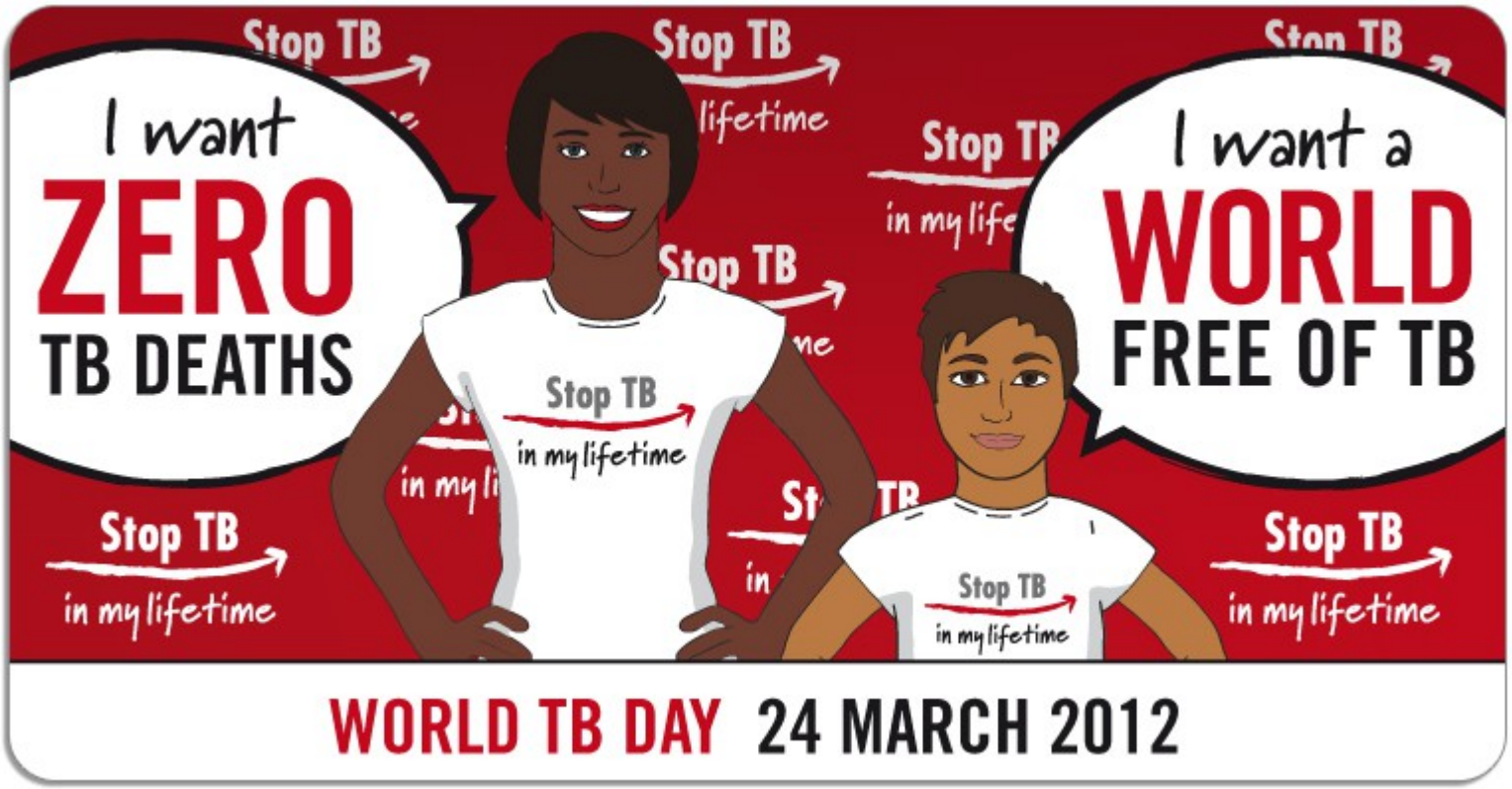
Paediatric TB



Stories from South Africa

"He was quiet when he died," reported Thabo's auntie. "He hardly made a sound. I would almost never have known if it hadn't been for the flies, really."

NDoH TB Mission Statement

To **prevent** TB and to ensure that those who do contract TB have easy access to **effective**, **efficient** and **high quality diagnosis**, **treatment** and **care** that reduces **suffering**.

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Mandela was treated for TB in 1988

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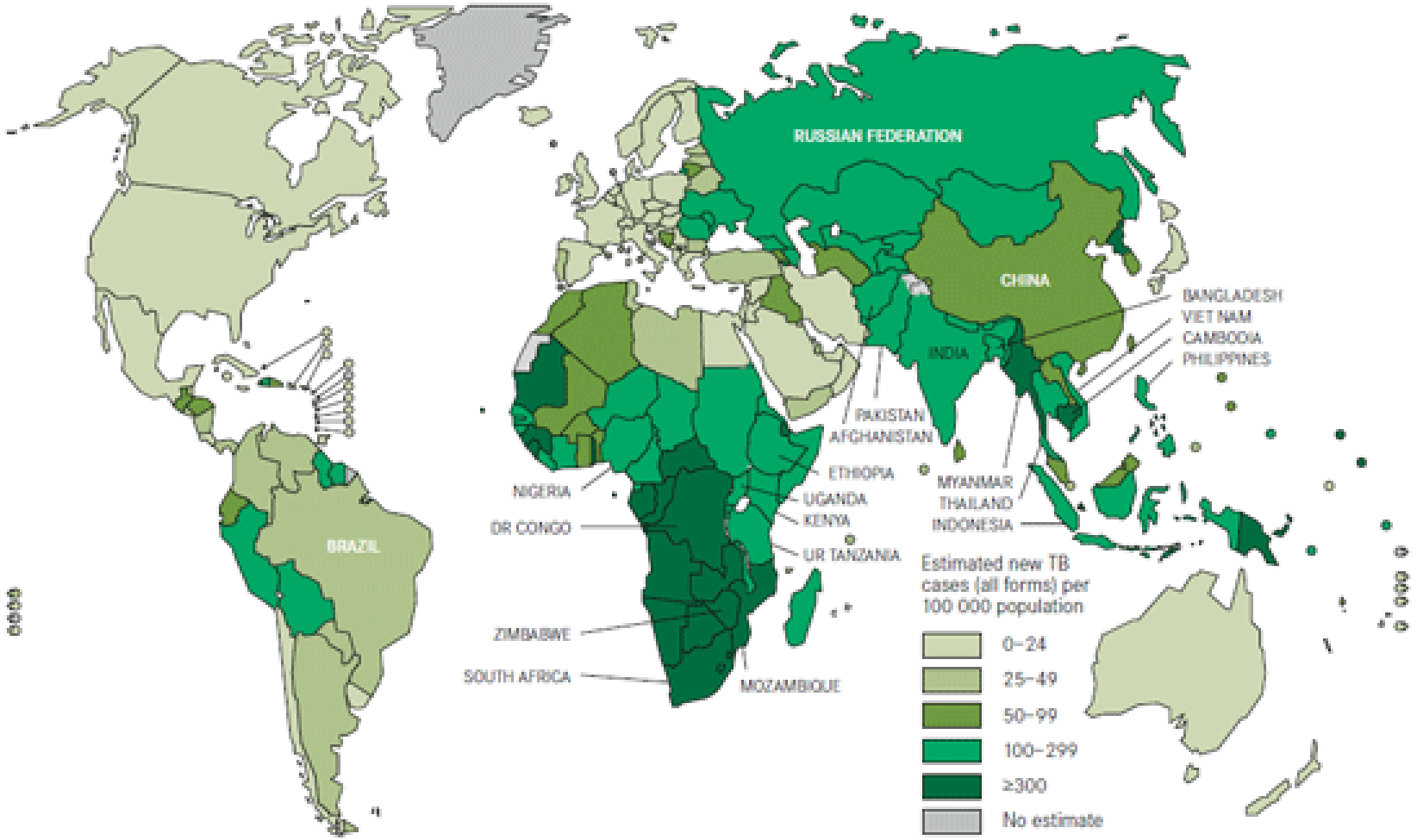
Global TB Burden



