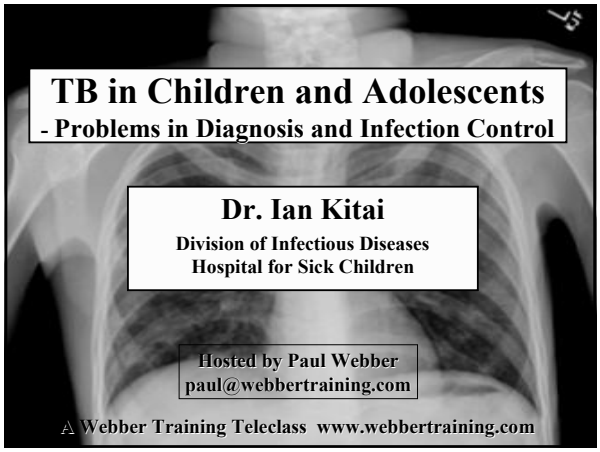


Young children with TB

Differ From Adults

- **Presentation**
- **Infectiousness- generally not infectious**
- **Progression to disease**
  - **Faster, more often, more extrapulmonary**
- **Response to treatment**
- **Side effect profile**

Adolescents with TB

- **Differ from young children**
  - **Presentation**
  - **Delay in diagnosis**
  - **Mood disorders**
  - **Compliance issues**
  - **Side effect profile**

Case 1

- 4 year old
- Unresolving pneumonia
- Chest X ray- hilar lymphadenopathy, small infiltrate
- Diagnosis- Pulmonary TB
- Gastric aspirates 1/ 3 –Positive by culture, occ AAFB's seen on 1
- Should there be contact screening?
- Should class be screened?

Do young children spread TB?

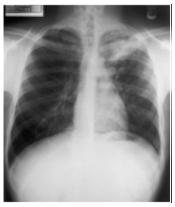
- **Standard response**
- Young children (approx less than 10) do not spread TB to others
  - Childhood Tb is paucibacillary
  - Children do not generate cough to spread TB

Little role for isolation

This message is largely true-

BUT there ARE a FEW exceptions which can be anticipated from the clinical circumstances

TB: IN CHILDHOOD:



Who Infects Children?

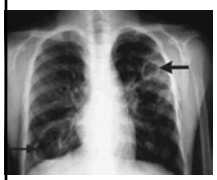
1. **Close contacts with multibacillary and cavitary disease and cough-ADULTS or ADOLESCENTS**
2. **Less often: smear negative culture positive patients**

Young children have RARELY spread TB to others

- 3 month old
- Spread TB to parents and close HCW's

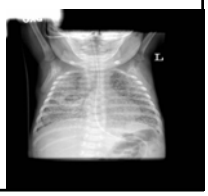
- But – has cavity
- Miliary disease
- And harsh cough – exceptional circumstances
- Reynolds et al **INT J TUBERC LUNG DIS 2006 10(9):1051–1056**

Children generally not infectious- some exceptions



- 9 yr old.- Infected ¾ household
- 10/32 bus riders
- 16/24 classroom contacts
- Curtis et al N Engl J Med 1999 Nov3411491-

3 mo old
Infected 2 HCW's
Parents



Both children had multibacillary disease with cavities

Who poses infectious risks in pediatric TB?

- Munoz et al- Texas children's
- Screened adult visitors of 59 consecutive children admitted with TB
- Isolation if thought have potential to be airborne
- 8 children required isolation
- 16/105 (15%) screened adult visitors --previously undetected pulmonary TB.

- **Risk- mainly from adults accompanying child**
- Infect Control Hosp Epidemiol 2002 10:568-72.

Case 1

- 4 year old
- Unresolving pneumonia, Chest X ray- hilar lymphadenopathy, small infiltrateGastric aspirates 1/3 –Positive by culture
- 1. Should class be screened? **No– provided no infectious adult visitor found.**
- 2. Once on treatment should child be kept from **class—no, especially after 2 weeks Rx**
- 3. Should there be contact screening? **Yes and quickly**.
- **Maternal Aunt - found to have infectious pulmonary TB.**

TB in children: Infection control issues

- Bottom Line
- Most children are not infectious and don't need isolation
- Exceptions: Cavitary disease, Multibacillary disease and cough
- Contact tracing after "isolated" pediatric TB
- disease IS important to identify infectious adults and adolescents
- Remember the adults accompanying child!

