

# Extra-pulmonary Tuberculosis

*James Sunstrum, M.D.  
TB Consultant  
Michigan Dept. of Health & Human Services*

*July 18, 2019*

**Beaumont**

1

## Objectives

- How does TB spread beyond the lungs?
- How can TB present in these sites?
- How is extrapulmonary TB treated?
  
- DISCLOSURES: none

**Beaumont**

2

## TAKE ON TB

Too many people in our country still suffer from tuberculosis (TB).

### 9,557 TB CASES REPORTED IN THE U.S. IN 2015

493

TB Deaths  
in 2014

180

days of  
medications

PLUS

- X-rays
- Lab tests
- Follow-up & testing of contacts

\$450

MILLION

Total cost to U.S. for TB cases in 2015.

Our progress towards elimination is slowing - the U.S. saw the first increase in cases in over 20 years!

### TB CAN HAPPEN ANYWHERE & TO ANYONE!

To eliminate TB, we must reach the hardest hit populations.

29x

Higher for  
Asians  
than whites.

8x

Higher for  
African Americans  
than whites.

8x

Higher for  
Hispanics/Latinos  
than whites.

2 out of every 3

TB cases occur among foreign-born persons.

3

**Figure 1** The spectrum of TB — from *Mycobacterium tuberculosis* infection to active (pulmonary) TB disease

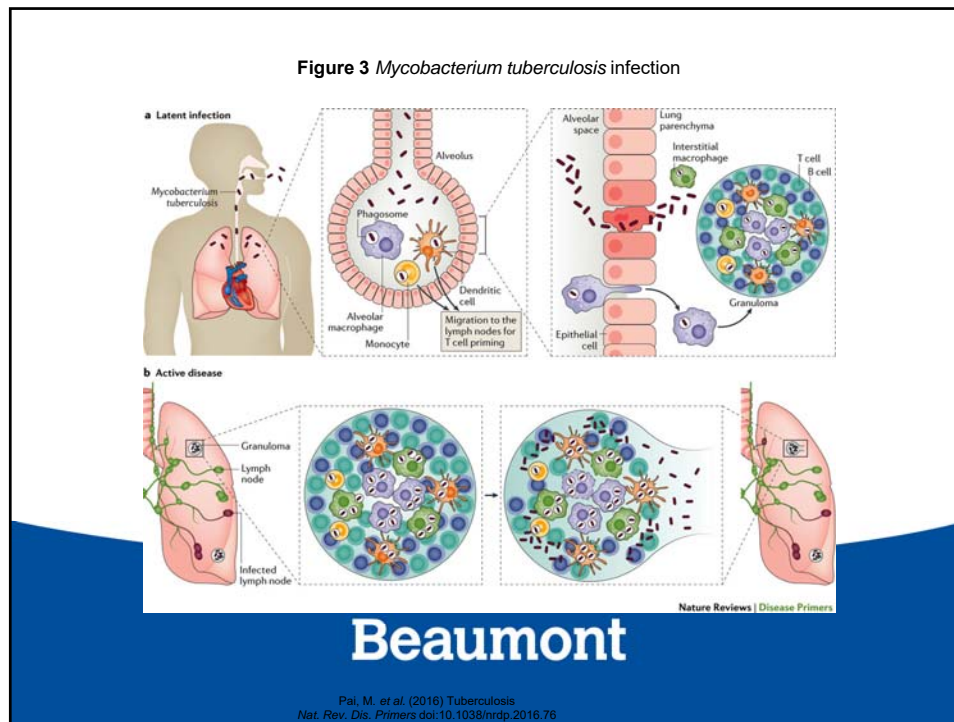
	Infection eliminated <small>With innate immune response* or With acquired immune response</small>	Latent TB infection	Subclinical TB disease	Active TB disease
<b>TST</b>	Negative	Positive	Positive	Positive
<b>IGRA</b>	Negative	Positive	Positive	Positive
<b>Culture</b>	Negative	Negative	Negative	Intermittently positive
<b>Sputum smear</b>	Negative	Negative	Negative	Usually negative
<b>Infectious</b>	No	No	No	Sporadically
<b>Symptoms</b>	None	None	None	Mild or none
<b>Preferred treatment</b>	None	Preventive therapy	Preventive therapy	Multidrug therapy

Nature Reviews | Disease Primers

Beaumont

Pal, M. et al. (2016) Tuberculosis  
Nat. Rev. Dis. Primers doi:10.1038/nrdp.2016.76

