

Extrapulmonary Tuberculosis

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TB Consultant

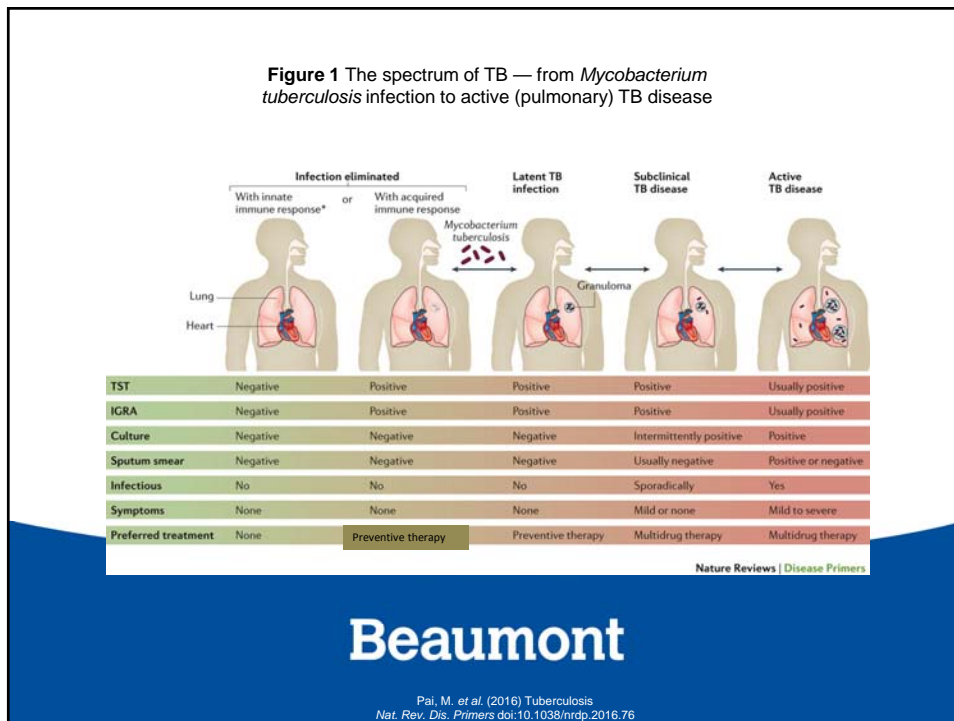
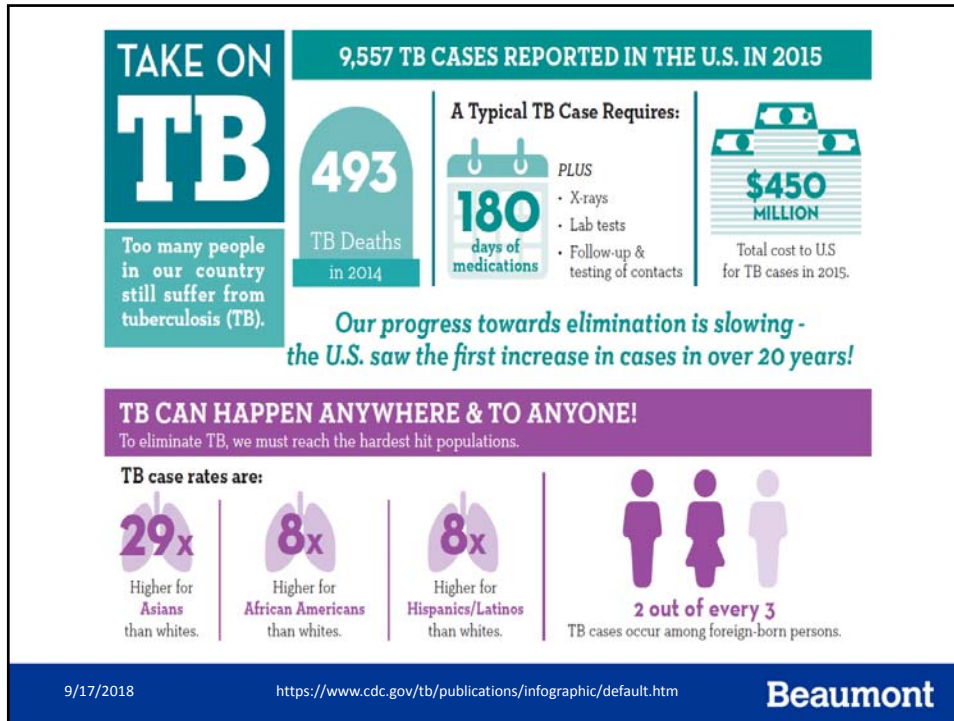
Michigan Dept. of Health & Human Services

