Extrapulmonary Tuberculosis

Germaine Jacquette, MD
Clinical Assistant Professor
NJMS Global Tuberculosis Institute
May 4, 2012

TB Cases by Site of Disease
United States, 2000 – 2010

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Cases</th>
<th>Pulmonary</th>
<th>Extra-pulmonary</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>16,309</td>
<td>13,086 (80%)</td>
<td>3,211 (20%)</td>
</tr>
<tr>
<td>2001</td>
<td>15,945</td>
<td>12,724</td>
<td>3,221</td>
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<tr>
<td>2002</td>
<td>15,055</td>
<td>11,901</td>
<td>3,148</td>
</tr>
<tr>
<td>2003</td>
<td>14,835</td>
<td>11,805</td>
<td>3,030</td>
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<tr>
<td>2004</td>
<td>14,499</td>
<td>11,523</td>
<td>2,976</td>
</tr>
<tr>
<td>2005</td>
<td>14,068</td>
<td>11,126</td>
<td>2,942</td>
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<tr>
<td>2006</td>
<td>13,732</td>
<td>10,848</td>
<td>2,884</td>
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<tr>
<td>2007</td>
<td>13,286</td>
<td>10,567</td>
<td>2,719</td>
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<tr>
<td>2008</td>
<td>12,905</td>
<td>10,261</td>
<td>2,644</td>
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<tr>
<td>2009</td>
<td>11,537</td>
<td>9,012</td>
<td>2,525</td>
</tr>
<tr>
<td>2010</td>
<td>11,181</td>
<td>8,709 (78%)</td>
<td>2,438 (22%)</td>
</tr>
</tbody>
</table>

E-P TB in USA - 2010

- Of 2438 E-P* cases in 2010
  - Included 2522 sites
  - 84 cases with > 1 site

*Excludes cases with assoc. pulmonary disease

Site of disease | # cases
---|---
Lymphatic | 1012
Pleural | 407
Bone & Joint | 259
Peritoneal | 142
Genitourinary | 138
Meningeal | 117
Other | 447


Are E-P TB Cases Stable?

<table>
<thead>
<tr>
<th>Site of disease</th>
<th>2009</th>
<th>2010</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphatic</td>
<td>45%</td>
<td>40%</td>
<td>(- 5%)</td>
</tr>
<tr>
<td>Pleural</td>
<td>19%</td>
<td>16%</td>
<td>(- 3%)</td>
</tr>
<tr>
<td>Bone &amp; Joint</td>
<td>10%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Peritoneal</td>
<td>6%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Meningeal</td>
<td>6%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>6%</td>
<td>5%</td>
<td>(- 1%)</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
<td>17%</td>
<td>(+ 9%)</td>
</tr>
</tbody>
</table>

**Demographics of E-P TB**

- Among HIV (+) >50% have extrapulmonary TB
- Lymphatic: more in younger ages, esp. in HIV (+), Asians (especially high rate among persons from Indian subcontinent in UK)
- Genitourinary: most prevalent in those > 35 years (long lag time from initial infection)
- TB meningitis: Hispanics, blacks, Amerindians
- Pericardial: blacks far outnumber other races


**Pathogenesis of E-P TB**

- Hematogenous/lymphatic dissemination of bacilli to multiple sites at time of initial infection
- Some tissues commonly involved, others rarely
- Tissues with increased arterial supply, high O₂ content favored
- Trauma may play a role (+ history in 30-50% bone/joint TB)
- Increasing evidence for role of innate immunity: host genetic susceptibility mediated by macrophage capacity


**TB Meningitis**

- (-) TST in up to 50%
- Abnormal c-xray 31-74%
- Cerebrospinal fluid:
  - TOpening pressure; protein; WBC (mainly lymphocytes) > occas. acellular in elderly and HIV (+)
  - ↓CSF glucose (< 40 mg/dl or < 0.5 of blood glucose)
  - (+) AFB smear (low yield); (+) NAA (higher than smear)
  - (+) culture (50-80%)