4



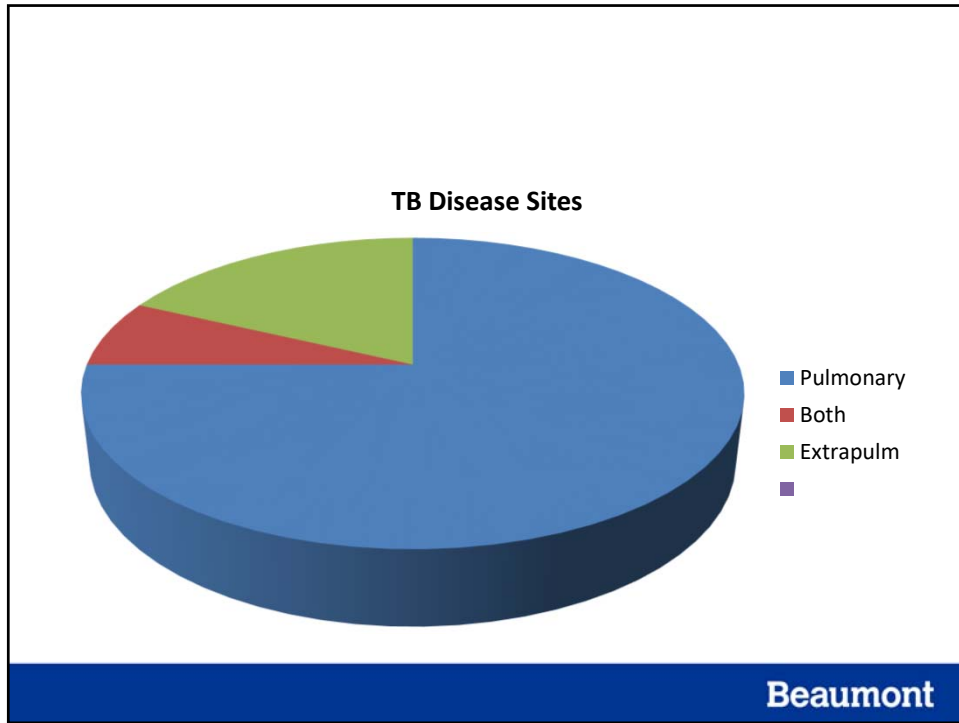
5

## Indiana statistics 2013-2017

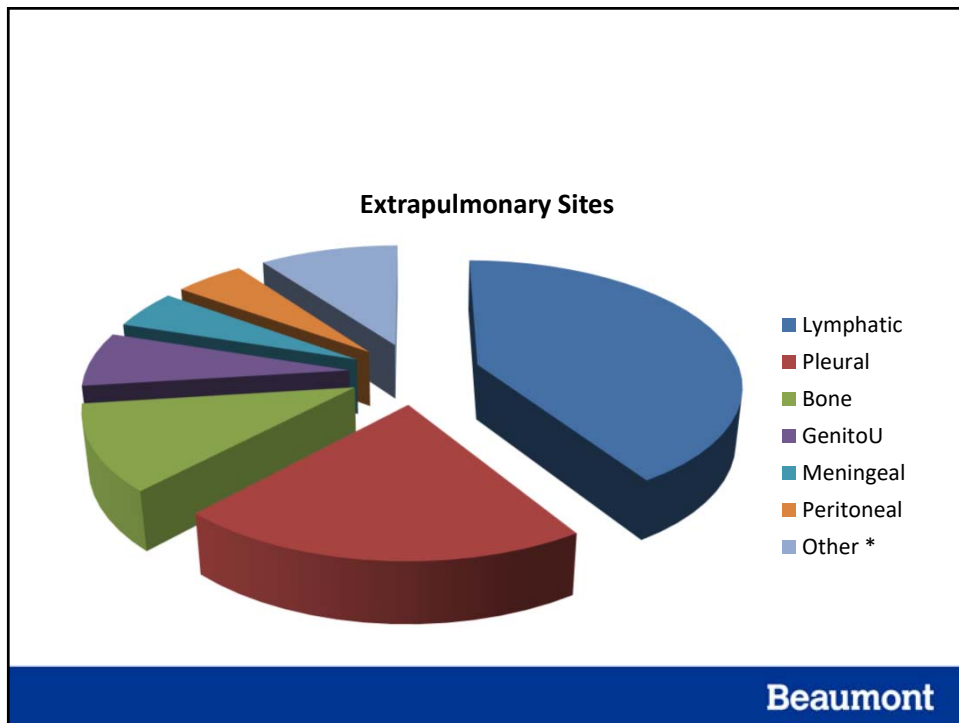
- Pleural 35 cases
- Lymphatic 33
- Bone/joint 21
- Genitourinary 13
- Peritoneal 11
- Meningeal 10
- Eye 9
- Pericardium 2
- 1 case of:
- Bile duct
- Small bowel
- Stomach
- Liver
- Rectum
- Salivary gland
- Breast