Burden of Disease in South Africa

- Rate of TB cases:
  - Globally **139 cases/100,000**
  - High burden countries **177 cases/100,000**
  - Africa - **363 cases/100,000** population
  - South Africa – **940 cases/100,000** population

Factors the Influence the TB Pandemic in Africa

- South Africa has the highest TB incidence in the world, 5x the rate of high-burden countries. WHY?
  - Poverty and rapid urbanisation
  - Impact of the HIV pandemic
  - Poor health infrastructure
  - Poor programme management with **inadequate case detection**, diagnosis and cure

TB in South African Children

- 948 per 100 000 population
- 9th heaviest TB burden in the world
- South African TB prevalence:
- 3% of children = annually infected with TB
- Median age = 12 – 15 months
- 8% of children presenting with acute lower respiratory tract infections have culture confirmed TB
- 48% of 138 cases culture confirmed TB present as acute pneumonia (Jeena PM et al Int J Tuberculous Lung disease 2002)

TB in South African Children

- HIV / TB co-infection in 35 – 52% childhood TB cases
  - MUST perform HIV test on all children with TB
- 38% of HIV-infected children at CHB were on TB treatment at the time of starting ART! But very few cases proven
- Risk of TB disease 4 times higher in children with a CD4 < 15% (12.4%) compared to children with a CD4 > 15% (3.3%) in children older than 3 years (Elenga et al PIDJ 2005)

Transmission of TB is person-to-person via airborne droplet nuclei.

- Cough – 3000 droplet nuclei
- Sneeze – up to 1 million droplet nuclei
- Singing, Aerosol-producing investigations
- 10-200 droplets can cause TB infection

TB Transmission

- Droplet nuclei can stay airborne for up to 72 hours (like dark, damp rooms, sunlight kills them
- The most infectious person has PTB and lung cavities – usually older than 12-years-old
- EPTB is generally not infectious unless they also have PTB
- Latent TB is not infectious

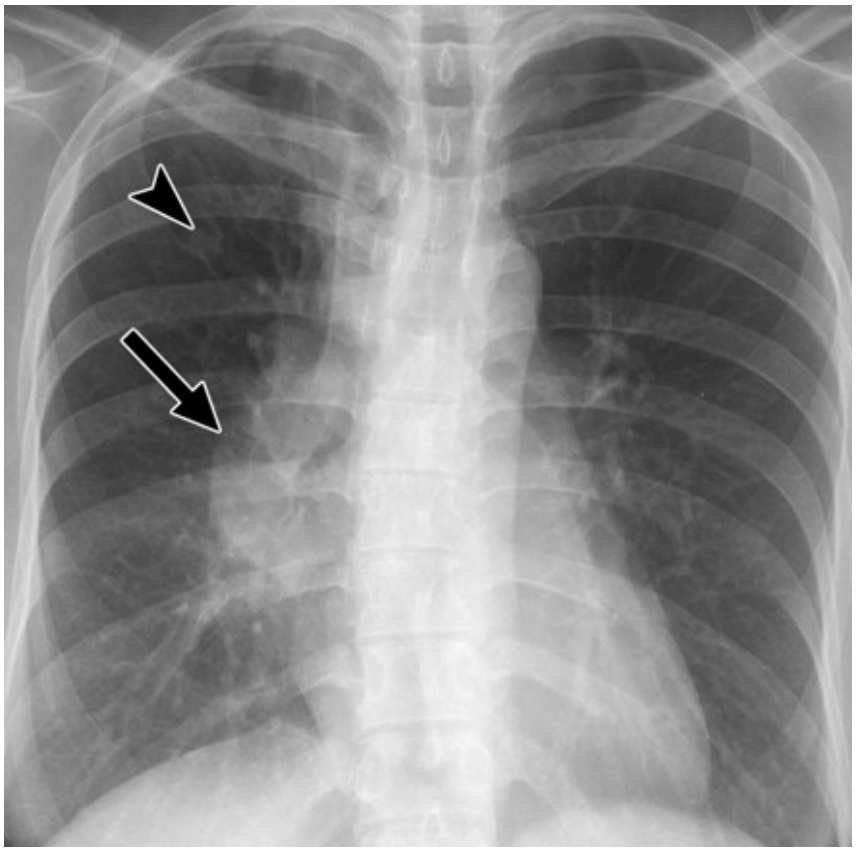
because TB is not replicating or causing them to cough

Primary TB infection: usually asymptomatic.

- Occurs on 1st exposure
- Inhaled droplet nuclei lodge in the **terminal alveoli**
- Are phagocytosed by **macrophages** causing a local immune response - **Ghon focus**
- Bacilli/antigens drain to the hilum causing hilar LAD = **primary complex**

Ghon Focus

Primary TB Infection



Primary Complex

- Eventually growth ceases and macrophages containing TB die and the **primary complex** is replaced by fibrous scar tissue (may have calcification
- Will have a +TST within 4-6 weeks

What are the risks of developing active TB after primary TB infection?

- Normal immunity 10% or 1:10
  - Risk is highest in the first 2 years after infection and again late in life especially for children <5 and elderly
- Decreased immunity – 50-60% will progress to active TB disease
- So: **IPT** for all under 5yo and for all with immune impairment

TB screening should be done at every medical encounter for every patient.

- Maintain a high index of suspicion bearing in mind the **high TB and HIV prevalence** in RSA
- **TB exposure** is especially relevant in children (trace adults to prevent TB in children!!)
- TB is a **paucibacillary** disease in children – do not rely solely on sputum

Children with HIV have an increased risk of developing TB disease.

- Increased risk of TB **exposure** from parents with HIV/TB
- Increased risk of progressing from primary TB **infection** to TB **disease**
- Progression to TB disease occurs **more rapidly**
- Clinically **more difficult to definitively diagnose** TB due to confusing CXR and cross-over of HIV and OIs with signs/symptoms of TB (cough, FTT, LAD, LIP, abnl CXR)
- More likely t and TB culture

Symptoms of TB

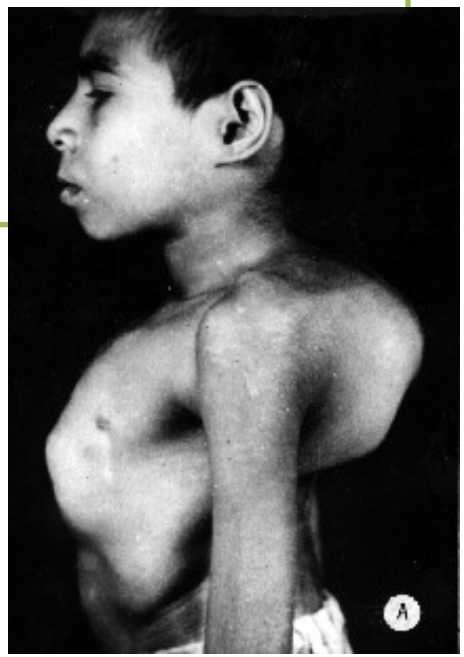
- **Cough** (2 weeks)
- **Fever** (2 weeks)
- **Night sweats** (drenching)
- **Weight** loss or poor weight gain
- Malaise and fatigue
- Loss of appetite
- Shortness of breath
- Chest pain

