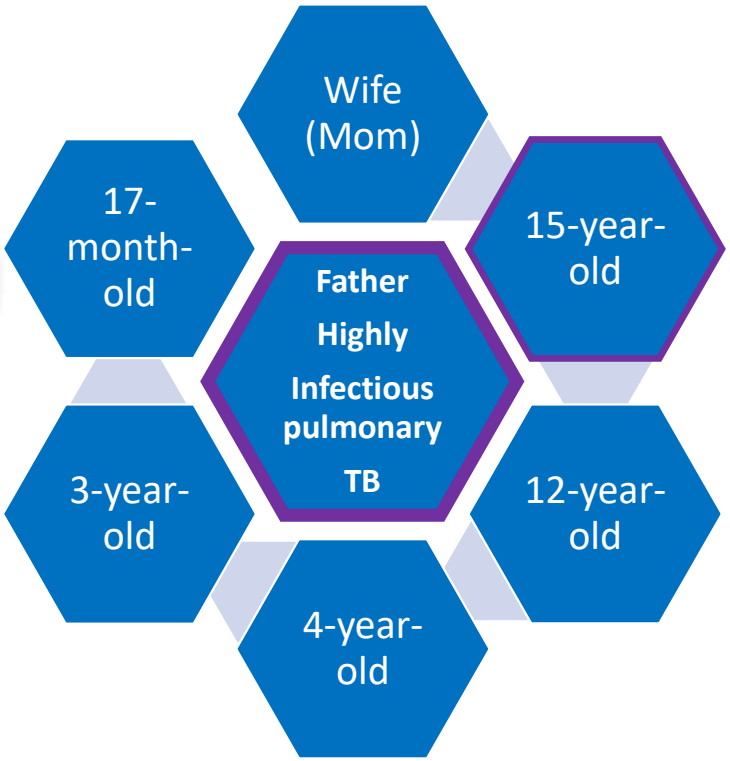

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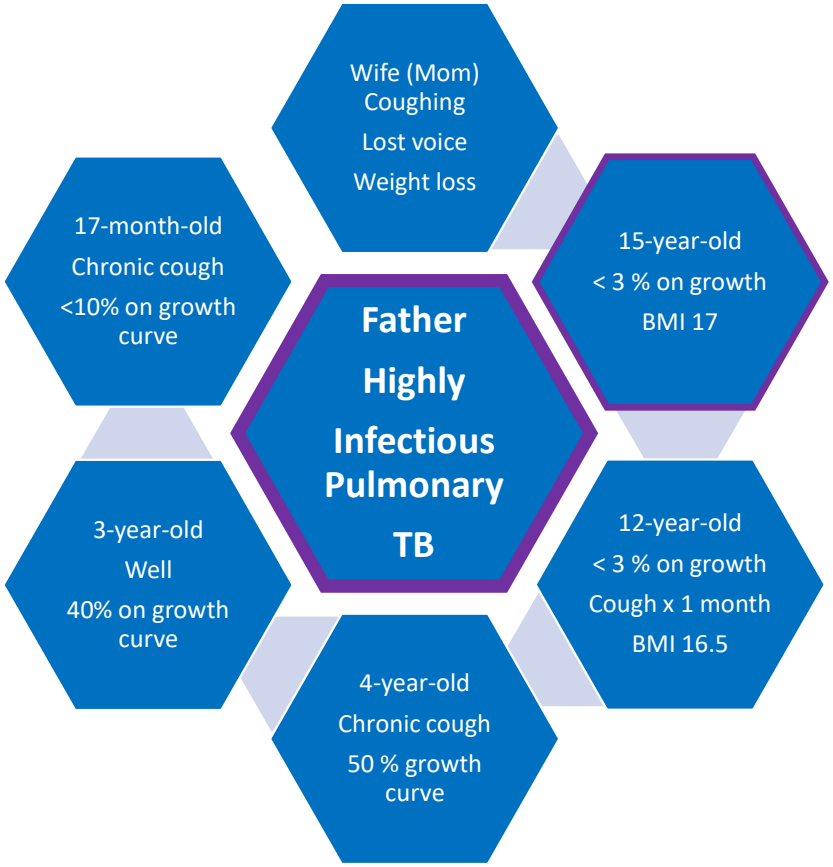
- CXR
- Sputum if coughing