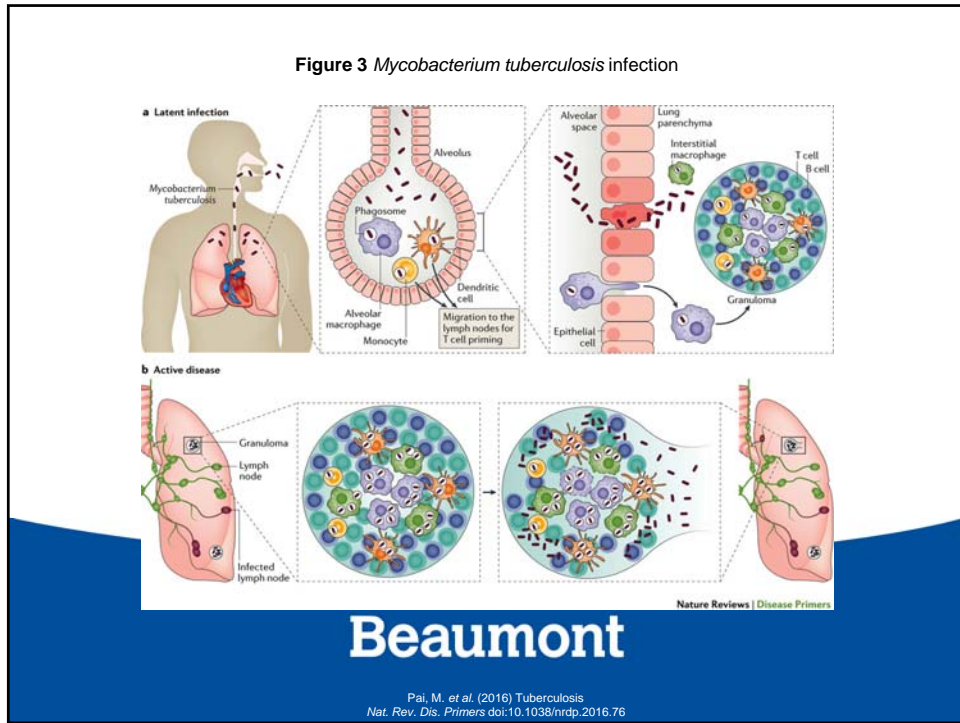
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Objectives

- How does TB spread beyond the lungs?
- How can TB present in these sites?
- How is extrapulmonary TB treated?

