Taking another look at Tuberculosis

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INCIDENCE AND MORTALITY RATES OF TUBERCULOSIS IN SRI LANKA
1984 - 2005

RANGE PER 100,000 POPULATION

PTB
TOTAL TB
Mortality Rate
24y old Tamil boy is brought to A & E department of PGH Badulla with severe dyspnoea. He is tachypnoeic and gasping for breath. 

O/E Pale, Cachectic and febrile with bilateral crepitation.

Within 2 hours of admission he had a Respiratory arrest & could not be revived despite ET intubation and manual ventilation.

He had been transferred from DH Passara where he had been treated one day and his sputum was found to be positive for AFB. 

20th November 2008
Chest x-ray revealed extensive bilateral fibrocavitatory disease with areas of consolidation.

Questioning the father in retrospect, it revealed that the patient was not resident of Passara but working in a tea boutique in Maradane-Colombo for 6 years.

He had been unwell with cough, wheezing and episodic fever for 1 1/2y. He had sought medications from over 8 doctors and had taken inward treatment from 2 teaching hospitals where he had been treated for bronchial asthma with repeated nebulizations.

At no point in his illness was chest x-ray or sputum examination performed!
The Problems Associated With Delayed Diagnosis

- Latent TB Infection
- TB Disease
- Anti TB Treatment

Spread of disease in the community
Progression of disease in patient
Respiratory Cripple
The key factors affecting the diagnosis of TB

- PATIENT
- DOCTOR
- COMMUNITY
- INVESTIGATIONS
Lack of awareness
Social stigmatization
Nature of Symptoms

Inaccessibility to Health care
Social stigmatization
Myths
SYMPTOMS OF PULMONARY TUBERCULOSIS

Nonspecific and Constitutional
- Unusual fatigue
- Tiredness
- Malaise
- Anorexia
- Pyrexia
- Weight Loss
- Night sweats
- Amenorrhoea

Respiratory
- Cough - 2 wks
- Haemoptysis
- Chest pain
- SOB
THE SUBTLE NATURE OF THE EARLY SYMPTOMS OF TUBERCULOSIS WITH POOR ACCESSIBILITY TO DIAGNOSTIC FACILITIES PLAYS A KEY ROLE IN THE DELAYED DIAGNOSIS OF THE DISEASE
SOCIAL STIGMA – IS IT REAL in 2009?

- Rejection by family
- Rejection by society
- Loss of employment
- Disqualification for middle east employment

- Social isolation
- Depression
- Homelessness
- Rejection at Marriage
- Suicide

Does TB deprive you of all Human Rights?
Lack of awareness
Nature of Clinical signs
Misdiagnosis
False image
Paucity of diagnostic aids
Low priority
CLINICAL SIGNS OF PULMONARY TUBERCULOSIS

Mild to moderate disease may have no clinical signs

Generalized
Pallor (Anaemia)
fever
weight loss

Respiratory
upper zone crackles
- post tussive
signs of consolidation

Localized wheeze

Chronic Tuberculosis
Tracheal deviation
flattened chest
cavity - amphoric
breath sounds
Differential Diagnosis

Differential Diagnosis

- Asthma
- C O P D
- Bronchiectasis
- Bronchial carcinoma
- Other infections, Eg: Bacterial pneumonia Lung abscess Pneumocystis carinii

Pointers to the Correct Diagnosis

- Intermittent symptoms, Expiratory wheeze
- Smoking, Chronic symptoms, generalized wheezing
- Large amounts of purulent Sputum / Haemoptysis
- Risk factor (Smoking) / clubbing
- Response to antibiotic
- Abscess with fluid level on CXR
- Dyspnoea prominent
High Risk Groups with Increased Susceptibility to Tuberculosis

Nonspecific Decrease in Resistance
- Adolescence
- Senescence
- Malnutrition
- Post gastrectomy states
- Diabetes mellitus
- Alcoholism
- Drug addicts

Decrease in Resistance Due to Hormonal Effects
- Pregnancy
- Therapy with adrenocortico steroids

Decrease in Local Resistance
- Silicosis

Decrease in Specific Immunity
- Lymphomas
- Uremia
- Immunosuppressive therapy
- Sarcoidosis
- Live virus vaccination

Acquired immunodeficiency syndrome (AIDS)

Exposure to TB Patients
- Family / close contacts
- People living / working in institutionalized Settings
  - Eg: Prisons, Nursing homes, Refugee Camps
- Healthcare Workers
Changing Profiles