**Beaumont**

6

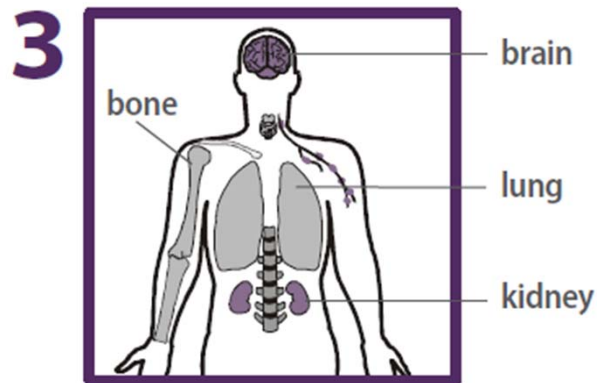


7



8

## TB Pathogenesis (6)



**A small number of tubercle bacilli enter bloodstream and spread throughout body**

**Beaumont**

9

## Is pleural TB considered extrapulmonary?

- Yes, in USA
- *No, in United Kingdom*
- Considerable overlap
- Pleural TB should have sputum examined
- Suspected pleural TB should be isolated until sputum carefully assessed

**Beaumont**

10

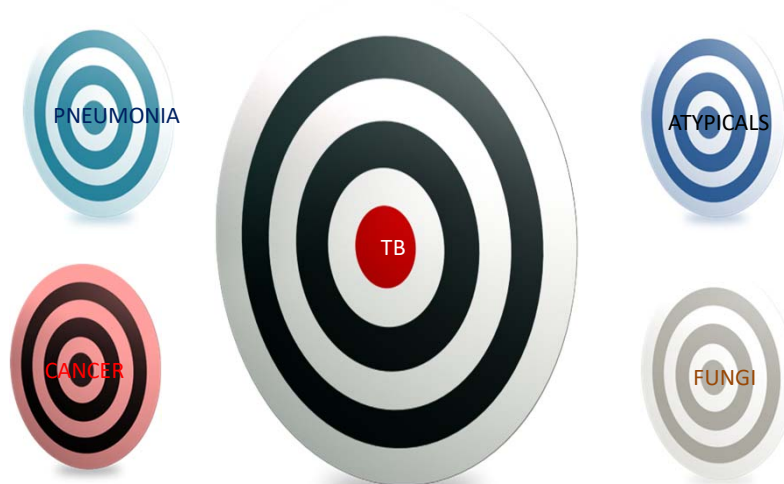
## Respiratory Tuberculosis

- Active infection of lungs, pleural cavity, mediastinal lymph nodes or larynx
- British Royal College of Physicians, 2006

Beaumont

11

## TB is difficult to diagnose



Beaumont

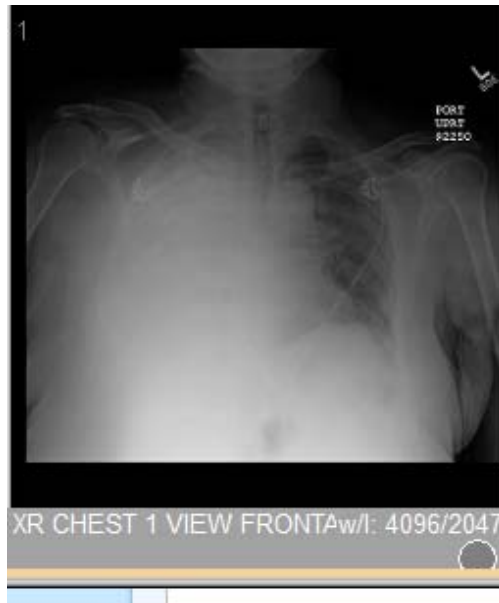
12

## AFB studies of body fluids

- Pleural
- Pericardial
- Peritoneal
- Cerebrospinal
- Joint
- Urine
- Stool
- Menstrual blood
- Tissue
- AFB smear usually negative
- AFB cultures only 20-40%
- Fluids “exudative”
- PCR or NAAT ? %

Beaumont

13



Beaumont

14

## Pleural fluid diagnosis

- pH > 7.3 usually
- Protein >4 grams
- Glucose <40 mg/mL
- WBC 300-5,000
- Lymphocyte predominance (wide range)

Beaumont

15

## Pleural fluid biochemistry

- Adenosine deaminase (ADA) enzyme increased
- Inconsistent studies of ADA

Beaumont

16



## Light's Criteria

- According to Light's criteria (1972), a pleural effusion is likely exudative if at least one of the following exists:
- The ratio of pleural fluid protein to serum protein is greater than 0.5
- The ratio of pleural fluid LDH and serum LDH is greater than 0.6
- Pleural fluid LDH is greater than 0.6 or  $\frac{2}{3}$  times the normal upper limit for serum. Different laboratories have different values for the upper limit of serum LDH, but examples include 200 and 300 IU/l.