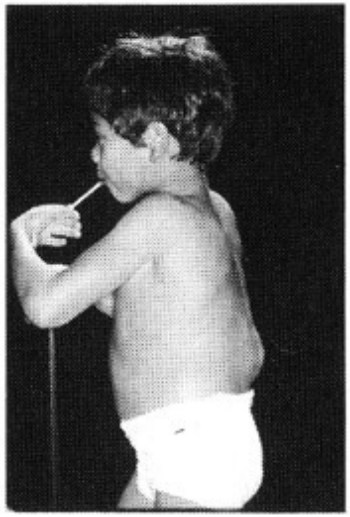
Signs of TB disease

- Painless LAD
- Hilar/mediastinal LAD
- HSM/abd pain on exam
- Acute angulation of the spine
- Scrofula
- CSOM
- HA- fits, vomiting, irritability
- Lung exam varies
- Others

sease

Destroyed vertebrae with Cold Abscess

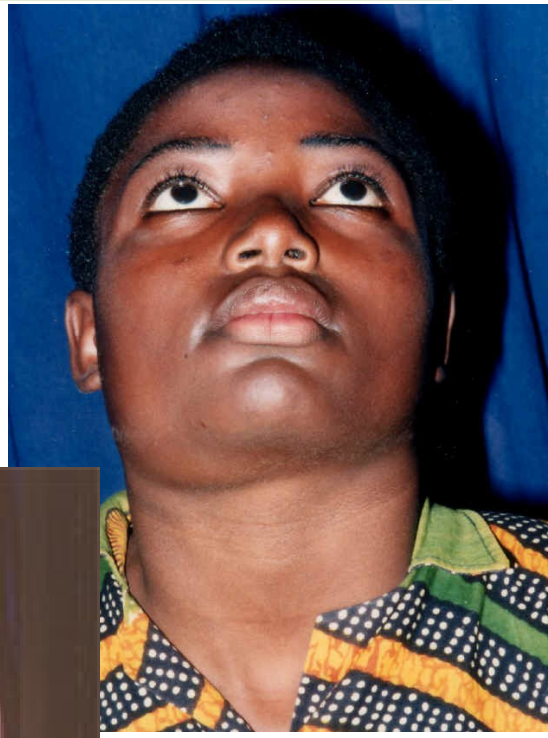


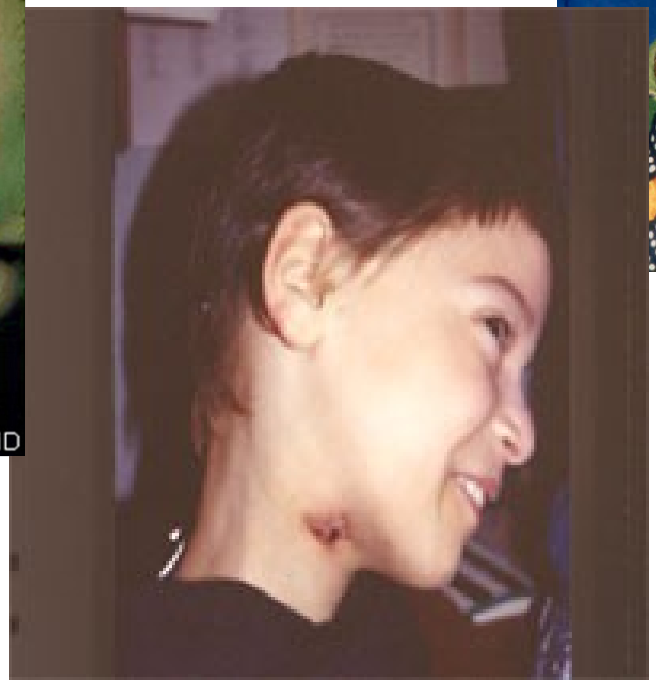


TB Meningitis

Scrofula

Primary Disease of Cervical Lymph Nodes

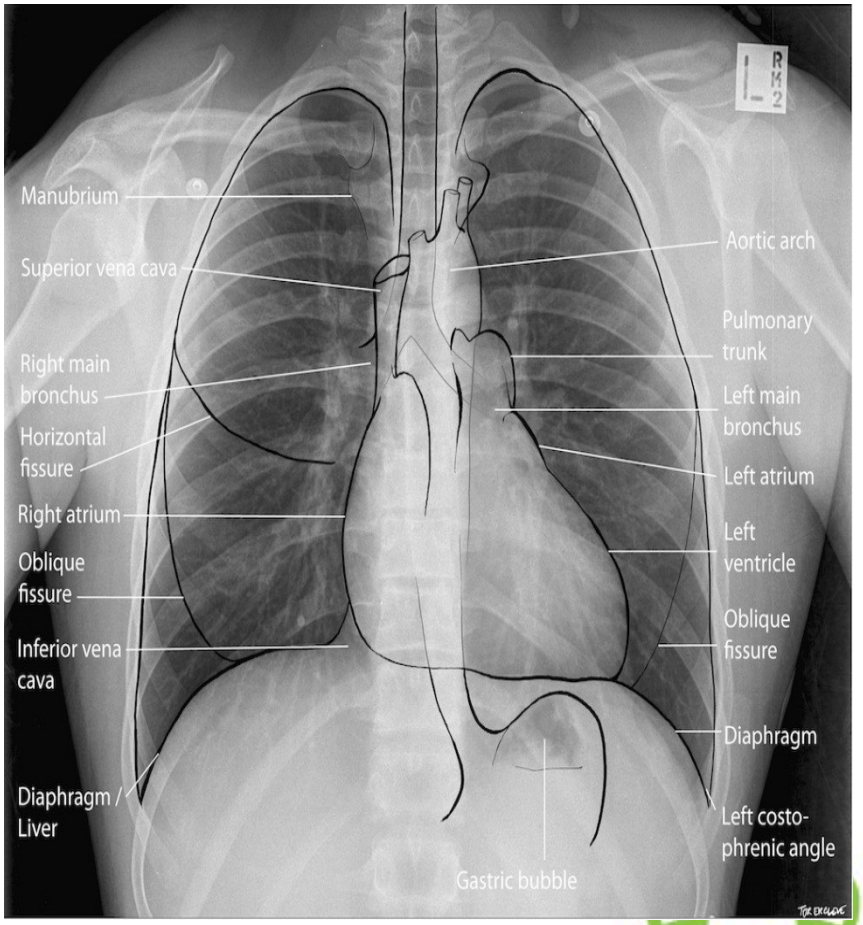




How useful are TB investigations?

CXR – NOT a stand-alone TB test

- Generally non-specific
- Hilar LAD (lateral is useful)
- Widened mediastinum
- Compression of the airways
- Opacification
- Millet-sized lesions (1-2mm) = miliary TB
- Pleural effusions (usu >6yo)
- Cavitary lesion (~12yo)
- May be normal (esp. EPTB)



Hilar Adenopathy

Figure 7.5 – Hilar adenopathy. A. Unmarked image. B. Marked image to outline the presence of bulky, bilateral hilar adenopathy. Occasionally even large lymph nodes like this are dismissed as pulmonary arteries.

