Navigating the uncertainties of TB Investigation & Management

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# OVERVIEW

- Introduction
- TB diagnosis
- TB treatment
  - Regimens
  - Duration
  - Formulation
- Conclusion
- The future

#### Tuberculosis incidence, 2019

Incidence of tuberculosis is the estimated number of new and relapse tuberculosis cases arising in a given year, expressed per 100,000 population. All forms of TB are included, including cases in people living with HIV.





Globally 1.1 million children (< Source: World Health Organization (via World Bank)

- 11 % of all TB cases globally
- 20% of these children die

Tuberculosis around 3 million

1800s Consumption

INTRODUCTION

• Phthisis in ancient Greece

• Captain of all these men c

• 1700s The White Plague

Highest prevalence in < 5 yrs in high TB burden areas

OurWorldInData.org/eradication-of-diseases • CC BY

# TB DIAGNOSIS

Young children Pauci-bacillary TB disease Cannot easily expectorate

Diagnosis based on combination of :-

Careful history

- Clinical examination growth assessment
- HIV testing
- TB Bacteriological testing
- CXR AP & LAT
- TB infection testing
- Relevant investigations for presumed EPTB



# WHO

#### TB INVESTIGATI(

- Children with a +ve TB contact
- Children with a +ve TB symptom screen
- HIV+ve children
- Children with SAM
- Prior to immunosuppressive therapy
- Clinical suspicion of TB

### **Tuberculosis Symptoms**



fatigue

fever



weight loss



# TB INFECTION VS TB DISEASE



### INVESTIGATIONS

Respiratory specimens

	Adv	Disadv	Sens (%)	Spec (%)
Sputum		Young children	73	97
GA	Young children	fasting	64	95
NPA	Young children		46	98
Stool	Non- invasive		53	98

1 respiratory sample for Xpert MTB/RIF Ultra

1 respiratory sample for TB MCS (excludes stool)

## INVESTIGATIONS

Radiology



### HIV test

### **HIV POSITIVE**

Urinary Lipoarabinomannan antigen (u-LAM) essay

- HIV+ adults with CD4 <100</p>
- Sens 52 83% specificity 80%
- Children 48 73%
- Utility in HIV- children with SAM

#### Pre-initiation/monitoring





### EPTB INVESTIGATIONS



Collection of appropriate specimens from affected site/s

- CSF
- FNA of lymph nodes
- Biopsies
- Fluid pleural, pericardial, peritoneal, synovial
- Urine
- Blood
- BMA&T
- Histology



# TB TREATMENT

• Various evolutions through the ages

- Romans fresh air, rest, nutrition, sunlight and moderate exercise
- Streptomycin first antiTB drug in 1943
  - 60 yrs after Robert Koch announced discovery of M. TB
- 1944: para-aminosalicylic acid (PAS)
- 1951: isoniazid triple therapy
  - Decrease resistance
  - Increased efficacy duration of therapy 24 months
- 1960s: Streptomycin/INH/**Ethambutol** duration 18 months
- 1970s: Rifampicin 9 months
- 1972: INH+RIF+**PZA** 6 months



# SHINE

Shorter Treatment for Minimal Tuberculosis in Children. NEJM, 2022





Table 2. Pri	mary Efficacy Analysis (Modif	fied Intention-to-	Treat Pop	oulation).*					
Outcome		4-Month Treatment (N=572)		6-Month Treatment (N=573)		Difference (95% CI)			
						Adjusted Analysis†	Unadjusted Analysis		
						percenta	ge points		
Unfavorable	e status — no. (%)	16 (3)		18 (3)	(	-0.4 -2.2 to 1.5)	-0.3 (-2.3 to 1.6)		
Death fi	rom any cause after 4 mo	7 (1)		12 (2)					
Loss to	follow-up after 4 mo but	0‡		1 (<1)					
Treatr Tu			No. of Patients	4-Month Treatment	6-Month Treatmer	n nt	Risk Differend	:e (95% CI)	
Ext			event		al no. (%)		percentage	percentage points	
Re	Primary outcome								
Favorable Modified intention-to-		eat population	1145	16/572 (3)	18/573 (3	)		-0.3 (-2.3	
	Per-protocol population		1121	14/563 (2)	17/558 (3	5)	-	-0.6 (-2.5	
	Intention-to-treat popula	ation	1204	44/602 (7)	44/602 (7	)		0 (-2.9	
	Key secondary outcome								
Modified intention-to-t		eat population	910	10/450 (2)	13/460 (3	5) 		-0.6 (-2.6	
	Per-protocol population		895	8/445 (2)	13/450 (3	-8 -4		-1.1 (-5.1	
						4-Mon Treatm Bette	th 6-Mon ent Treatm r Bette	th ent r	



Considerations

- 2/3 Paediatric TB is non-severe pauci-bacillary disease
- Used dose-optimised DT FDC HRZ (50/75/150mg)
  - DT ethambutol (E 100mg)
  - DT HR (50/75mg)
- Chest x-ray
- Sputum smear microscopy
- Xpert MTB/RIF Ultra
  - Request semi-quantitative result
- Excluded
  - Younger than 3 months
  - SAM
  - Required hospitalisation
  - Treated for TB within 2 years



### SUMMARY DS-TBTreatment

#### **Pulmonary TB**

- 1. 4 month regimen 2HRZ(E)/2HR
- 2. 6 month regimen 2HRZ(E)/4HR

#### Children ≥ 12 yrs

- 1. 4 month regimen 2HPZM/2HPM
- 2. 6 month regimen 2HRZ(E)/4HR

#### Extra-pulmonary TB (DS-EPTB)

- 1. Peripheral LN TB eligible for 2HRZ(E)/2HR or 2HRZ(E)/4HR
- All EPTB: 6 month regimen 2HRZ(E)/4HR
  ☆TBM
  - ♦ 6HRZEto
  - ◆2HRZE/10 HR
  - Osteo-articular TB
    2HRZE/10 HR

# Adjuvant Therapy

Steroids TBM TB pericarditis Airway obstruction by TB lymph nodes

Regimens Prednisone 2mg/kg/d (max 6omg/day) Dexamethasone 0.3 – 0.6 mg/kg/d

Duration 4 weeks Tapered over 2 – 4 weeks





**Response to treatment** Bacteriological response Clinical response



Drug interactions BOOST Lopinavir/rit with ritonavir BOOST dolutegravir-reg with DTG

Manage co-morbidities

Nutritional support & monitor for drug toxicity



# Conclusion & Future

Limitations and strengths of every weapon in your TB arsenal

- Diagnostic
- Therapeutic

Avoid the pitfalls and landmines – walk a steady path on shaky ground

Future

- TB Prophylactic therapy guidelines
- New SATB guidelines (2013 & 2014)
- Paediatric trials of DS-TB
  - OptiRif Kids
  - TBM-KIDS
  - SURE
- Paediatric trials of DR-TB

Desired decline in global TB incidence rates to reach the 2035 targets

### **STRATEGY**

#### A WORLD FREE OF TB

ZERO deaths, disease, and suffering due to TB

END TB

90%

0%