Beaumont

17

**Ocular TB**  
**Henry Fraimow, MD**  
**Cooper University Hosp**

Beaumont

18

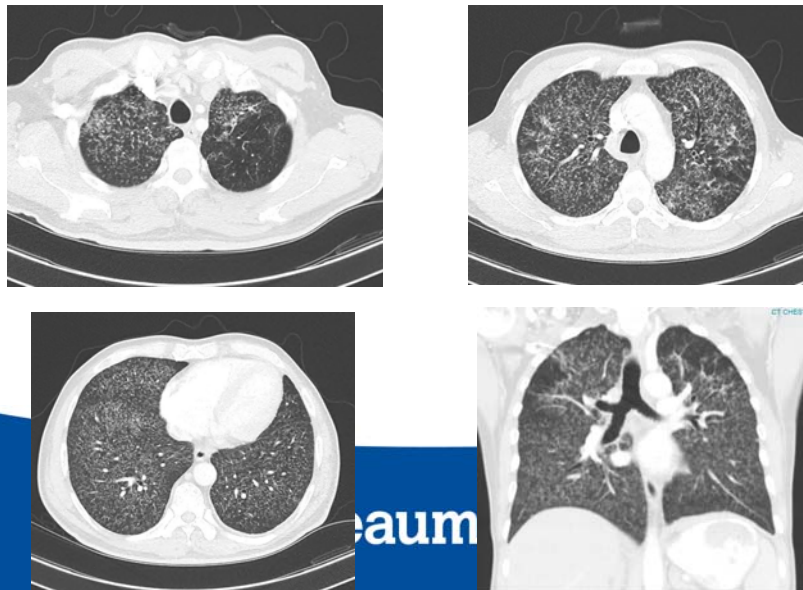
## Patient 1

- **Physical Exam:**
  - 131.2 lb (baseline 167 lb) 99.6° F
  - Vision 20/25 in both eyes, color blind
  - Mild conjunctival injection Right eye
  - Dry crackles anteriorly, Right > Left
  - Right knee mildly boggy and swollen, not warm
- **Pertinent Labs:**
  - Glucose 118; **Creatinine 1.42**; Uric Acid 6.1
  - AST 20 ALT 19 **Alk Phos 281** Bili 0.6
  - WBC 11.2 Hg 12.5, platelets 320, **ESR 81**
  - HIV, Hepatitis C, Hepatitis B Negative

Beaumont

19

## Chest Imaging at Start of Treatment



20

## Patient 1

- **Started on Treatment**
  - Regimen: RIPE plus B6
  - Recent films done of right knee requested
- **F/U Visit 3 weeks**
  - Feeling better, gained 3 lbs, decreased cough, Right knee “the same”
  - **Increased redness and complaining of some pain of the Right eye;** on exam vision unchanged, Pupil reactive
  - Sputum cultures growing MTB
  - Labs: Glucose 292, Hg A1C 7.3, Uric Acid 11.5, LFTs stable, Alk phos decreasing

Beaumont

21

## Back to our Question

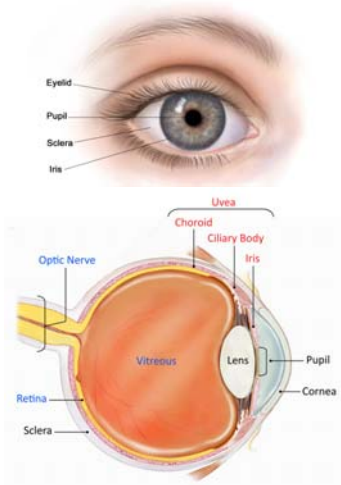
So did this Patient with extensive Pulmonary TB and probable TB osteoarthritis of the knee also have Ocular tuberculosis?