TB Meningitis:
CT for diagnosis of Hydrocephalus
Rx: ventriculostomy or V-P shunt

TB Meningitis – Treatment
• Need effective CSF-penetrating agents
• Standard RIPE treatment
  – Good penetration: INH, PZA, SM; less good: RIF, EMB
  – Parenteral forms of INH, RIF: give highest dose in range
• In children: EMB > SM (WHO), EMB > ETH (AAP)
• 90% deaths early: avoid treatment interruptions
• Corticosteroids recommended at all stages¹

¹ G. Thwaites, Nguyen & Nguyen. NEJM. 2004

CNS Tuberculoma
• May develop during steroid taper in TB meningitis
• Biopsy unless TB diagnosis established elsewhere
• Use serial CTs or MRIs to follow mass lesions
• High dose steroids given if paradoxical response
• Treatment for 12 months or longer, and until edema surrounding lesions has resolved¹

¹ S. Poonoose et al. Neurosurgery, 2003 & personal communication, overseas experts
Bone & Joint TB

- Disease of antiquity: in 1900 common crippling disease
- Now 3rd most common form
  - ~ 3-4% of all TB cases, 10-11% of all E-P
  - higher in HIV (+) persons
- Pain, impaired function, swelling; subtle, slow course
- Co-existence of pulmonary disease 30-50%

TB Spondylitis

Origin of vertebral osteomyelitis in anterior inferior edge of vertebra adjacent to disc

Abscess filled with necrotic debris ("cold" as opposed to "hot," filled with pyogenic pus)

Vertebral TB, Paraspinal Abscess

Image of chest X-ray showing vertebral TB and paraspinal abscess

Vertebral TB, Paraspinal Abscess

Image of CT scan showing vertebral TB and paraspinal abscess with surgical intervention
Vertebral TB – Surgical Indications

- Neurologic deficit
- Spinal deformity with instability or pain
- No response to medical therapy
- Epidural abscess
- Large paraspinal abscess
- Non-diagnostic percutaneous needle biopsy

Disseminated TB

- TB disease at more than one noncontiguous sites
- Diagnosis at 2nd site may not require (+) culture
  - Clinical data may supports TB in 2nd site
  - (+) *M. tuberculosis* culture from initial site within 30 days
- In USA, shift from pediatric age group to adults
- Called “miliary” if lesions 1-2 mm in diameter

Medical risk factors for dissemination
- Immunosuppression, HIV/AIDS, age extremes
- Cancer, cancer chemotherapy
- TNF-a inhibitor agent, etc.

Surgical risk factors for dissemination
- Partial resection of lymph node
- Tubal surgery
- TURP; lithotripsy
- Vertebral curette in pre-antibiotic era

Disseminated TB Case # 1

- 34 y/o Philippine-born male in US x 8 years
- H/o (+) TST, no TLTBI
- “Shoulder bursitis” Rx oral steroids
- Weight loss (patient self-induced fast?)
- Acute R chest pain: R apical cavity, and R pleural effusion on CT angio
- HIV (-); (-) AFB smears, sputum, BAL; shoulder plain film (-)
E-P TB Case #1

- Shoulder:
  - MRI – para-deltoid fluid collection
  - Drainage fluid: (-) cultures
  - Bx: non-caseating granulomas

- Pleural effusion
  - Resolving BUT collection under diaphragm, communicating with pleura
  - Abdominal imaging: fluid tracking to L2 vertebra

- Lumbar Spine MRI
  - L1-L2 vertebral destruction, no cord compression; paraspinal, psoas abscess (Pott’s)

E-P TB Case # 1

- Chest clinic
  - More sputum samples
  - ESR 85 mm/hr
  - Dilemma: send back to hospital for more procedures? (pleural tap & biopsy, more complete w/u of shoulder) or trust that sputum cultures will grow?
  - Chose latter, RIPE begun 11/7/11
  - Application for charity care initiated to facilitate outpatient procedures

E-P TB Case # 2

- 48 y/o Chinese male
- H/o BCG
- Foot pain with draining lesion
- (+) TST, negative IGRA test (Quantiferon-Gold)
- Bone culture (+) for *M. tuberculosis*
TB Lymphadenitis: Inspiration for Fashion Trend