2019 Contact Investigation in Family

Epidemiology is Critical Information



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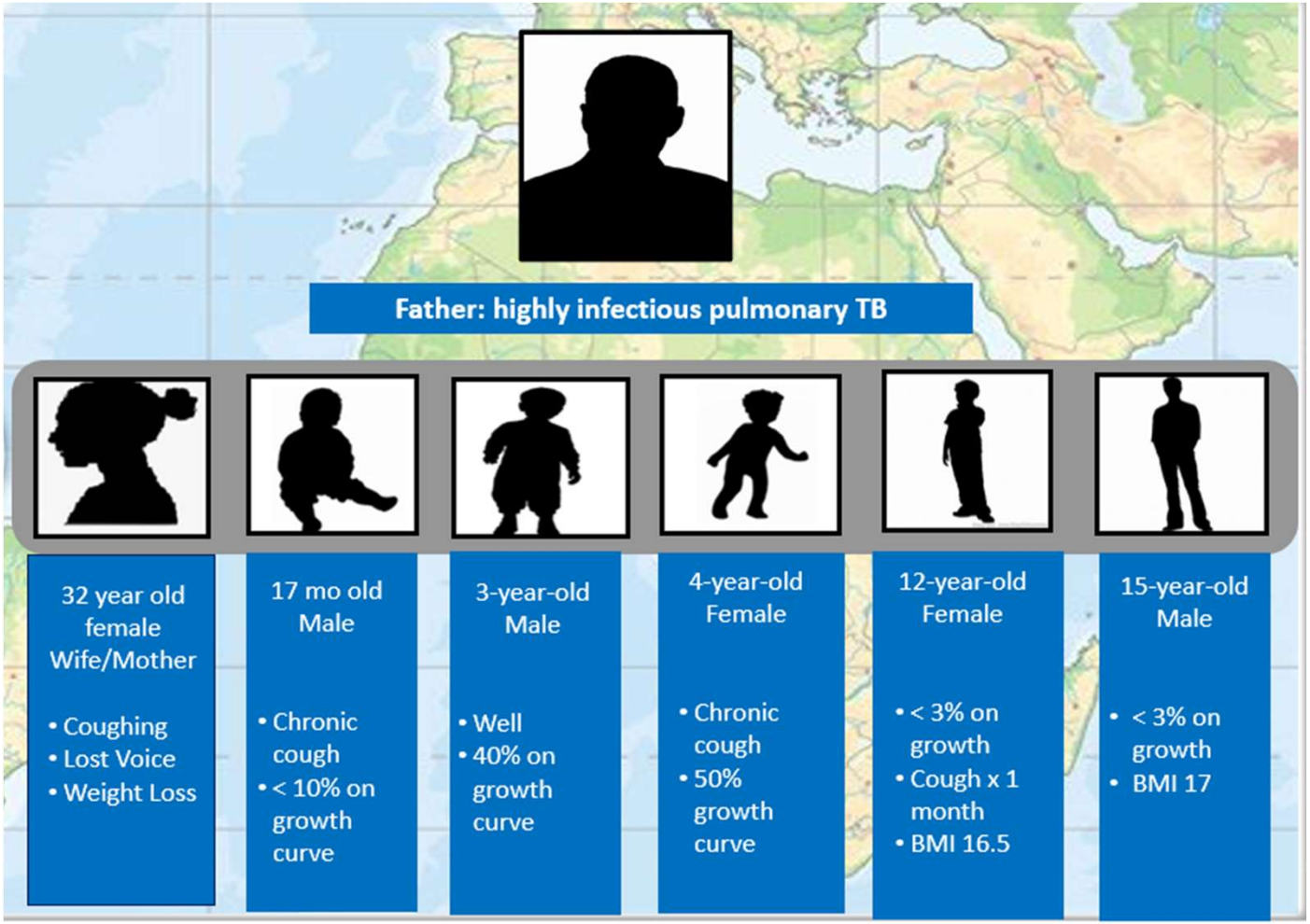
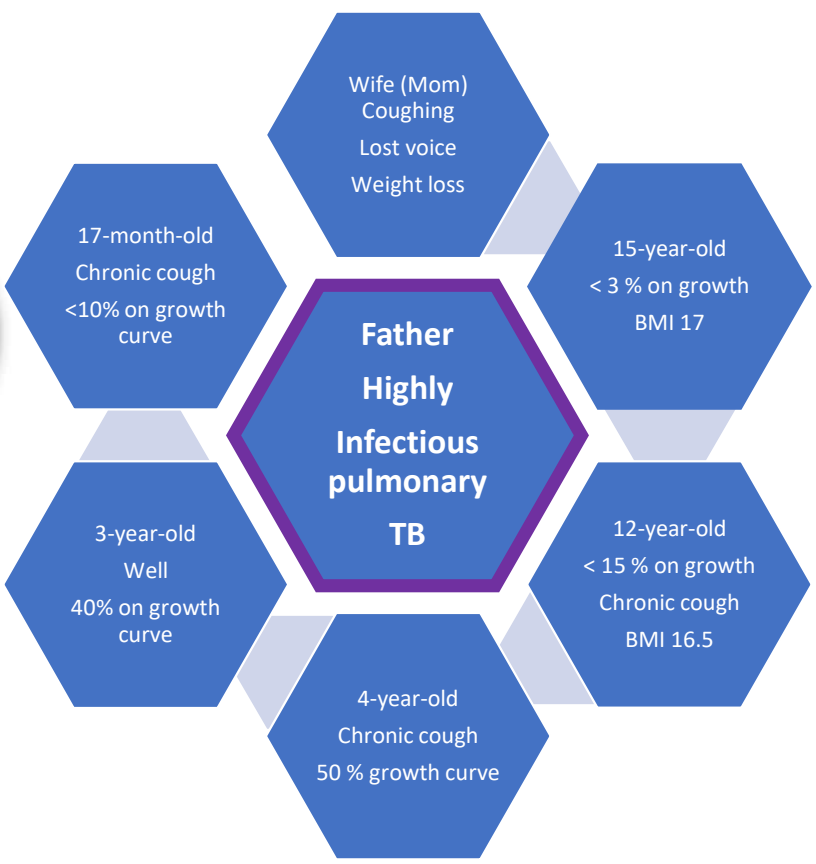