AGE DISTRIBUTION

0-14
15-55
>55

25%
1%
74%

Wasted
Cache tic
Haemoptysis
Elderly

Healthy looking
Mild cough
Low grade fever
Young
Sites of Attack

80% PREDOMINENTLY LUNGS

BRAIN
EYES
LIVER
INTESTINE

SPINE
PRIMARY TUBERCULOSIS

Lung - most important portal of entry

Disease transmission

Inhalation → Aerosol of TB Bacilli → Coughed up by a smear (+) TB patient
PRIMARY TUBERCULOSIS
WHAT HAPPENS TO THE INHALED BACILLUS

TB Germ

(Magnified Approximately 30,000 times)

Majority

INFECTED

Germ - inactive
No Symptoms
Do not feel sick
Do not spread the disease
TB skin test (+)

Natural Immunity

DISEASE

10% Minority

Germ - active
Symptoms
Mild & Non Specific Pleurisy
Signs unusual

Immunity
Clinical Features

Nonspecific and Constitutional
- Unusual fatigue
- Tiredness
- Malaise
- Anorexia
- Pyrexia
- Weight Loss
- Night sweats
- Amenorrhoea

Respiratory
- Cough
- Haemoptysis
- Chest pain
- SOB
**POST PRIMARY TUBERCULOSIS**

**Signs**
Mild to moderate disease may have no clinical signs

**Generalized**
Pallor (Anaemia)  
fever  
weight loss  
clubbing

**Respiratory**
upper zone crackles  
- post tussive  
signs of consolidation  
Localized wheeze

**Chronic Tuberculosis**
Tracheal deviation flattened chest  
cavity - amphoric  
breath sounds

**EPTB-** 10% (Cervical lymphnodes  
pleural effusions)
6 MILLION PEOPLE ARE CO-INFECTED - HIV- TB
HIV PATIENTS ARE 25 TIMES MORE LIKELY TO GET TB
Pathogenesis of TB / HIV

TB → Immunity → CD4

• Active TB → CD4

• Immune Stimulation – TNF α

• HIV / TB - Opp Infection

CD4 T lymphocyte

HIV
# Clinical Picture of Pulmonary TB in HIV Seropositive Persons

<table>
<thead>
<tr>
<th>Features of Pulmonary TB</th>
<th>Stage of HIV Infection</th>
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<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td>Clinical Picture</td>
<td>Often resembles Post –primary TB</td>
</tr>
<tr>
<td>Sputum smear result</td>
<td>Often positive</td>
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<tr>
<td>Chest X-ray</td>
<td>Often cavities are seen</td>
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</tbody>
</table>
INVESTIGATIONS

Sputum Microscopy
Chest X ray
Mantoux Test
TB Culture

PCR
Gamma Interferon
Rapid Culture
Adenosine De Aminase
Sputum microscopy

Mycobacterium Tuberculosis
SPUTUM MICROSCOPY

Major tool for rapid diagnosis

- Not popular among Doctors & patient
- Lack of facility
- Incorrect sample collection – saliva
- Inadequate samples
- Improper reading
SPUTUM MICROSCOPY

Three Specimens Optimal

- Spot sample - 1st visit – give container
- Early morning sample - collected by patient
- Spot sample – 2nd visit

Cumulative Positivity

- First: 81%
- Second: 93%
- Third: 100%
Sputum collection

? Deterrent to the Diagnosis
TB Diagnosis

Microscopy is appropriate technology

Indicates
- Infectiousness
- Risk of death
- Priority for treatment

Specificity

- AFB Microscopy: 98%
- X-ray: 50%
CURRENT TRENDS IN INVESTIGATING PTB IN SRI LANKA
THE FACTS

The 1st line investigation

• Sputum microscopy - mainly confined to Chest Clinics
• ESR and Chest X ray - main tools used by the majority followed by Sputum Microscopy

NEED WE RELOOK AT INCEASING X RAY FACILITIES ALONG WITH SPUTUM MICROSCOPY?
TB Diagnosis

Over-diagnosed

Diagnosed by X-ray alone

Actual cases
Tuberculin Skin Test

Limited Value if TB prevalence is high

Results:
- 0 - 9 mm - Negative
- > 10mm - Positive
- > 20mm - Strongly Positive
TB INFECTED POPULATION

1/3 OF THE WORLDS POPULATION - 1.7 BILLION

South – East Asia accounts for nearly 1/3rd of all Tuberculosis cases

> 50% IN SRI LANKA.
ARE WE OVER RELIANT ON MATOUX AND ESR?

