TB and the Future
(although not much on the future!)

UPdate

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Conflicts of Interest

- No relevant conflicts of interest to declare

Case 1: Anna

- 25 year old primigravida
- HIV-positive, virally suppressed, on TDF/FTC/EFV
- Pulmonary TB:
  - Xpert positive (No Rif-resistance detected)
  - Smear positive
  - CXR: RUL fibro-cavitatory changes
- Started on RHZE 1 week ago
- Delivered healthy term baby today
- Hoping to breast-feed

Case 1: Anna

1. What is Congenital TB?
2. What is Perinatal TB?
3. How do newborns get TB?
4. How would you investigate for TB?
5. What about BCG?
6. What about chemoprophylaxis?
7. Can she breast feed?

Epidemiology

- ‘Exceedingly rare’ – though underdiagnosed
- Median age of incident TB cases < 30 years
- Increasing proportion of females
- Therefore, increasingly babies born to parents with TB disease
- Also, expanded families, resulting in exposure to elderly etc.
- HIV → increase in extra-pulmonary TB
- Often (60-70%) undiagnosed/unsuspected maternal TB
- Mortality: 20-40% - improved with treatment

Pathogenesis

- Genital tract TB → contiguous spread
- TB bacillaemia → placental infection
- Placental granulomas
  - Haematogenous spread via umbilical vein
    - 1° focus in **liver**
  - Rupture in amniotic fluid, then inhaled or ingested
    - 1° focus in **lung**/GIT/upper respiratory tract
- Direct contact with lesions during birth

Clinical Features

- Median age at presentation = ~24d
- Almost all TST-negative, though often convert later
- ± half with normal CXR
- Often non-specific
  - May mimic acquired infections, congenital cardiac disease, inborn errors, other congenital infections, etc.

Diagnostic Criteria

- **Beitzki (1935)**
  - Isolation of Mtb
  - 1° focus in liver OR
  - Evidence of TB within days of birth, AND
  - No adult contact identified

- **Cantwell (1994)**

  Proven TB lesion + 1 of:

  - Lesions in 1st week
  - 1° hepatic complex
  - Maternal genital or placental TB
  - Exclusion of postnatal transmission