Hilar Adenopathy

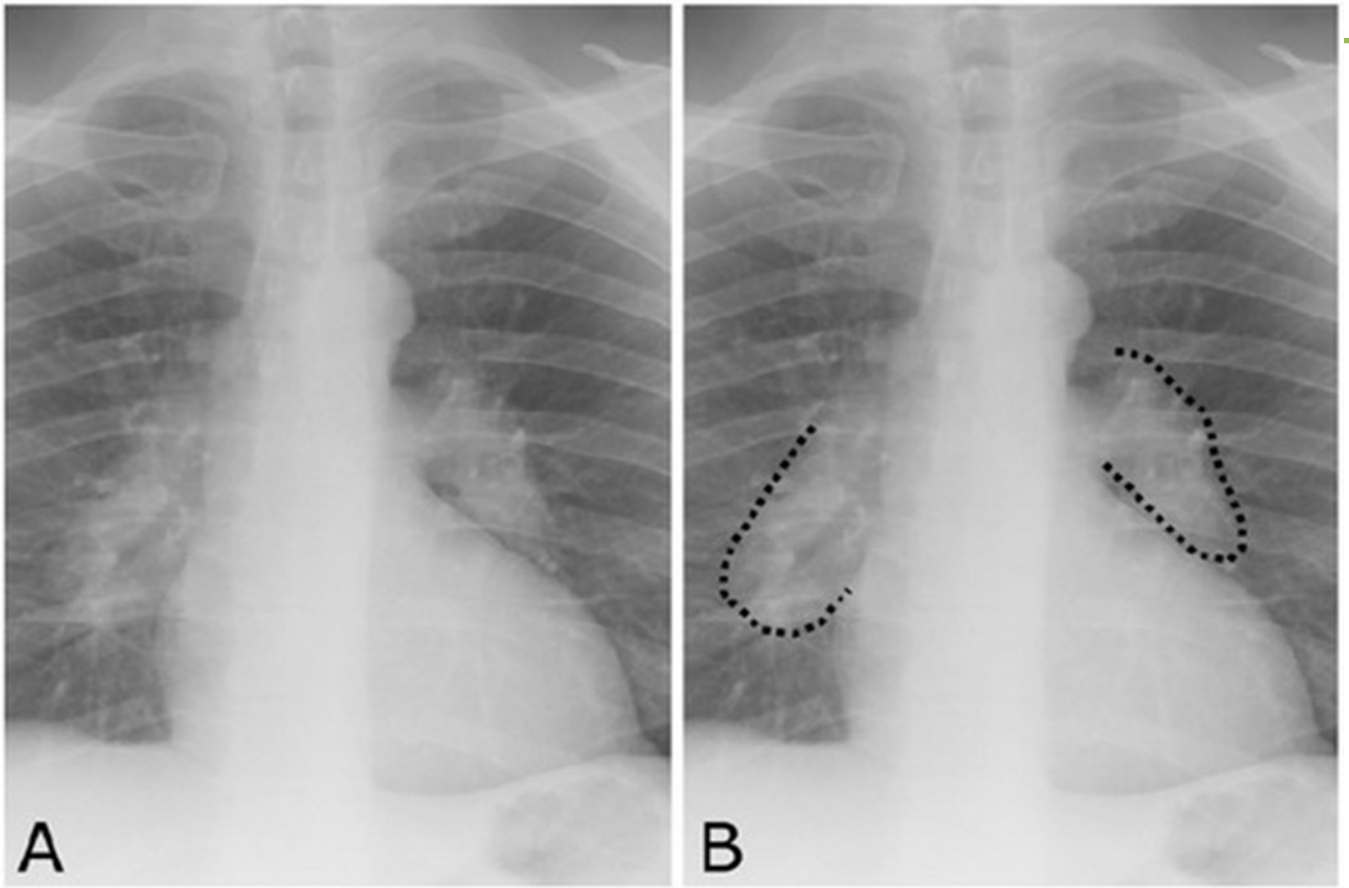
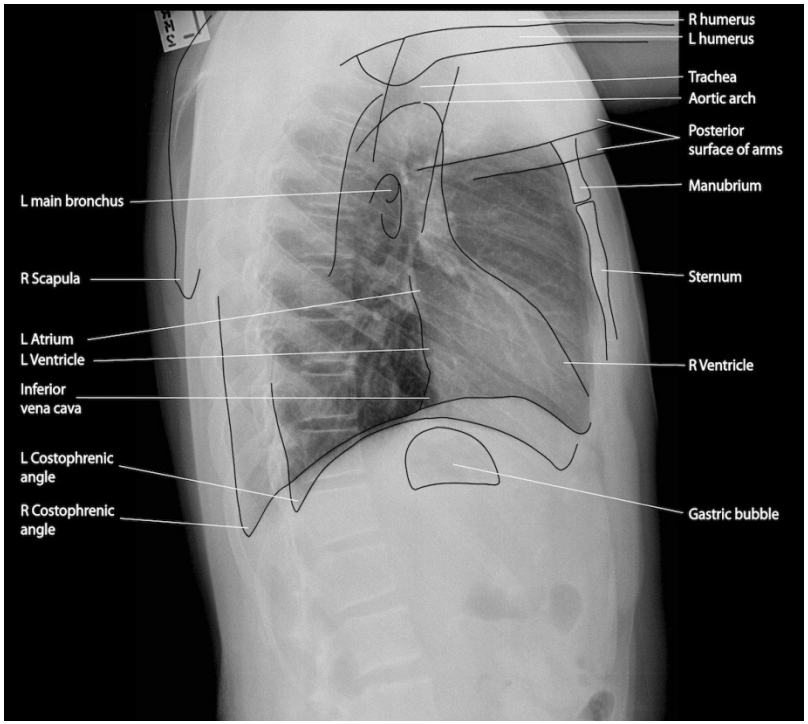


Figure 7.5 – Hilar adenopathy. A. Unmarked image. B. Marked image to outline the presence of bulky, bilateral hilar adenopathy. Occasionally even large lymph nodes like this are dismissed as pulmonary arteries.