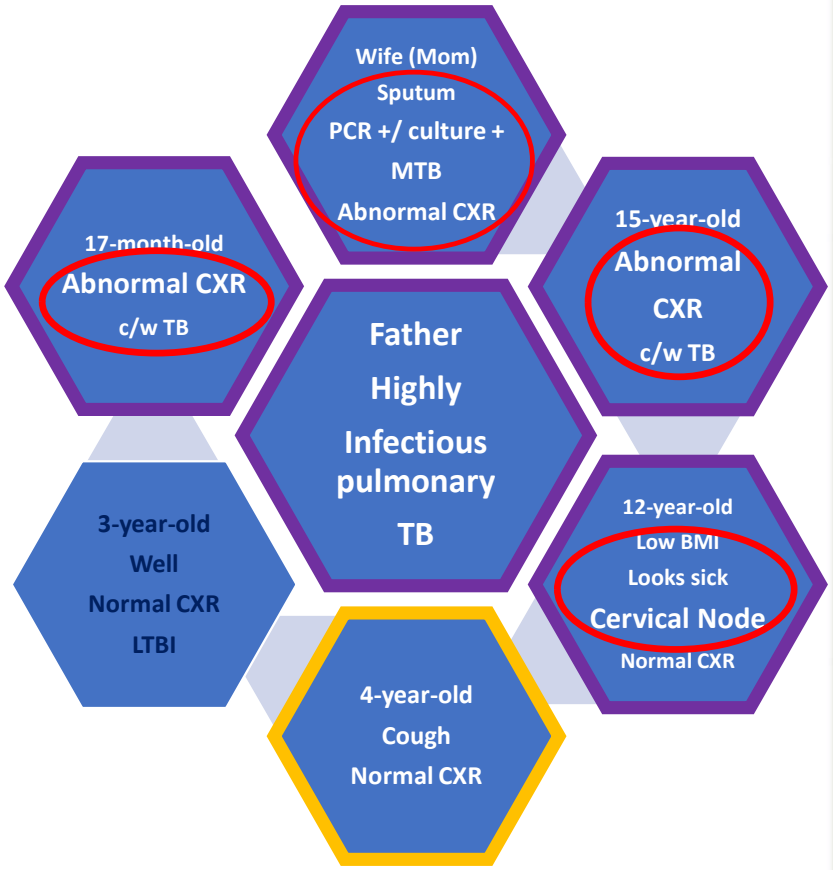
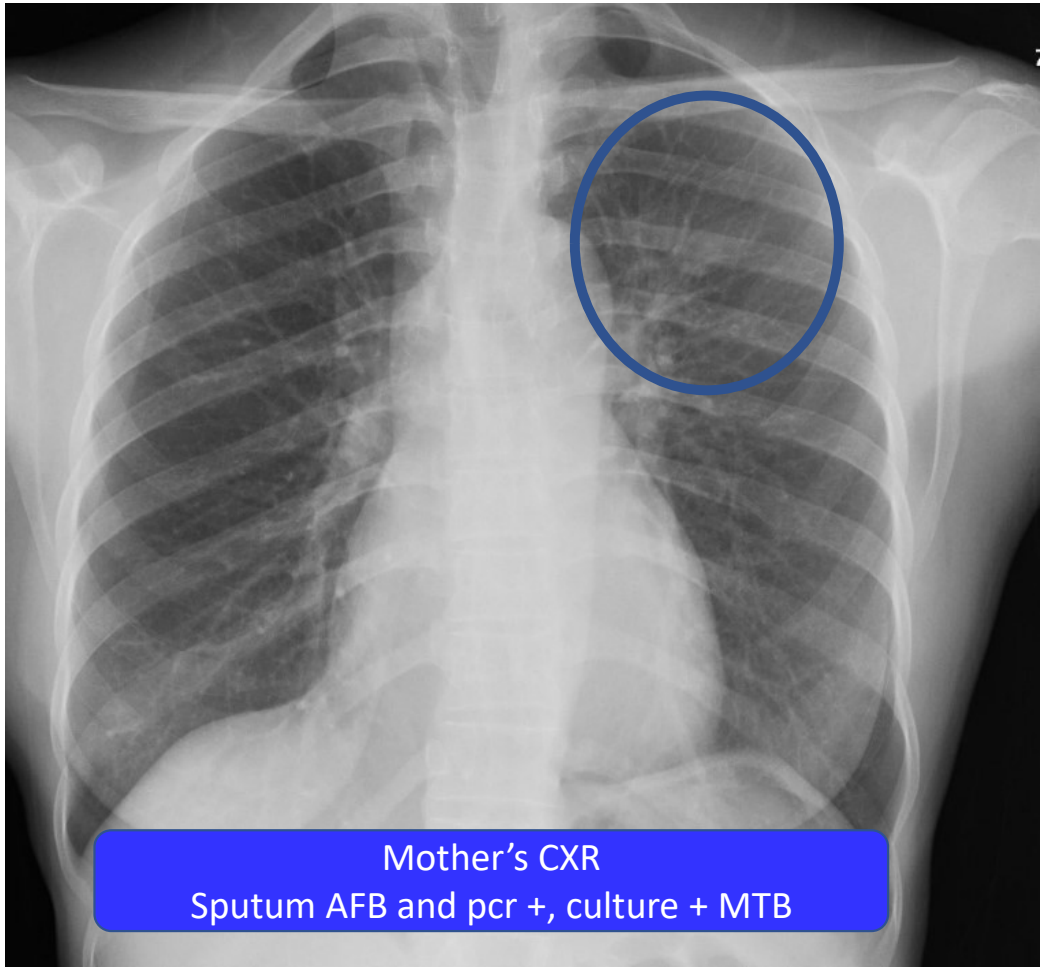