Pediatric and adolescent TB disease in N America

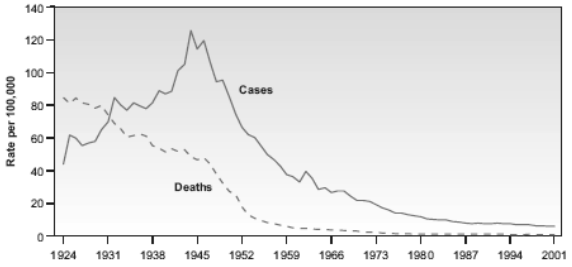
- Many asymptomatic –detected through contact screening (Ontario = about 20%)

Others: present with disease at any site

Typically immigrants from high incidence countries .

TB in Canada -epidemiology

Figure 1
Tuberculosis incidence and mortality rates – Canada: 1924-2001



TB: Epidemiology

- Should class be screened?

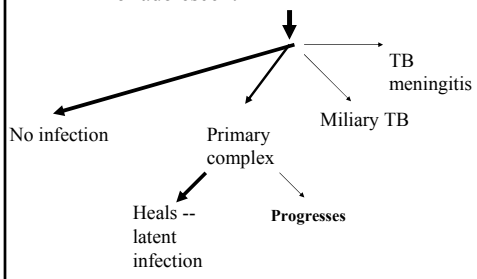
TB- Definitions

- Latent TB Infection--- a few bacilli sequestered somewhere, walled off by host defenses and not detected clinically.
  - Practically- well, N exam and CxR
  - Positive test for LTBI- Mantoux, Quantiferon
- TB disease– signs or symptoms, any site.

TB IN CHILDHOOD: PATHOGENESIS

EXPOSURE

Child exposed to bacilli from adult or adolescent



TB in the very young

- 3 month old
- Hx pertussis like cough
- Fever
- Canadian Born
- Unwell

TB in the very young

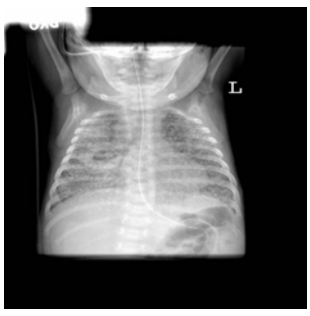
Unwell

Hemophagocytoisis

Hepatosplenomegaly

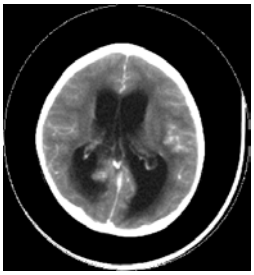
ICU admission

Cavitary disease – infected close contacts.

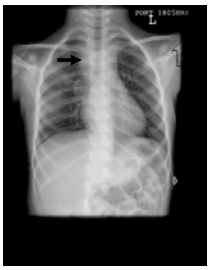


TB in the young

3 year old



- 6 WEEKS FEVER LETHAGY WT LOSS
- Coma



TB Meningitis

- Good response to RX
- Coma- sitting-walking
- Strabismus- improved
- Some motor deficits
- Cognition?? too young to be sure

- **Permanent sequelae are common**.

TB in the very young

- Rapid progression to TB disease
- Often disseminated
- May be miliary, TB meningitis

TB EXPOSURES:

- **The younger child the more urgent the need for prophylaxis.**

TB: Management of Contacts

X ray and PPD – all children

PPD negative: clinically well

Preventive Rx to all < 5 (variations 4-6)

Rpt test after 3 months

D/c Rx if repeat skin test –ve.