Hilar Adenopathy

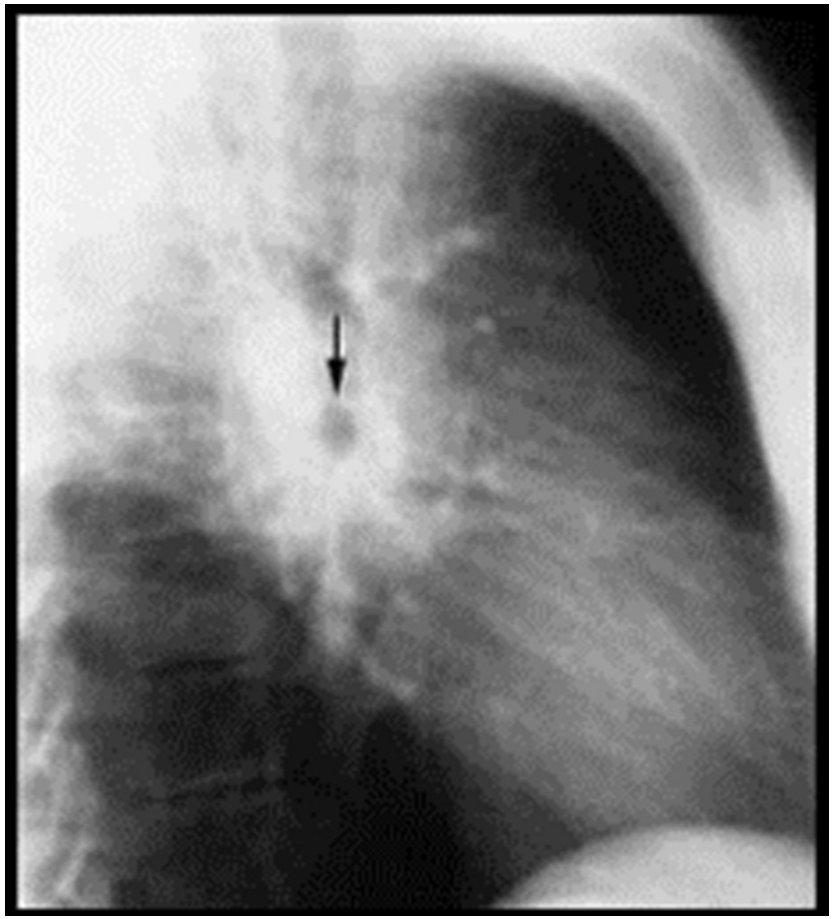
Lateral Chest X-Ray

Labelled lateral CXR

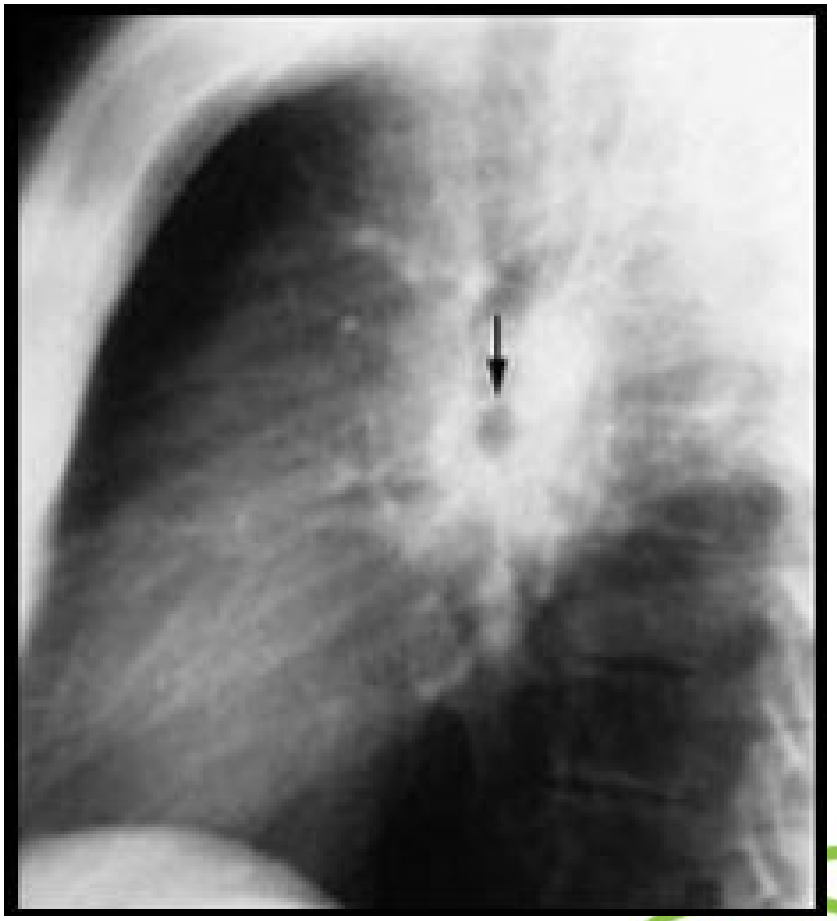


Normal Lateral CXR

Normal and Abnormal Lateral CXR

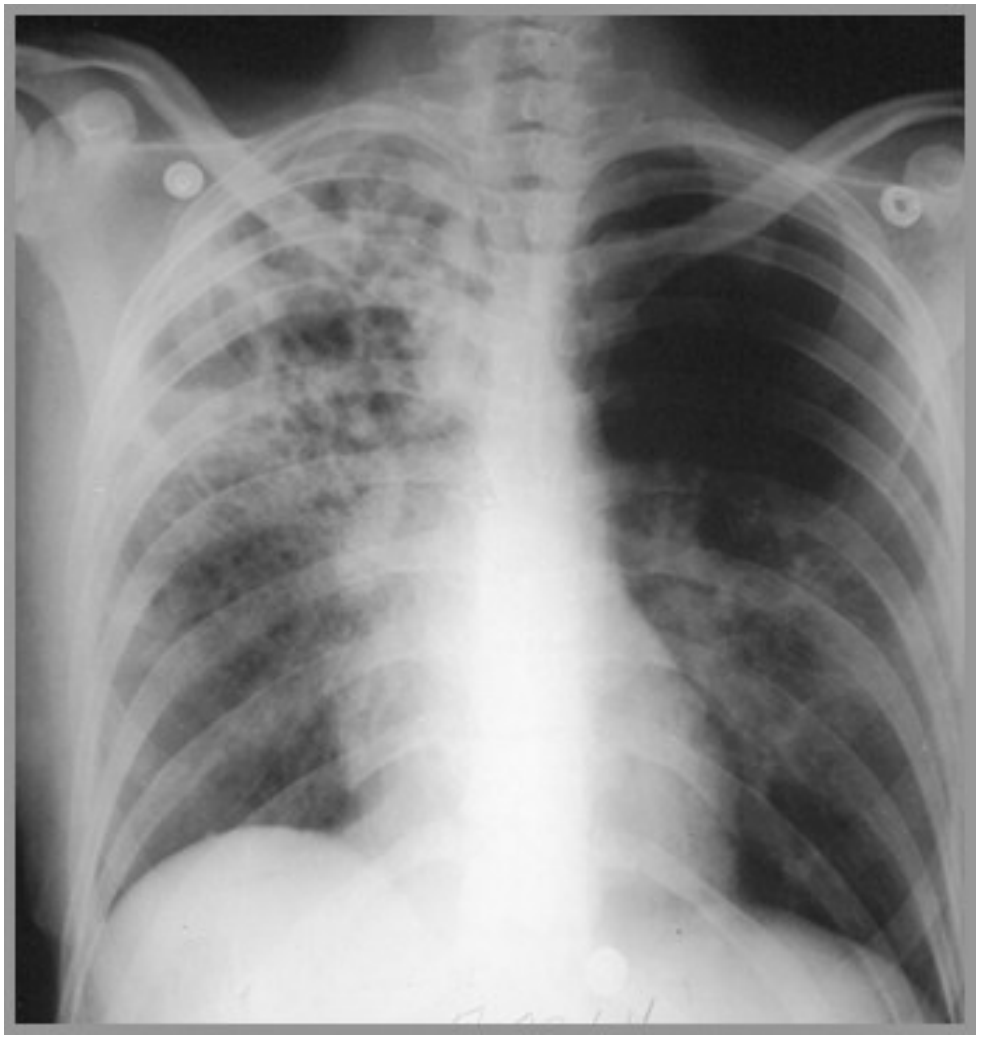


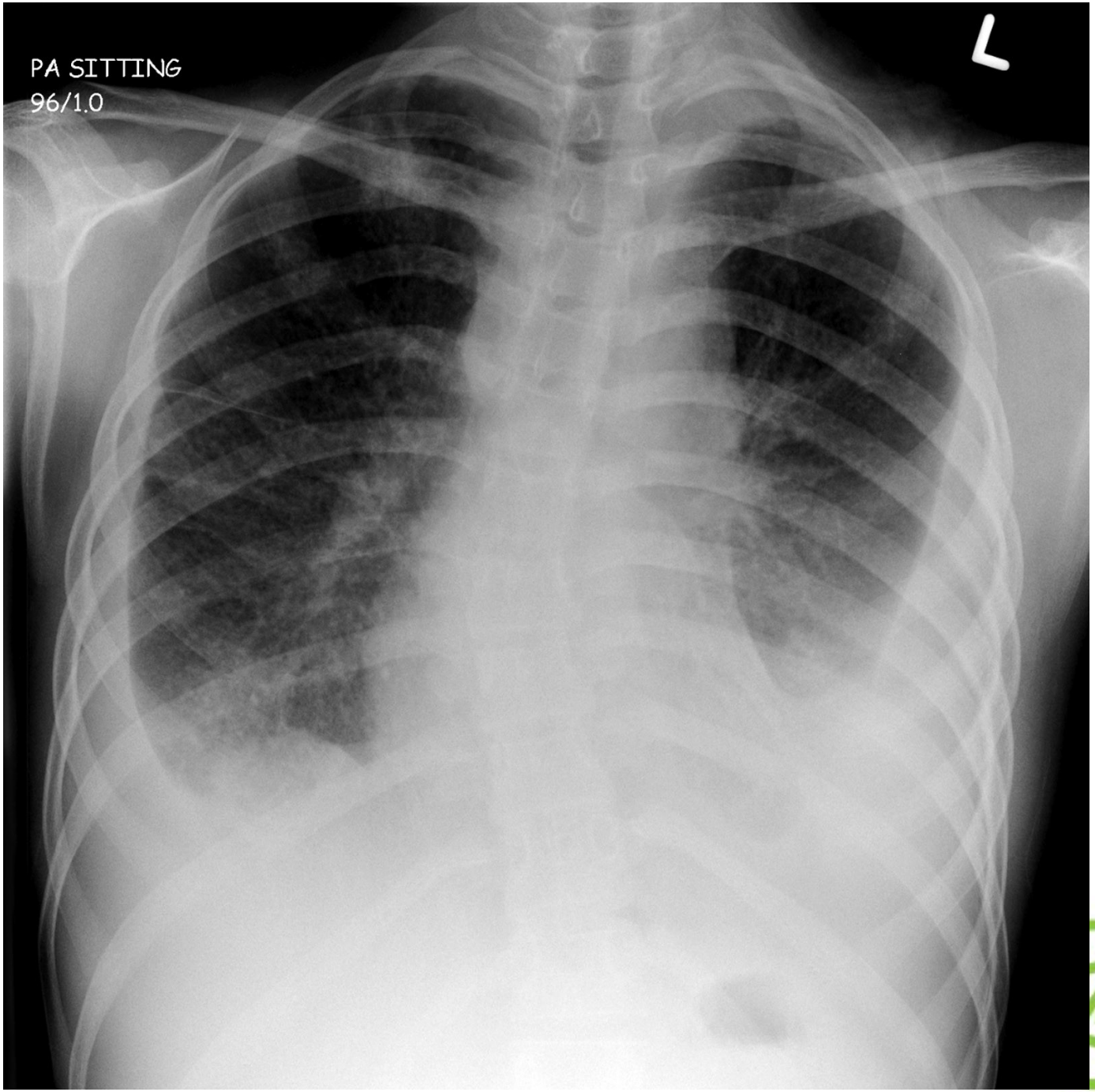
Lateral View of Hilar Adenopathy



Miliary TB

Cavitary Pulmonary TB




PA SITTING
96/1.0
L

TB AFB and Culture in Children

Egyptian beggar with likely spinal TB – 3rd century B.C.

TB Smear and Culture

- Paucibacillary disease in children (low organism load) so unlikely to have AFB/cx
- Collection of a good sample is difficult (esp. <8yo)
- Gastric aspirates are difficult to attain in clinic
- Sputum induction not always available
- FNA useful from lymph nodes – stain and cx

TB Lymphadenopathy (EPTB)

- Most common EPTB
- Usually cervical
- Present >14 days
- Usually non-tender
- No response to antibiotics
- FNA useful (especially for culture) but not required
- **Caution** to RX without firm diagnosis in setting HIV infection
- TST may be positive

How is TB Diagnosed in Children

- Exposure
- History/clinical presentation
- Exam (including weight)
- Labs/studies (+/-)
- Rx with abx and wait
- Clinical judgement
- ALWAYS test for HIV in children as in adults

Documented TB exposure

Close contact with an adult or adolescent with pulmonary TB or child with smear-positive TB

Close contact is defined as any household contact or contact outside the household that is of sufficient duration and proximity to pose a high risk of infection.

Are there any current symptoms or signs suspicious of TB?

Cough, wheeze, fever, lethargy, fatigue, weight loss, or visible mass in the neck

No current symptoms or signs

<5yrs or HIV-infected

INH for 6/12

≥5yrs and HIV-uninfected

No preventive therapy

Observe for symptoms
Evaluate / refer if symptoms indicative of TB

Symptoms or signs present

Investigate for TB

Not TB

Follow up after 1-2 weeks

Child is well

Persistent non-remitting symptoms

Refer to hospital

TB diagnosed

Treat for TB
Enter into TB register

WRHI

TB Treatment Regimens for Children

- **Uncomplicated PTB that is smear-negative** and less severe forms of EPTB (**LAD**)
  - Treat with 3 drugs (HRZ) x 2 mo/2drugs (HR) x 4 mo