2019 Contact Investigation in Family
All IGRA positive except 17-month-old - 20 mm blistering TST







Mother's CXR
Sputum AFB and pcr +, culture + MTB

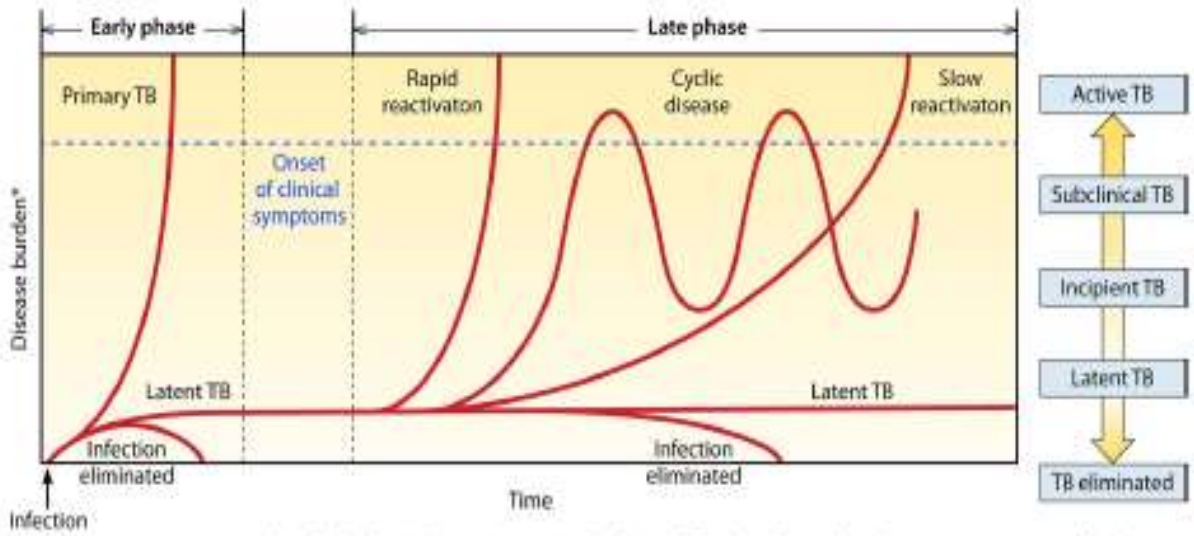
CXR read as normal

CXR can be normal -
Make sure your patient's really is.

Pathways of TB Disease Progression

Drain et al.