If positive (>5mm)- reevaluate and RX for LTBI or disease

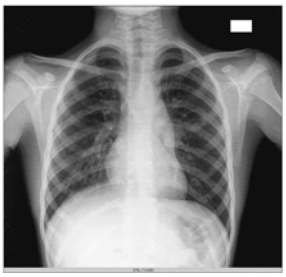
Risk Factors for Progressive Tuberculosis Disease

- **extremes of age (particularly < 4)**
- **recent tuberculin conversion**
  first 2 years
- **HIV seropositivity**
- **diabetes mellitus, antiTNF agents**
- **Immunodeficiency: HIV, IL 12 , γ interferon**

TB IN CHILDHOOD: Clinical

	CLINICAL FEATURES
EXPOSURE **Child inhales bacilli from adult or adolescent**	NONE
↓	
PRIMARY REACTION Small parenchymal lesion & regional node	Usually NONE X ray may show node and small parenchymal change

TB in older child



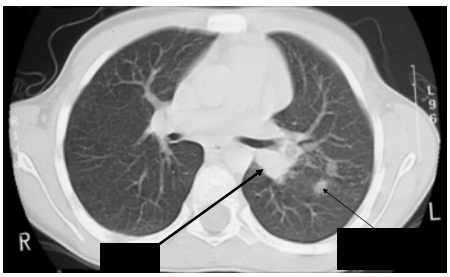
- 8
- Close contact
- CxR

" normal"

Mantoux 22mm

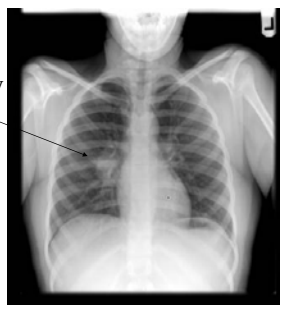
Asymptomatic

Primary TB: CT



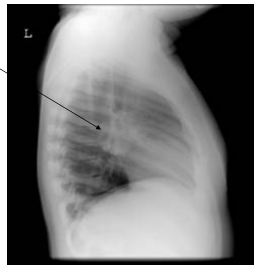
TB

- Hilar lymphadenopathy
- Hallmark of primary TB

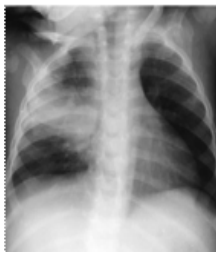


TB disease

- **Hilar nodes-**
- **Lateral view important**

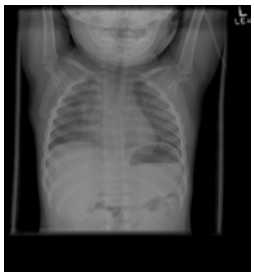


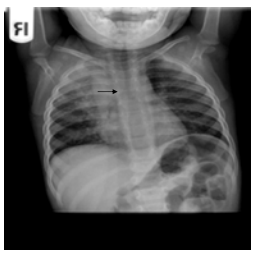
Primary complex : progresses



- Segmental pneumonia- result of bronchial obstruction

Progression—wheeze and stridor





Lymph node compression of bronchus or trachea

▪TB in childhood: Management

- **Protect yourself and others - parents**
- **Obtain isolate before Rx:**
- **Hard copy of contact strain**
- **Gastric aspirates – still best**
- **Sputum, Biopsies**
- **DON'T RELY ON EMPIRIC Rx – can't predict sensitivities**

Is skin test helpful to diagnose disease

14 mo

- **Referred – persistent fever cough. 4 week hx**
- **Canadian Born Visit to East Africa 3 months before**
- **Exam: nil to find**

Childhood TB in GTA

- **CxRay – "normal"**
- **Mantoux 22 mm**
- **Gastric Aspirates x3**

Placed Immediately in GL kit (contains sodium carbonate)