- **Smear positive or cavitary TB** = high bacillary load
  - Treat with 4 drugs (HRZE) in intensive phase
- **Severe TB** – child very ill/malnourished, HIV with very low CD4 count, meningitis, bone, abdomen, miliary: treat with 4 drugs and intensive phase duration may need to be prolonged – consult guidelines/expert

Regimen 3A: Uncomplicated TB with a low bacillary load for children up to 8-years-old

Body weight kg	Intensive Phase: 2 months		Continuation Phase: 4 months
	RH 60,60 R: Rifampicin H: Isoniazid	PZA 500 mg PZA: Pyrazinamide	RH 60/60
2–2.9 kg	½ tablet	Expert advice on dose	½ tablet
3–3.9 kg	¾ tablet	¼ tablet	¾ tablet
4-5.9 kg	1 tablet	¼ tablet	1 tablet
6–7.9 kg	1½ tablets	½ tablet	1½ tablets
8–11.9 kg	2 tablets	½ tablet	2 tablets
12–14.9 kg	3 tablets	1 tablet	3 tablets
15–19.9 kg	3 ½ tablets	1 tablet	3 ½ tablets
20–24.9 kg	4 ½ tablets	1 ½ tablets	4 ½ tablets
25–29.9 kg	5 tablets	2 tablets	5 tablets

Regimen 3A: Uncomplicated TB with a low bacillary load for children >8-yo and adolescents

Body weight (kg)	Intensive Phase (2 months) Treatment given 7 days a week	Continuation Phase (4 months) Treatment (DOT) given 7 days a week	
	RHZE (150,75,400,275)	RH (150/75)	RH (300,150)
30-37 kg	2 tablets	2 tablets	
38-54 kg	3 tablets	3 tablets	
55-70 kg	4 tablets		2 tablets
> 71 kg	5 tablets		2 tablets

Regimen 3B: Complicated TB, High bacillary load, retreatment cases. (e.g. extensive PTB, spinal/osteo-articular TB, abd TB, meningitis*).

Weight kg	Intensive Phase 2 months			Continuation Phase 4 mos
	RH 60, 60	PZA 500 mg	Ethambutol 400mg tab or 400mg/8ml soln	RH 60, 60
2-2.9	½ tab	Expert advice	1 ml	½ tab
3-3.9	¾ tab	¼ tab	1.5 ml	¾ tab
4-5.9	1 tab	¼ tab	2 ml	1 tab
6-7.9	1 ½ tab	½ tab	3 ml	1 ½ tab
8-11.9	2 tab	½ tab	½ tab	2 tab
12-14.9	3 tab	1 tab	¾ tab	3 tab
15-19.9	3 ½ tab	1 tab	1 tab	3 ½ tab
20-24.9	4 ½ tab	1 ½ tab	1 tab	4 ½ tab
25-29.9	5 tab	2 tab	1 ½ tab	5 tab

Regimen 3B: retreatment cases for children >8-yo and adolescents

Weight kg	Intensive Phase: 3 months	Continuation Phase: 5 months		
	RHZE 150,75,400,275	RH 150,75	Ethambutol 400mg tab	RH 300,150
30-37	2 tabs	2 tabs	2 tabs	
38-54	3 tabs	3 tabs	2 tabs	
55-70	4 tabs		3 tabs	2 tabs
>70	5 tabs		3 tabs	2 tabs

Complicated TB: Individual drugs may be better – or not.