• Mantoux is non specific and influenced by many factors
• ESR does not correlate well with disease activity
• ESR may be normal with active disease though a very high ESR may indicate TB

MICROBIOLOGICAL / HISTOLOGICAL CONFIRMATION OF TUBERCULOSIS SHOULD BE GIVEN TOP PRIORITY
Gamma Interferon

MTB produces antigens

– not seen in BCG & Non TB Myco bacteria

• Early Secretory Antigen Target 6 – ( ESAT 6)

• Culture Filtrate Protein 10 – ( CFP 10)

Pt’s Lymphocytes – culture with Antigens

Gamma Interferon
TB CULTURE

- Highly specific
- Grossly underutilized
- Time consuming
- Luxury test in state sector

Very helpful in species identification
Identify Drug sensitivity patterns
EPTB
Smear negative TB

Rapid Culture Methods
Radiometric methods
Oxygen consumption
TB growths 7 – 10 days earlier
Costly
TB Diagnosis

- Polymerase Chain Reaction (PCR)
- Mycobacterial Antibodies
- TB - Gamma Interferon
- Adenosine De Aminase
TB though deadly is completely curable.

- Completely Free
- Very Cheap
- Long Duration
- Multiple Drugs.

4 Antibiotics x 2 months
2 Antibiotics x 4 months.
# Essential Anti-TB Drugs

<table>
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<tr>
<th>Drug</th>
<th>Mode of Action</th>
<th>Potency</th>
<th>Side Effects</th>
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<tbody>
<tr>
<td>Isoniazide (H)</td>
<td>Bactericidal</td>
<td>High</td>
<td>Peripheral Neuropathy / Hepatitis</td>
</tr>
<tr>
<td>Rifampicin (R)</td>
<td>Bactericidal</td>
<td>High</td>
<td>Nausea / Hepatitis / OCP</td>
</tr>
<tr>
<td>Pyrazinamide (Z)</td>
<td>Bactericidal</td>
<td>Low</td>
<td>Joint Pains / Hepatitis</td>
</tr>
<tr>
<td>Ethambutol (E)</td>
<td>Bacteriostatic</td>
<td>Low</td>
<td>Optic Neuritis</td>
</tr>
<tr>
<td>Streptomycine (S)</td>
<td>Bactericidal</td>
<td>Low</td>
<td>Auditory / Vestibular Damage</td>
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**Intensive Phase**  
- **RHEZ** Two Months  
  Non Infective in Two Weeks

**Continuation Phase**  
- **R H** Four Months  
  Smear Negative in Two Months
Prophylaxis in TB

**INAH** – 6/12

**INAH + Rifampicin** – 3/12

**Primary Chemoprophylaxis**

- Person exposed but not infected
- Eg: Breast Fed Baby with sputum + Mum.
- HIV Positive / Mx Negative

**Secondary Chemoprophylaxis**

- Person infected but no clinical disease
- Eg: HIV + / Mx +
- Recent Mx Converters
- Mx > 10mm with Risk factor
- Mx > 10mm High prevalence groups
TREATMENT PROBLEMS

- Incorrect Chemotherapy Dose / Duration
- Non compliance / Incomplete treatment
- Irregular Drugs Supply
- Poor Quality Drugs

CONSEQUENCES

- Common Drugs Ineffective
- Second line drugs – Severe adverse reactions / not very effective
- Very High cost
- High Mortality.
The “New” TB
MDR-TB

> 50 million infected with MDR-TB


Russia
150,000 Civilians
6,000 MDR
140,000 Prisoners
20,000 MDR
12 billion dollars
Second Line Drugs

- Amikacin
- Kanamycin
- Capreomycin

- Ethionamide, Prothionamide

- Cycloserine,

- PAS

- Ofloxacin, Ciprofloxacin,

Surgical Resection
XDR – TB

- Extreme Drug Resistant TB
- Form of MDR TB – resistant to
- Quinolones + Injectables – Amikacin, Capreomycin, Kanamycin – classes of the second line drugs
- 4 – 19% of MDR Cases
  - South Africa – Kwazulu – Natal – HIV positive population
  - Very high mortality – 52 out of 53 cases dead within 25 days

TDR – TB

- Totally Drug Resistant TB
- 2009 – Iran
DOTS is the most cost effective strategy available for controlling the TB epidemic.
DOTS Ensures Treatment

- With the right drugs
- In the right dose
- At the right intervals

- Political commitment
- Diagnosis by microscopy
- Adequate supply of SCC drugs
- Directly observed treatment
- Accountability
The key factor to the diagnosis of Tuberculosis is the Awareness that this Disease still Exists.

Thank you