Beaumont

22

## Some Important Terminology

- **Uveitis:** inflammatory diseases involving the uvea (includes choroid, ciliary body, iris)
- **Anterior uveitis:** Most common form: front of eye, "iritis"
- **Intermediate uveitis:** involves ciliary body, often see inflammatory cells in vitreous
- **Posterior uveitis:** involves choroid and retina, includes "chorioretinitis"
- **Pan-uveitis**
- **"Granulomatous" uveitis:** presence of large "greasy" keratic precipitates (KPs)



Source: <https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0022373/>

Beaumont

23

## Ocular tuberculosis masquerading as a tumor

*Thérèse M Sassalos, Rajesh C Rao,  
Hakan Demirci  
University of Michigan*

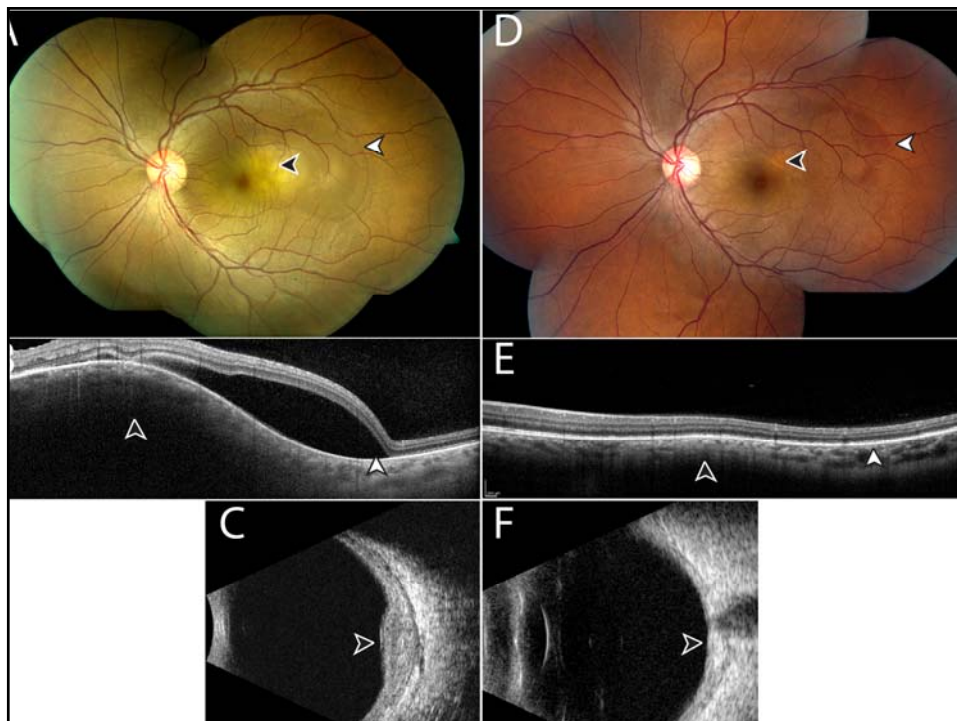
Beaumont

24

- A 31-year-old healthy woman presented with 4 days of blurry vision and 3 weeks of periorbital pain of the left eye.
- Mexico 11 years ago.
- Close contact with a friend, who was recently abroad, and who was “constantly coughing”.
- Quantiferon ++
- CXR normal

Beaumont

25



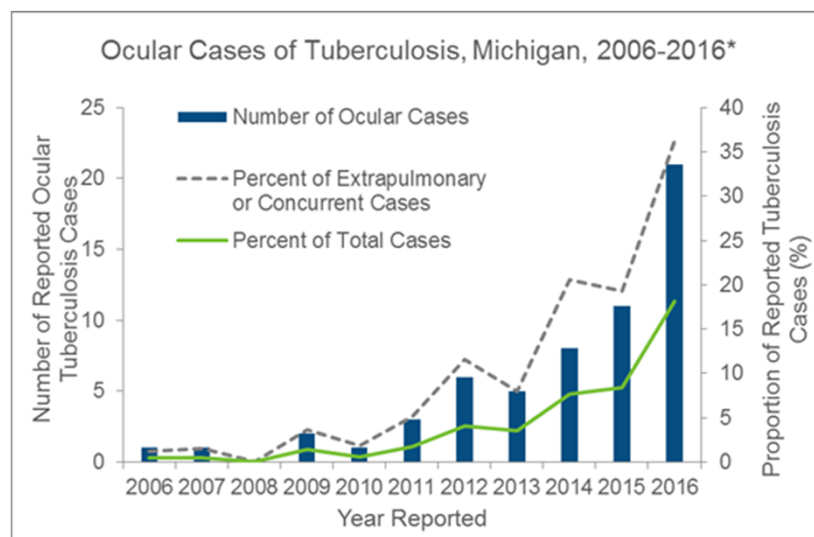
26

## How does TB get to the eye?

- Pathogenesis of Ocular Tuberculosis
  - Haematogenous spread
  - Exogenous infection
    - Direct extension from surrounding tissues
    - Self contamination from sputum
  - Immune, non-infectious syndromes
    - Inflammatory response to TB antigens?
    - Eales disease (retinal perivasculitis)
    - Serpiginous choroiditis