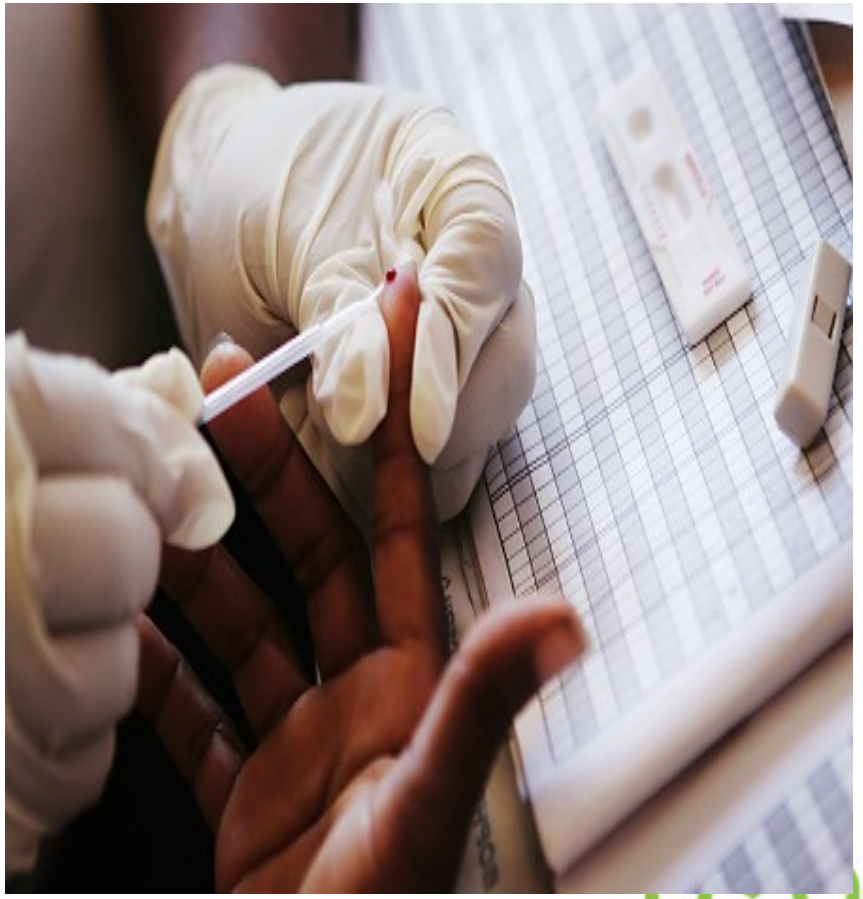
Drug	Dose (mg/kg)	Range (mg/kg)
Isoniazid (H)	10	10-15
Rifampicin (R)	15	10-20
Pyrazinamide (P)	35	30-40
Ethambutol (E)	20	15-25
Streptomycin (S)	15	12-18

Response to TB Rx

- Younger children review monthly until 3 months
- Weight and resolution of symptoms
- Older children smear + sputum at 2 & 5 months(reg. 1) and 3 & 7 months (reg.2)
- CXR not recommended as resolution slow
- If the child not responding NEED to INVESTIGATE FURTHER (? MDR, ? MAC, ?lymphoma)

Concomitant TB RX and ART

- Test all paediatric TB cases for HIV
- ART may be started 2 weeks after TB rx
- Watch for IRIS
- Remember to double dose the Kaletra or to add Ritonavir if child is on Aluvia/Kaletra and is started on TB rx



TB Rx and Kaletra

- Need to “boost” Kaletra (4:1 concentration lopinavir: Ritonavir)

Indications for Steroids in TB

- TB **meningitis**
- TB **pericarditis**
- **Mediastinal/hilar LAD** obstructing the airways.
- Severely ill children with **disseminated** TB (miliary)
- **IRIS** (sometimes)
- The dosage is prednisone 1-2 mg/kg daily orally for 4-6 weeks added to the TB drugs. The dose can be tapered to stop over 2 weeks.

Documented TB exposure

Close contact with an adult or adolescent with pulmonary TB or child with smear-positive TB

Close contact is defined as any household contact or contact outside the household that is of sufficient duration and proximity to pose a high risk of infection.

Are there any current symptoms or signs suspicious of TB?

Cough, wheeze, fever, lethargy, fatigue, weight loss, or visible mass in the neck

No current symptoms or signs

<5yrs or HIV-infected

INH for 6/12

≥5yrs and HIV-uninfected

No preventive therapy

Observe for symptoms
Evaluate / refer if symptoms indicative of TB

Symptoms or signs present

Investigate for TB

Not TB

Follow up after 1-2 weeks

Child is well

Persistent non-remitting symptoms

Refer to hospital

TB diagnosed

Treat for TB
Enter into TB register

WRHI

Baby Suzie

PHYSICAL EXAM

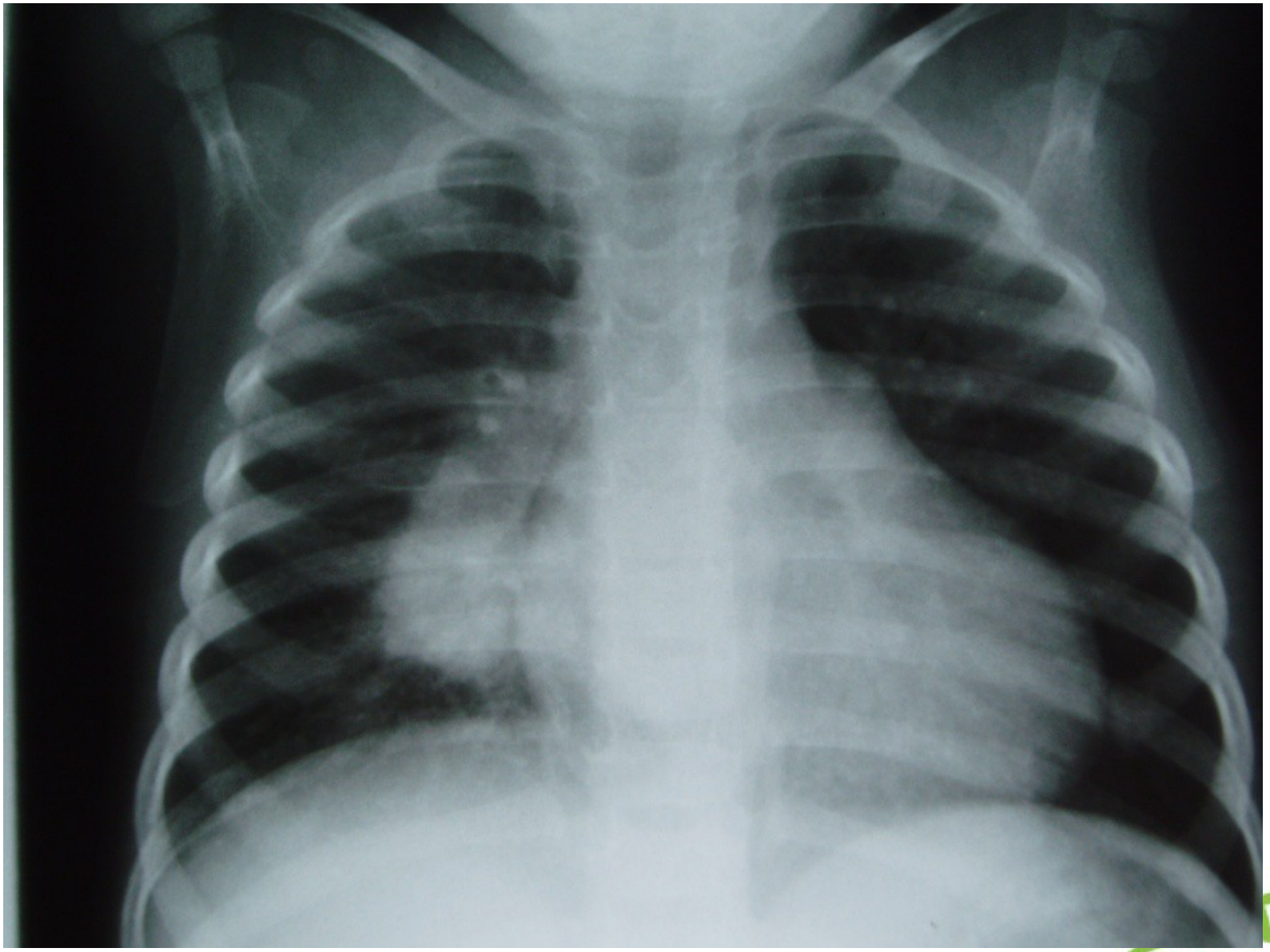
- She is failing to thrive with weight the same as on discharge, < -2 z-score
- Generalised LAD
- Scattered crepitations, left chest
- 3 cm hepatomegaly
- 2 cm splenomegaly