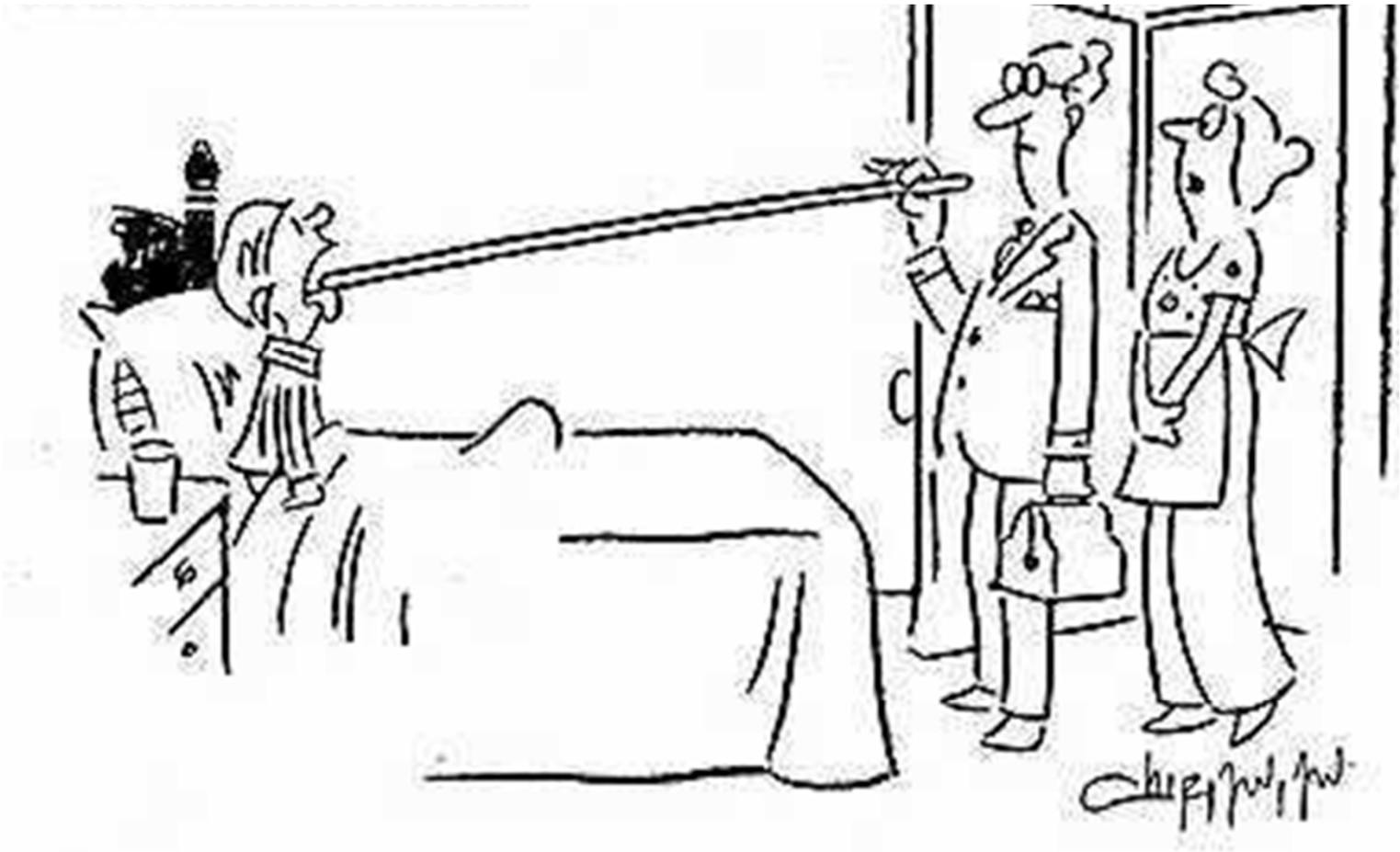
Prevention

- Variety of similar approaches
- Largely expert-opinion based
- Predominantly INH x 6m
  - Alternative = Rifampicin + INH x 3m
- Some guidelines suggest TST at 3-6m
- Always require close clinical follow-up
- Aggressive investigation and treatment if symptomatic

Managing asymptomatic neonates

Scenario	Action 1	Action 2
Asymptomatic neonates born of mother's with infectious drug-susceptible tuberculosis	Treat with daily rifampicin (15 mg/kg), isoniazid (10 mg/kg), PZA (35mg/kg) for 6 months.	At the end of the treatment period, • Screen the infant for TB again • If negative, BCG must be given after 2 weeks[1].
Asymptomatic neonates born of mother's with infectious drug-resistant tuberculosis	Give prophylaxis with high dose INH (15-20 mg/kg) daily for 6 months and followed up monthly to exclude clinical tuberculosis disease (usually drug-resistant) and to monitor side effects. Consider adding pyridoxine when INH is given.	**If child is well and does not develop signs of TB whilst on prophylaxis,** Continue prophylaxis until end of 6 months stop prophylaxis and BCG given 2 weeks later.
		If TB disease develops whilst on prophylaxis refer to the MDR-TB Unit
Asymptomatic neonates born of mother's with non infectious drug-susceptible tuberculosis[2]	Screen the infant for TB clinically, radiologically and bacteriologically (gastric aspirates)	If no tuberculosis is confirmed (negative), give prophylaxis with Isoniazid (10 mg/kg/d) for 6 months If child is well and has no signs of TB at 6 months, prophylaxis can be stopped and BCG given 2 weeks later.
		If TB is confirmed or infant has signs suggestive of TB, A complete course of TB treatment must be given BCG must be given 2 weeks after completing treatment.

[1] BCG is a life vaccine, which is affected by the use of TB drugs (including INH)
[2] Non infectious means the mother has completed at least 2 months of anti-tuberculosis therapy prior to delivery of the baby with confirmed negative smear microscopy/ culture



"Is it contagious, doctor?"

Case 2: Sipho

- 6 year old boy
- Close, prolonged contact with adult with PTB:
  - Xpert-positive
  - Rifampicin-resistant
  - Recently started out-pt: H-Z-E-Am-Mfx-Eto-Trd
- Asymptomatic
- Thriving

Case 2: Sipho

- Any additional information required about his contact?

- Any further investigations on Sipho?
- Does Sipho's HIV-status change your approach?

- Any chemoprophylaxis?

- What follow-up is required?

Case 2: Sipho

- After 5 months of hd-INH Sipho presents with:
  - Fever
  - Weight loss
  - Cough
  - Lethargy

  } X 4 weeks

- CXR:
  - Bilateral patchy changes, hilar lymphadenopathy

Case 2: Sipho

- How would you investigate and manage Sipho?
  - Role of TST/IGRA/LAM?
  - Interpretation of Xpert, LPA, DST results
  - Standardized vs. Individualised Regimens

Group	Drugs
Group 1: First-line oral drugs	Ethambutol (E) Pyrazinamide (Z)
Group 2: Injectable drugs	Kanamycin (Km) Amikacin (Am) Capreomycin (Cm) Viomycin (Vm)
Group 3: Fluoroquinolones	Levofloxacin (Lvx) Moxifloxacin (Mfx) Gatifloxacin (Gfx)
Group 4: Oral bacteriostatic second-line drugs	Ethionamide (Eto) Prothionamide (Pto) Cycloserine (Cs) Terizidone (Trd) Para-Aminosalicylic Acid (PAS)
Group 5: Drugs of unclear efficacy (Not recommended for routine use in MDR-TB patients)	Clofazimine (Cfz) Amoxicillin/clavulanate (Amx/Clv) Clarithromycin (Clr) Azithromycin (Azr) Linezolid (Lzd) Thioacetazone (Th) Imipenem High-dose INH

Figure 1. The morning pill burden for a teenage boy on ART and treatment for MDR-TB. (Photographer: Damien Schumann).

In the dark days, before doctor-patient confidentiality.

Future of Paediatric TB

- Diagnostics
- Chemoprophylaxis
- Drug Therapy
- Vaccines


ANY
QUESTIONS
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