Beaumont

27

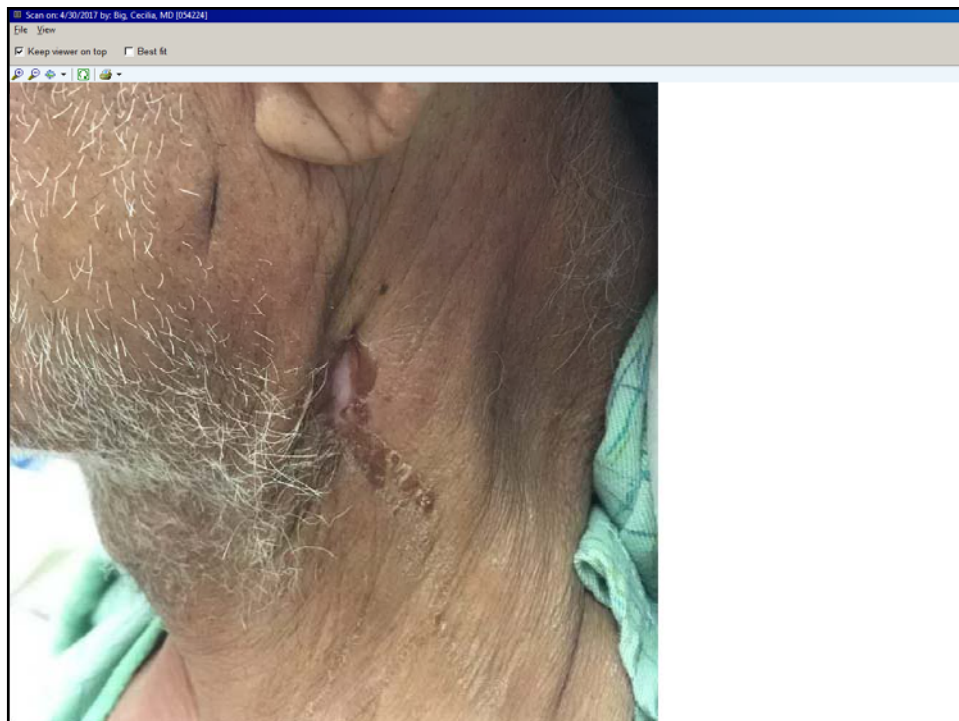


Beaumont

28



29



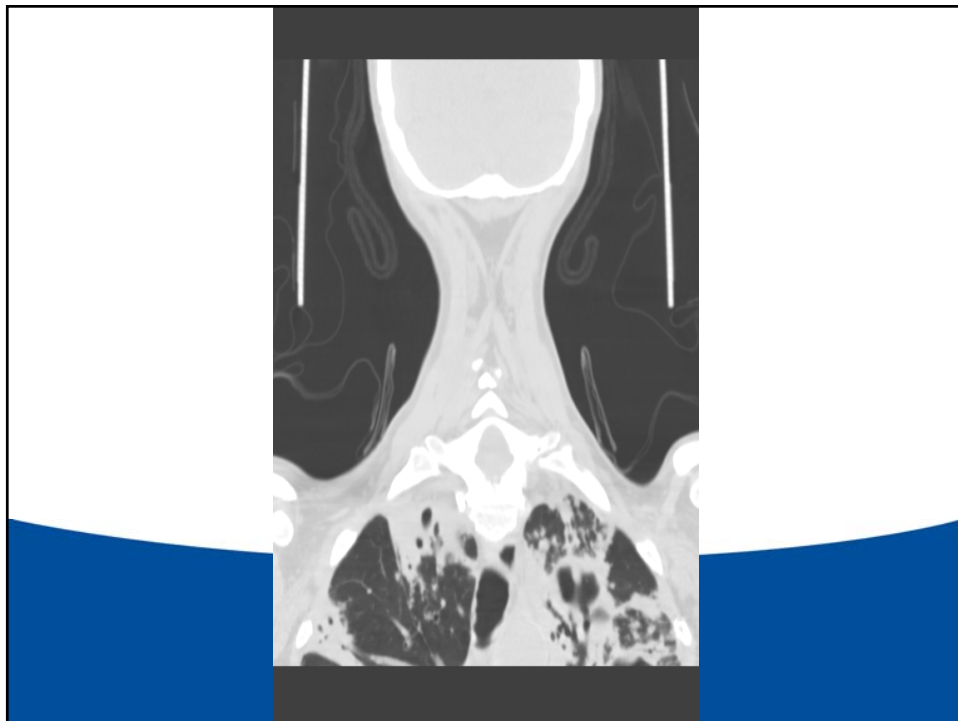
30

## CT Scans April 2017

- *“Large mucosal ulceration involving left pharyngeal tonsil extending to the sternocleidomastoid muscle with air along the tract compatible with fistula formation*
- *Cavitary lesions within bilateral lung apices”*