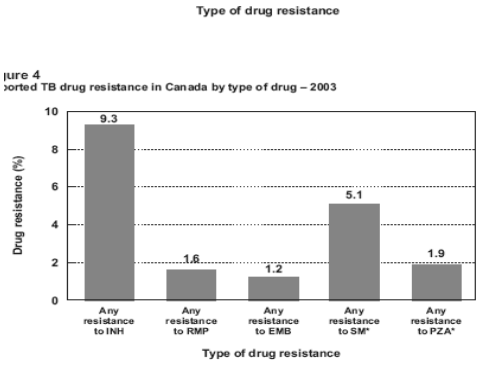
Public Health Labs

TB GTA

1/3 aspirates pos MTB
Fully sensitive

- **Rx INH x 21 days until culture result**
- **Then PZA, RIF, INH x 7 months**

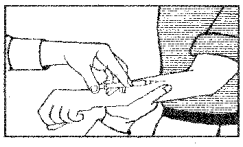
- Grandmum (Kenya)+ve pulm TB



Chidhood TB- diagnostic tests

- Gastric aspirates
  - Need buffer solution
- Chest X rays- technique NB
- CT sometimes helpful -? radiation risk
- Skin tests – 2 HCW's

TB: Tests



- **Mantoux test**
- Intradermal
- 0.1ml PPD 5TU
- Discard vial after 1 mo
- Bevel up
- Wheal of 6-10mm
- Hold arm still

Newer Tests- quantiferon gold

- Whole blood assay for gamma interferon
- Antigens- ESAT 6 and CFP-10: Not found in BCG or M Bovis
- Avoids 2 visits and lack of standardisation
- Not great for detecting disease
- Licensed by FDA, not enough pediatric data

Childhood TB

- Ususally Paucibacillary
- Usually non infectious
- SPECTRUM of paucibacillary to multibacillary disease–

distinction between latent infection and disease is artificial

- More bacilli- more drugs to prevent resistance and obtain cure.

TB IN CHILDHOOD: PATHOGENESIS

EXPOSURE

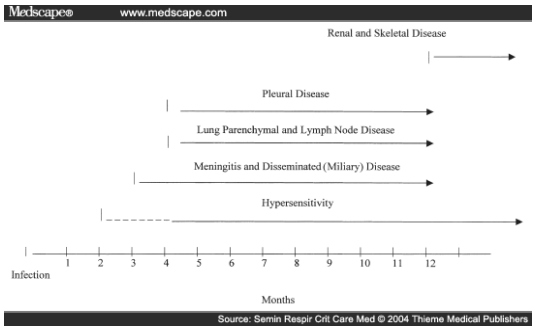
Child exposed to bacilli from adult or adolescent

Primary complex → **Bacilli disseminate to lung apices, meninges, bone, spine, nodes**

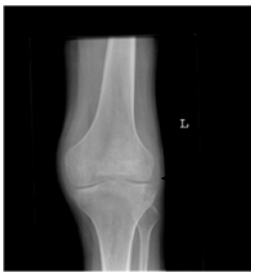
No infection | Heals | Progresses

Rapid progression | Dormant, site of reactivation TB

Timeline

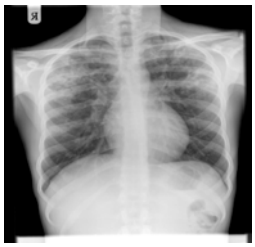
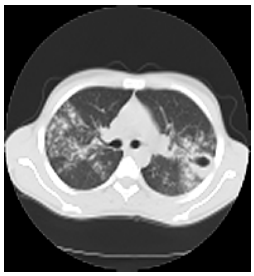


Knee pain in 17 year old



- Knee pain for 1 year
  - Saw family doctor and orthopedic surgeon
  - X-ray: soft tissue swelling
  - Bone scan: avascular necrosis of tibia and knee synovitis
  - Advil for some relief
  - Walking with a cane x 4 months
  - Wt loss 35 lbs?/depressed

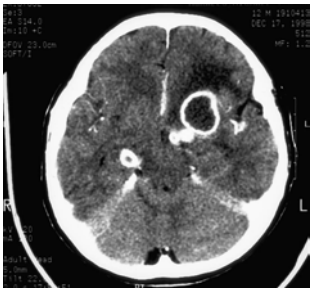
Knee pain- referred to adolescent medicine