Clinical Microbiology Reviews
October 2018 Vol 31

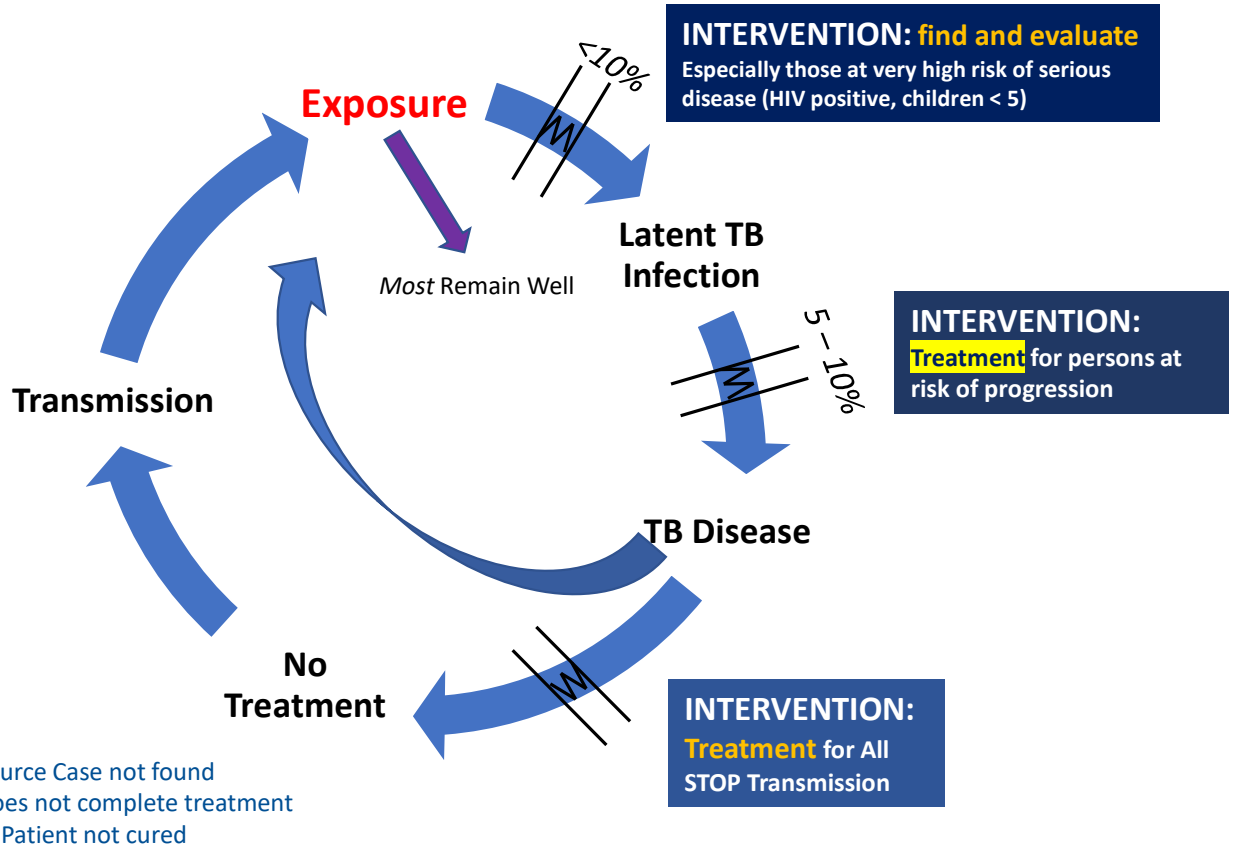


*Rising TB burden implies an increase in abundance of TB and pathogen biomarkers, compartment-specific changes in immunological responses, and a decrease in the probability of disease resolution in the absence of treatment.

FIG 1 Pathways of tuberculosis disease progression. After initial exposure, *M. tuberculosis* may be eliminated by the host immune response, persist as a latent infection, or progress to primary active disease. Following the establishment of latent infection, disease may persist in a latent form, naturally progress in a slow or rapid fashion to active tuberculosis, or cycle through incipient and subclinical states before developing into symptomatic disease or eventual disease resolution. Although not all possibilities for regression of disease burden are depicted, spontaneous recovery may occur in any of these clinical trajectories.

How Can TB be “Ruled Out?”

Treatment is Prevention



Source Case not found
Patient does not complete treatment
Patient not cured

Think TB

TREATMENT IS PREVENTION – WE DO NOT HAVE AN EFFECTIVE VACCINE – YET

TREATMENT STOPS TRANSMISSION