Beaumont

31



32



## Final diagnosis

- Cervical lymph node and cavitary pulmonary tuberculosis
- No head and neck cancer

Beaumont

33

## Cerebrospinal fluid in TB meningitis

Test	Results	Comment
Opening pressure	Elevated	
Appearance	Clear early; turbid to cloudy	
WBC	100-500+ PMNs in early Up to 95% mononuclear chronic	Normal <5
Protein	100-500 mg/mL	Normal <50
Glucose	40-50 mg%, rarely <20	Compare with blood glucose
AFB smear	20-37%	
AFB Culture	40-80%	

Beaumont

34

## 2016 TB Treatment Guidelines

- PICO Question 8: Does the use of adjuvant corticosteroids in tuberculous meningitis provide mortality and morbidity benefits?
- Recommendation 8: We **recommend initial adjunctive corticosteroid therapy** with dexamethasone or prednisolone tapered over 6–8 weeks for patients with tuberculous meningitis (strong recommendation; moderate certainty in the evidence).

Beaumont

35

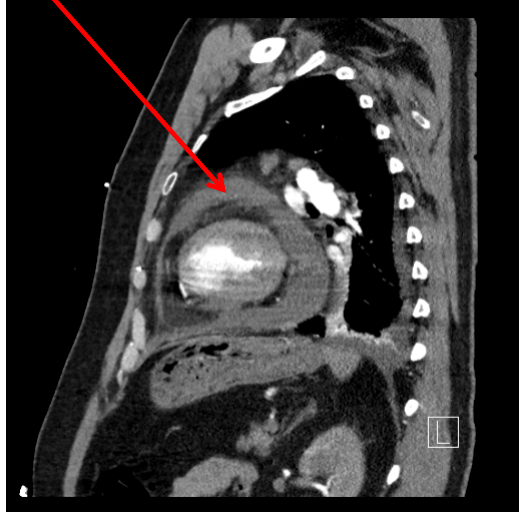
## Peritoneal TB

Finding	%
Abdominal pain	60%
Abdominal swelling	53-100%
Weight loss	50-90%
Fever	45-100%
Concomitant respiratory TB	30-53%

Beaumont

36

## Pericardial TB



Beaumont

37

## Pericardial TB

Finding	%
Fever	73-93%
Paradoxical pulse	23-71%
Pericardial rub	37-84%
Neck vein distension	46-74%
Edema	24-64%
Ascites	30%

Beaumont

38

## 2016 TB Treatment Guidelines

- PICO Question 7: Does the use of adjuvant corticosteroids in tuberculous pericarditis provide mortality and morbidity benefits?
- Recommendation 7: We suggest initial adjunctive corticosteroid therapy **not be routinely used in patients with tuberculous pericarditis** (conditional recommendation; very low certainty in the evidence).