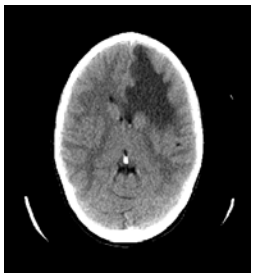
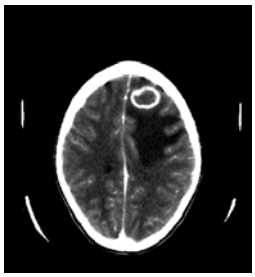
▪TB Disease

- **13**
- **Headache**
- **Visual disturbances**

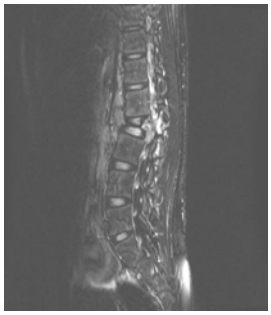
?Brain tumor



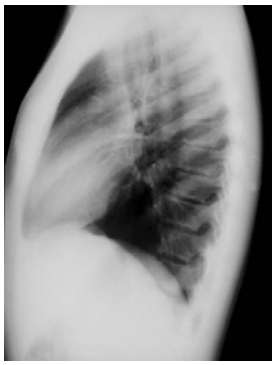
Severe headache and visual loss in 15 year old

Extrapulmonary disease

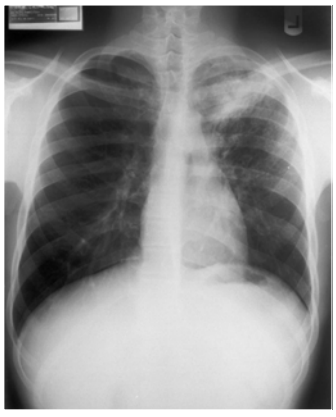


- 14
- Backache x 1 year
- Bx Outside hospital– granulomas



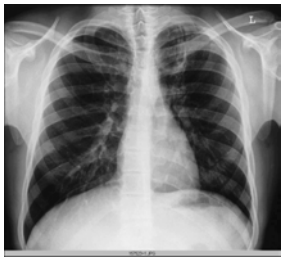
- 1994 – Canada from Highly endemic country
- 1999: Treated for depression> I year
- Clinical bulge at sternum and over foot

- TB DISEASE "typical"
  - 16 yr old
  - Cough , Fever
  - Nightsweats
  - Smear pos for 3months on Rx

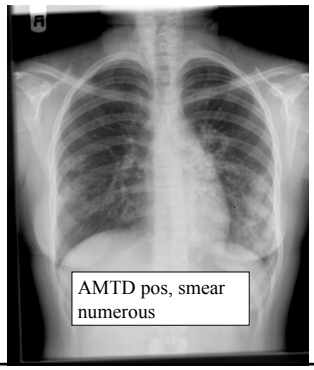


TB DISEASE

- After 6 months of treatment



TB Disease

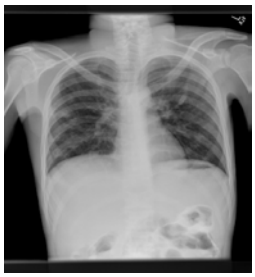


- Cough for 3 months
- Immigrant 4 yrs ago
- Saw family MD at onset
- 3 courses of antibiotics
- Then sputum

2 yrs previously declined INH-mantoux 14mm

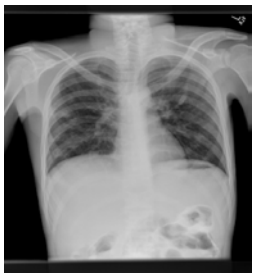
?BCG

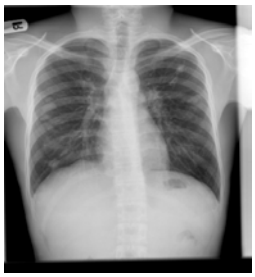
Adolescent TB



- 14 Immigrated 3 years previously
- Abdominal pain, marked weight loss
- Abdominal mass
- TB peritonitis

TB in adolescence- compliance





After 2 mo Rx

Request for intermittent Rx

After 4 months

New infiltrates.