• Most frequent site of E-P disease
• Higher % foreign-born with TB; in 40% of HIV (+) persons
• Usually occur within 6 months of primary infection: most regress
• Excisional biopsy preferable; reduces fistulas
• Send sputum cultures even if chest x-ray negative

E-P TB Case #3

• 39 y/o f Dominican school aide
• H/o (+) TST
• Developed cervical lymphadenopathy
• FNA was “non-diagnostic”
• 3 months later had malaise, followed by dizziness and unsteady gait; admitted to r/o stroke
• Head CT showed multiple small mass lesions; CXR: negative; chest CT scan: multiple small cavitating nodules; AFB sm (+); grew M. tb

Paradoxical Reaction – Enlargement of TB Lymph Nodes

1E. Lincoln & E. Sewell. Tuberculosis in Children. 1963
IRIS / Paradoxical Reaction

- Temporary exacerbation of symptoms, signs, or radiographic manifestations of TB after beginning anti-TB treatment
  - High fevers
  - Esp. increase in size of lymph nodes/new lymph nodes
  - Worsening of infiltrates or pleural effusions
  - Expanding central nervous system lesions

- Most common among HIV(+) on ART; can occur in immunocompetent

- Treatment: NSAIS or steroids if severe

Pericardial TB

- Although uncommon, has potentially lethal outcome

- Probably arises from adjacent lymph nodes, occasionally hematogenously

- Dyspnea, cough, chest pain, night sweats, ankle swelling most common symptoms

- Cardiomegaly, pleural effusion, low voltage EKG

- Echocardiogram confirms pericardial effusion

Pericardial TB

- Indirect diagnosis (TB at other site, e.g., pleura), by pericardiocentesis, or presumptive diagnosis

- Prompt treatment indicated if diagnosis likely

- RIPE and corticosteroids recommended

- Follow-up monitoring with echocardiogram to rule out constriction

- May require pericardiectomy

E-P TB Case # 4

- 42 y/o Haitian male adm. with shortness of breath

- Chest x-ray: cardiac enlargement

- ECHO: large pericardial effusion

- (+) TST; fluid suggestive for TB

- Refused steroids!

- Serial ECHOs: impaired chamber filling

- Surgical procedure: pericardiectomy
Peritoneal TB

- **Most at-risk**
  - Young child-bearing age women
  - Older men, often alcoholic

- **Presentation**
  - Ascites
  - Abdominal pain, with or without signs of obstruction

- **CA125 can be markedly elevated**
  - Marker for epithelial ovarian cancer
  - Seen in also some benign conditions
  - False (+) with TB; repeat test on or after treatment

E-P TB Case # 5

- 25 y/o Mexican female
- Noted increased abdominal girth, (-) beta-HCG
- **Elevated CA-125; dx ovarian cancer**
- Laparoscopy: multiple small yellowish nodules studding peritoneum, histopathology showed granulomas; culture (+) *M. tuberculosis*
- Responded well to anti-TB therapy despite some non-adherence

E-P TB Case # 6

- 20 y/o Mexican male
- Cough, anorexia, weight loss x 9 months
- Hospitalized with pulmonary cavitary TB; Rx RIPE
- On therapy developed abdominal pain, mass
- Underwent hemi-colectomy for enteric TB with tuberculous phlegmon; delayed wound healing
- Post-op gained 30 pounds

Pleural TB

- Acute > subacute chest pain
- Fever, shortness of breath, cough, common
- Usually unilateral, small to very large
- Associated pulmonary lesion (higher frequency on CT scan than on chest x-ray)
- Exudative effusion by laboratory analysis
- Adenosine deaminase (ADA) used little in US
**Pleural TB**

- Best microbiologic yield: pleural tissue > pleural fluid
- Yield from sputum culture high: collect sputum even when no parenchymal infiltrate
- Role of steroids in treatment unclear
- Resolution without treatment usual BUT pulmonary TB usually occurs in months or years if no Rx
  - Treat for active TB even if spontaneous resolution has occurred