Baby Suzie

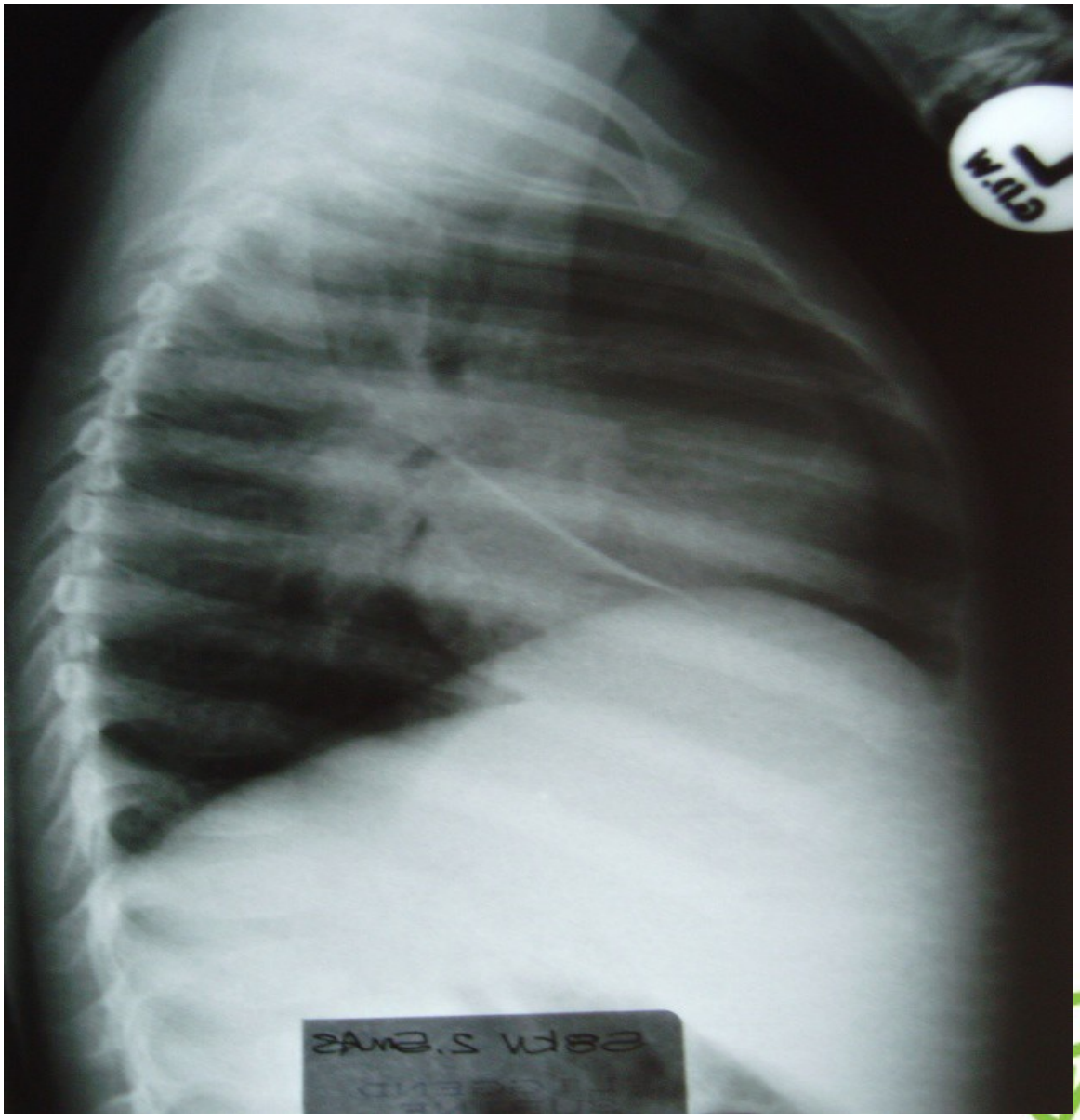
LABORATORY RESULTS

- Her HIV DNA PCR result is positive
- CXR - Bronchopneumonic changes bilaterally, hilar LAD
- Mantoux non-reactive
- Gastric washings – negative for AFB's, culture pending

- Pre-initiation lab results:
  - CD4% - 5%, CD4 - 276
  - Viral load - 300,000 copies/ml
  - FBC normal



Hilar LAD



Does Suzie have TB??

Yes	No
Recurrent LRTI	PPD negative
FTT	Gastric washings negative for AFB's
Hilar adenopathy on CXR	No TB contact
HIV positive	

Suzie is started on TB treatment

- She is given Rimcure 1 tablet daily
- Is this the correct management?
- Does she qualify for ART?
- When should we start ART?
- Which drugs?
- Do we need to make any changes to her ART regimen?
- What do we need to be cautious of if she starts ART?

Case 2 Simphiwe

- Simphiwe's mother Dorothy was diagnosed with TB in her last month of pregnancy
- She is HIV positive and received ART for 2 months prior to his birth
- Her TB was diagnosed as she had a cough for 2 weeks, night sweats.
- Her geneXpert result was positive, sensitive to rifampicin
- How should we manage Simphiwe at birth and beyond?

Mom has TB

- Mom diagnosed in last 2 months of pregnancy or failed to convert to smear negative or has no documented smear conversion:
  - No BCG at birth
  - Needs TB treatment if TB cannot be excluded
  - Needs IPT if TB is excluded
- Give BCG
  - After IPT is completed if asymptomatic
  - If HIV infected give after IPT and after stable on HAART

Breastfeeding if Mom has TB

- HIV-uninfected mother on TB treatment should be encouraged to breastfeed
- HIV-infected mother should also be encouraged to BF exclusively (or formula feed exclusively) in line with national guidelines
- TB drug concentrations are too low to protect the infant from TB or to be toxic to the baby

Baby asymptomatic

- If continues to be asymptomatic, BCG administered after completion of the preventive treatment
- If baby HIV+ may delay BCG until on HAART and immune reconstituted
- Tuberculin available, test after 3 months of INH treatment
- TST negative and the mother sputum smear-negative, the INH can be stopped and the child given BCG vaccination

After exclusion of TB disease, INH prophylaxis should be given to:

- All children under 5 years of age and HIV-infected children (irrespective of age) in contact with an infectious case of TB (drug susceptible TB and MDR-TB)
- All children under 5 years of age with a positive Mantoux (10 mm in diameter or greater)
- All HIV-infected children, irrespective of their age, with a positive Mantoux (5 mm in diameter or greater)

Key Points

- Control of TB is a nation-wide priority
- Advocate for TB infection control (esp. workplace)
- Screen for TB at every medical encounter
- Must have a high index of suspicion to diagnose TB disease in children because investigations usually do not definitively diagnose TB
- ALWAYS double-dose Kaletra/Aluvia or add Ritonavir if child is on this drug as part of HAART

Thank You

health

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Health
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