TB- compliance

- Missing 50% of visits
- Instituted daily observed therapy
- "Measures could be taken"
- Frequent reports from public health
- Added 2 drugs to regimen
- Significantly improved in 1 month

TB in adolescence

- Often infectious
- Late diagnosis– lack of clinical suspicion
- Protean with extrapulmonary disease
- Recent immigrants <5 years, sometimes sooner
- Mood disorders common
- Compliance issues

Young children with TB

Differ From Adults

- **Presentation**
- **Generally not infectious**
- **Progression from infection to disease:**
  - **Faster, more often, more extrapulmonary**
- **Response to treatment**
- **Side effect profile**

Adolescents with TB

- **Differ from young children**
  - **Presentation**
  - **Delay in diagnosis**
  - **Mood disorders**
  - **Compliance issues**
  - **Side effect profile**

TB: Management

- **Protect yourself and others**
- **Obtain isolate before Rx:**
  - **Hard copy of contact strain**
  - **Gastric aspirates – still best**
  - **Sputum, Biopsies**
- **DON'T RELY ON EMPIRIC Rx – can't predict sensitivities**

TB Disease: Rx

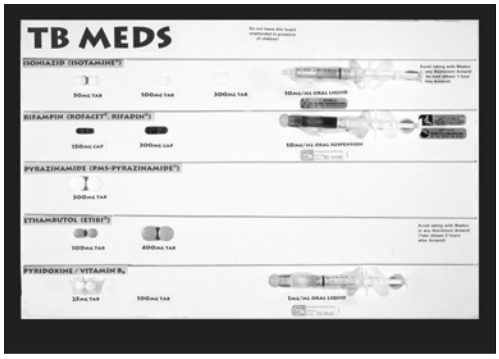
Higher Risk for Resistant disease

most patients we see

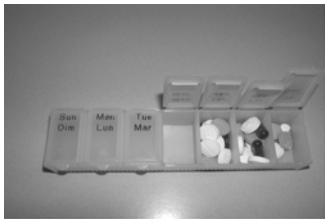
- **Begin with 4 drugs – eg INH, Rif, PZA, Ethambutol**.
  - Then modify based on sensitivities

TB Disease: Rx

- **Low risk** :
  - **PROVE it's susceptible Adult source or patient**
  - **Or low risk- non immigrant**
- **INH, Rif, PZA x 2 mo**
  Then INH Rif x 4 mo
- **Monthly clinical follow up : nausea, vomiting, jaundice**



TB Treatment



- DOT

Biggest recent advance

- compliance check

- **SUSCEPTIBILITY TESTING PHL**
  SITE PAROTID NECK NODE
  RESULT MYCOBACTERIUM
  TUBERCULOSIS COMPLEX Verbal Report:
  2004/07/13 HIGH LEVEL INH Resistant.
- **Streptomycin Sensitive**
- **Rifampin Resistant 2mg/L**
- **Isoniazid Resistant 0.1mg/L**
- **Pyrazinamide Resistant 100mg/L**
- **Ethambutol Sensitive 2.5mg/L**
- **Amikacin Sensitive 1mg/L**
- **Rifabutin Resistant 0.5mg/L**
- **Ofloxacin Sensitive 2mg/L**
- **PAS Sensitive**

TB Monitoring

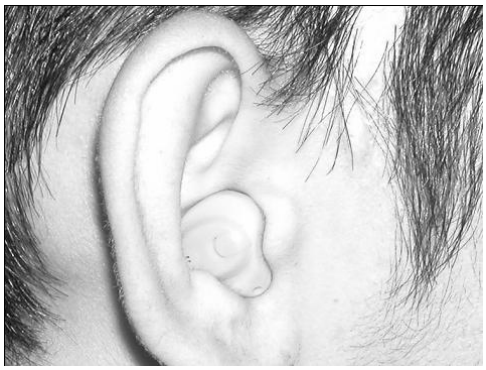
INH and Rifampin:

- **Liver function tests not routine**
  - Check if anorexia, nausea, vomiting, jaundice

  MONTHLY. If any clinical concern d/c and check

  INH- transient elevation common, clinical hepatitis rare, fulminant<1%.