Beaumont

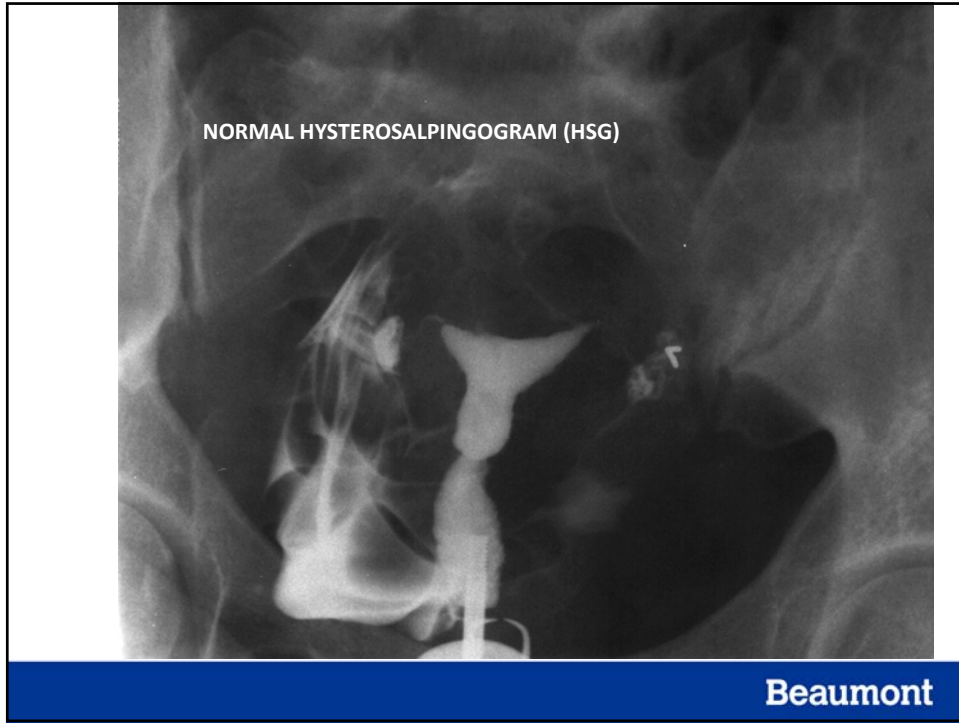
39

## Genitourinary TB

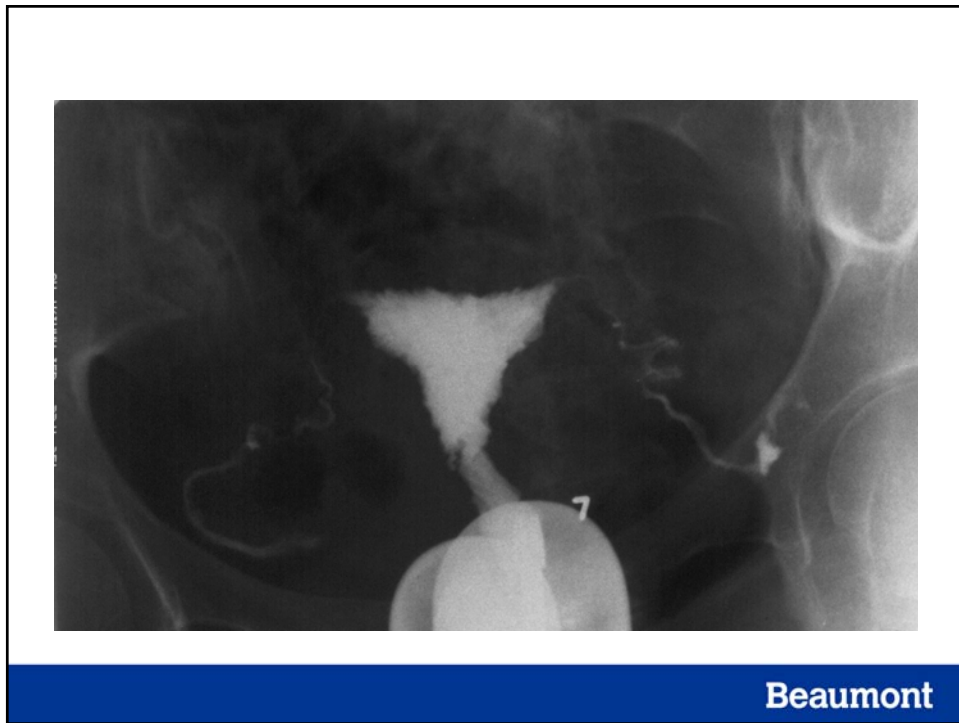
- Kidneys, bladder, ureter
- Fallopian tubes, endometrium, ovaries
- Prostate, epididymis, testes

Beaumont

40



41



42

## Uterine TB diagnosis

- Curettings from D&C
- Sent for histology, culture
- Menstrual blood cultured for AFB

Beaumont

43

## Paradoxical Reactions to TB Treatment



Beaumont

44

## Immune Reconstitution Inflammatory Syndrome (IRIS)

- Transient worsening of tuberculosis symptoms and lesions in response to antituberculous therapy
- HIV negative and HIV positive patients
- Not uncommon with treatment of lymph nodes, even after completion of treatment

Beaumont

45

## Treatment of TB Disease (3)

- Intensive phase should contain the following four drugs:
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)



Example of pills used to treat TB disease. From left to right: isoniazid, rifampin, pyrazinamide, and ethambutol.

Beaumont

46

## Duration of Extrapulmonary TB Treatment

- TB meningitis 9-12 months
- Bone & joint TB 6-9 months
- 6 months for most other cases

Beaumont

47

## In summary

- TB disease may occur in any organ of the body.
- Diagnosis is difficult, often multiple tests are needed
- Empirical TB treatment is more often necessary.

Beaumont

48