  1. personal communication, Dr. William Harris, NYCDOHMH

**Genitourinary TB**

- Renal TB usually hematogenous in origin
  - Urinary abnormalities: hematuria, pyuria
- Male genital TB through urine or contiguous spread from another organ
  - Bladder, epididymis, testes, and/or prostate
  - Local presentation; rarely systemic symptoms
  - May have superinfection (treated with quinolone!)
  - 50% sterile

**E-P TB Case # 7**

- 37 y/o Ecuadorian male, identified as contact of contagious TB case in household
- (+) TST, very large induration
- No respiratory symptoms, negative chest x-ray
- Review of systems: (+) G-U abnormalities: h/o scrotal swelling, spontaneous drainage in Ecuador; visible scarring on scrotum
- Tender epididymis, (+) urines for M. tuberculosis

**Genitourinary TB**

- Genital TB (female): lympho-hematogenous spread from pulmonary or other focus to tubes, endometrium, ovaries; rarely sexually transmitted

- Presentations
  - Pelvic pain
  - Menometrorrhagia; vaginal discharge
  - Infertility (common in developing world)
E-P Case # 8

- 26 y/o white multiparous female gave birth to an infant diagnosed with congenital TB at age 9 weeks (failure to thrive, tuberculous otitis media)
- Mother's symptoms at 3 months post-partum
  - Lower abdominal pain
  - Irregular menses
- Findings
  - (+) TST (conversion over 2 years)
  - Atelectasis on cx-ray
  - Granulomatous endometritis on biopsy
  - *M. tuberculosis* from biopsy matched infant’s strain

E-P TB: Diagnostic Pitfalls

- Historical clues often overlooked
  - Origin from (or travel to) high TB prevalence country
  - Past TB exposure; FH of TB
  - Past TB disease or LTBI, treated or untreated
  - Radiologic evidence for prior, healed TB disease
- Misinterpretation of negative tests
  - TST, IGRA can both be false-negative
  - Absence of AFB on smear
  - Absence of granulomas on biopsy
  - Negative mycobacterial culture
- Failure to obtain sputums

Management of E-P TB

- Consult textbooks, guidelines, and experts¹
- Do thorough literature review
- May need serial procedures to evaluate resolution, rely on “clinical improvement”
- Teach providers in your communities to recognize E-P TB

¹Regional Training and Medical Consultation Centers (RTMCCs); National Jewish Medical Research Center; State medical consultants, other experts
Supplementary Handout
Extrapulmonary TB

CDC data for known HIV (+) and HIV (-) TB cases for years 1998 and 2008:

**HIV(+) FB:**
- 1998: 19% E-P, 27% both = 46% total
- 2008: 26% E-P, 26% both = 52% total

**HIV(+) US-born:**
- 1998: 14% E-P, 18% both = 32% total
- 2008: 20% E-P, 16% both = 36% total

**HIV(-) FB:**
- 1998: 22% E-P, 7% both = 29% total
- 2008: 22% E-P, 9% both = 31% total

**HIV (-) US-born:**
- 1998: 15% E-P, 6% both = 21% total
- 2008: 16% E-P, 8% both = 24% total

**TB Meningitis Parameters**
- ↑ opening pressure
- ↑ CSF protein (100-500 mg/dl usual; can be > 2G and cause spinal block)
- ↓ CSF glucose (< 40 mg/dl or < 0.5 of blood glucose)
- Occas. acellular in elderly and HIV (+)
- (+) AFB smear in 10-40% initial specimens; NAA possibly more sensitive
- (+) AFB (+) culture in 50-80% of cases (large volume increases yield)

**Stages of TB meningitis**

- **Stage 1** – no neurologic deficit
- **Stage II** – confused or have neurologic signs such as cranial nerve palsy or hemiparesis
- **Stage III** – patients stuporous or comatose with more severe neurologic signs

**Texts and Guidelines**
ATS, CDC, IDSA. *Treatment of Tuberculosis.* MMWR. June 20, 2003.