- **Pyridoxine**
  - Milk and meat deficient diets, breastfed infants.



Side effects- amikacin

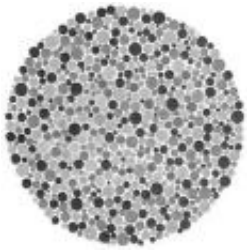
- Weekly creatinine, urea, trough amikacin level
- PICC line
- CBC's in small children.

Baseline and

Monthly audiograms

Ethambutol toxicity

- RARE
- Use 15mg/kg/day
- Acuity and colour vision testing
- Ishiara's plates
- - baseline and monthly



Tuberculosis: screening

- **Why screen?**
- **Who to screen?**
- **How to screen?**
- **What to do with results?**

TB: why screen?

- **Many contacts & children from high incidence countries infected**
- **High risk of progressive disease in young**.

  < 4 yrs old ppd positive:

  5-40% à disease

  20% of disease extrapulmonary

Data from 1950's and 60's Some prospective cohort

TB: why screen?

- Estimated 5-15% LTBI becomes disease over a lifetime - next generation of infectious adults. ↓
  - Data poor
- INH for 9 months lifetime risk of disease by 75%+
  - Data derived from institutions, outbreak situations
  - Ist UPHS trial included 33% c abnormal X rays
  - Mount et al Engl J Med 1961;265 713-23

▪TB: who to screen?

DON"T TEST LOW RISK POPULATIONS

Majority of positives false +ves -

e.g. Canadian born to low risk family

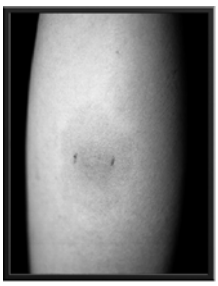
Assume test specificity and sensitivity 95%

TB prevalence	Positive Pred Value
20%	**83%**
1%	**16%**
0.5%	**9%**

▪TB: Who to screen?

- **TB contacts**
- **Origin from high prevalence country**
  especially in Canada < 5 years.
- **Travel to HPC – 5 and 11 years**
- **Suspected TB disease.**
- **Medical risk factors for TB disease.**
  beginning immunosupressive therapy
  HIV infection.

▪TB skin testing



- Positive Mantoux
- > 15 mm always +ve
- **Note marks to measure induration**

Definitions of Positive Mantoux

- Induration > 5 mm
  - **Close contact with infectious TB**
  - **Suspected TB disease**
  - immunosuppressive Rx
    immunocompromised (including HIV)

Definitions of Positive Mantoux

- Induration > 10 mm (including BCG)
  - **increased risk of disseminated disease**
    - **< 4 years of age**
    - medical risk factors: malnutrition, malignancy….
  - **increased environmental TB exposure**
    - **Child/parents born in high prevalence area**
    - **travel to high prevalence area**
    - **Adult contact is HIV positive/ homeless/ IVDU/ institutionalized**

TB: Management

LTBI
FIRST EXCLUDE DISEASE

Source likely INH sensitive

INH 10 mg/kg (max 300 mg), daily x 9 mo

Source likely INH resistant-- refer

Rifampin 6months if rif sens—DOPT preferred.

TB Monitoring

- **Liver function tests not routine**
  - Check if anorexia, nausea, vomiting, jaundice
- **Pyridoxine**
  - Milk and meat deficient diets, breastfed infants.

TB Screening. Two step testing: principles

- Hypersensitivity wanes
- Skin test years after infection ànegative reaction.
- BUT
- **This** skin test may boost reactivity subsequent tests--> positive
- Boosted reaction may be misinterpreted as new infection.

TB Screening. Two step testing

- For **initial** test of adults who will be retested periodically,
- eg. health care workers.
- ***If*** first test -ve, do second test 1 - 3 weeks later.
- Positive second test -->boosted reaction, not conversion
- "Classify as previously infected and care for accordingly."

Problems with 2 step testing

- There is almost no place for 2 step testing -2 weeks apart-in childhood (Don't confuse this with retesting 3 months after break in contact which is very important)
- There are very few data on significance of a test positive only on step 2– data suggests good correlation with prior BCG.
- Don't retest "to see if we can make it positive"
- Don't do 2 steps more than once, after that if periodic testing continues a single test should be done.

▪Tuberculosis: Evaluation

- Hx of TB contact
- BCG – but ignore for mantoux interpretation
- Weight
- Height
- Alertness, any change in behaviour,
- BCG scar

TB: Take Home

- Resistance: Highly prevalent and increasing
  - Organism and sensitivities essential
  - Don't rely on empiric Rx for disease
- Screen high risk
  contacts recent immigrants
- Monitor clinically for INH reactions
- REFER RESISTANT TB

Take Home

- Young children at high risk for severe disease- prophylaxis NB
- Extrapulmonary disease common in children, (+maybe in adolescents.)
- Adolescents may be diagnosed late, have mood disorders and compliance issues.

TB Team HSC

- **Patricia Malloy -- C N P**
- **Debra Louch Clinic Nurse**
- **Wayne Moore Info**
- **Robyn Salter Goldie– Social Worker**
- **Fellows, residents**
- **Toronto Public Health, Translation services.**

Also thanks to Pediatricians RN's RVHS

Team vital part of management

- Social Worker
- Nurse Practitioner
- Physicians
- Nurses
- Translation Services
- Public Health Nurses and Physicians

The Effect of Initial Drug Resistance on Treatment Response and Acquired Drug Resistance during Standardized Short-Course Chemotherapy for Tuberculosis

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Background. In Tomsk Oblast, Russian Federation, during the period of 1996–2000, most previously untreated patients with tuberculosis received standardized short-course chemotherapy, irrespective of drug-susceptibility testing results. A retrospective analysis was done to determine the effect of initial drug resistance on treatment outcome and acquired drug resistance in new patients receiving standardized short-course chemotherapy.

Methods. During the period of 1 November 1996 through 31 December 2000, a total of 2194 patients received a category 1 treatment regimen. Drug susceptibility test results for 1681 patients were available for analysis. Drug resistance patterns before and during treatment were compared for 73 patients whose culture results were persistently positive during treatment. Acquired resistance was defined as new drug resistance (during or at the end of treatment) that was not present at the beginning of treatment.

Results. Pretreatment drug resistance was strongly associated with treatment failure. In patients who had strains with pretreatment resistance patterns that included isoniazid or rifampin resistance, but not resistance to both, 17 (70.8%) of 24 cases involving treatment failures acquired new multidrug resistance. In patients with pretreatment pan-susceptible or streptomycin-monoresistant strains, 13 (41.9%) of 31 cases involving treatment failures acquired new multidrug resistance.

Conclusions. Early diagnosis of drug-resistant tuberculosis and judicious use of second-line drugs is recommended to decrease transmission of drug-resistant strains and to prevent the creation of multidrug-resistant strains. Finally, if drug susceptibility tests are not available or results are delayed, physicians should recognize that patients who do not respond to directly observed empirical short-course chemotherapy are at high risk of having multidrug-resistant tuberculosis and should be treated accordingly.

The Next Few Teleclasses

November 21 ***Catheter Associated Urinary Tract Infections***
… with Lauren Tew, Infection Control Nurse Consultant, UK

November 30 ***Preventing Surgical Site Infections***
with Loretta Litz Fauerbach, University of Florida

December 7 ***Preventing Central Line Associated Infections***
… with Robert Garcia, Brookdale University Medical Center

December 14 ***C. difficile – Where are We Now?***
… with Dr. Michelle Alfa, St. Boniface General Hospital

For the full teleclass schedule – www.webbertraining.com
For registration information www.webbertraining.com/howtoc8.php