- DISCLOSURES: none

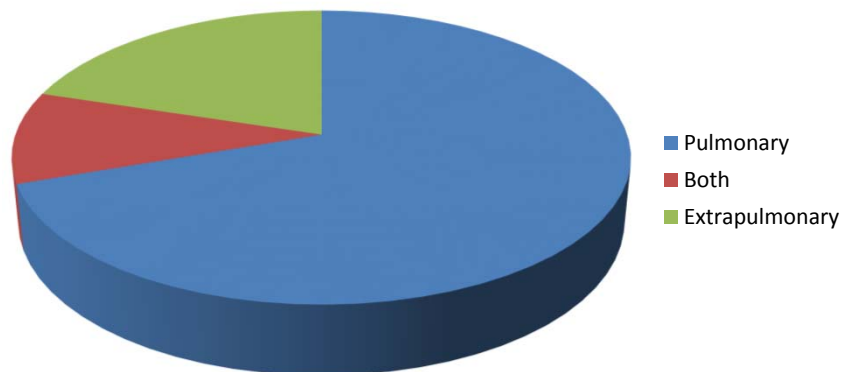




Indiana statistics 2013-2017

- 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

TB Disease Sites



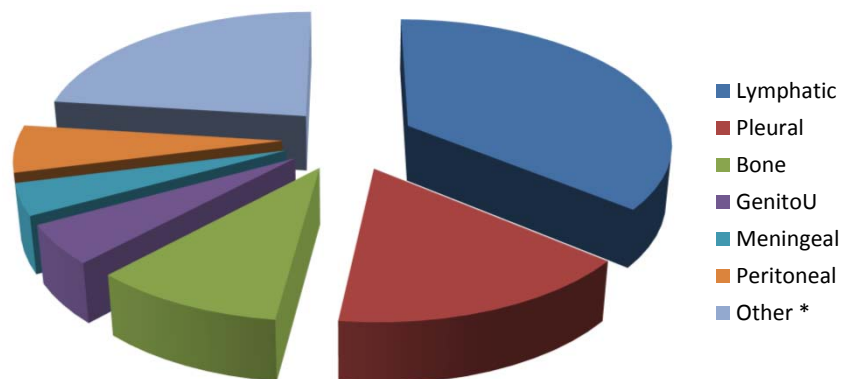
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Table 37

https://www.cdc.gov/tb/statistics/reports/2016/pdfs/2016_Surveillance_FullReport.pdf

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Extrapulmonary Sites



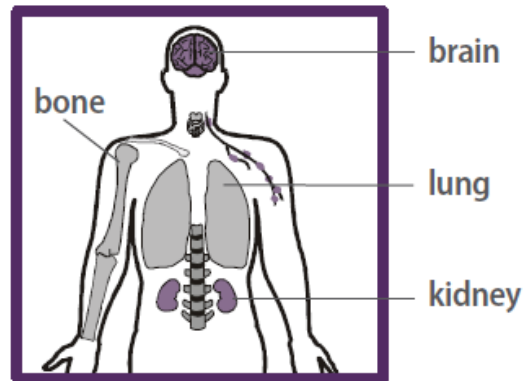
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Table 38

https://www.cdc.gov/tb/statistics/reports/2016/pdfs/2016_Surveillance_FullReport.pdf

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TB Pathogenesis



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

Module 1 – Transmission and Pathogenesis of Tuberculosis

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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

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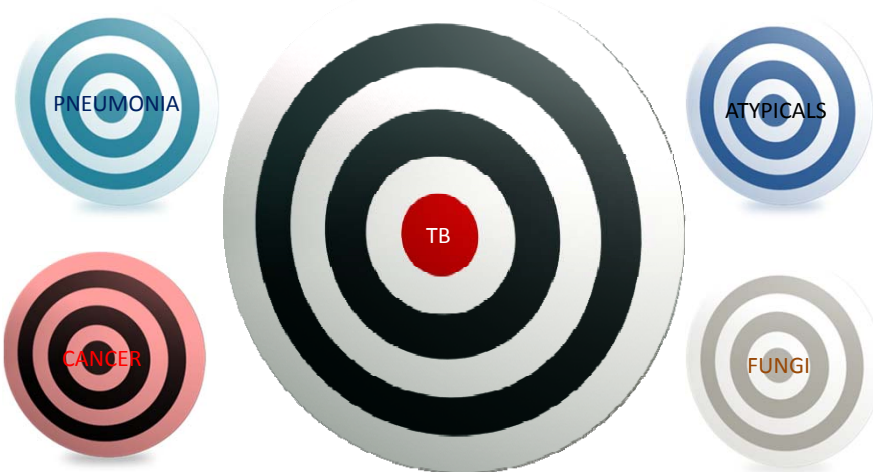
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Respiratory Tuberculosis

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

TB is difficult to diagnose



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 ? %

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Pleural fluid diagnosis

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

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Pleural fluid biochemistry

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

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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

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Ocular TB
Henry Fraimow, MD
Cooper University Hosp

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Patient 1

- **Physical Exam:**

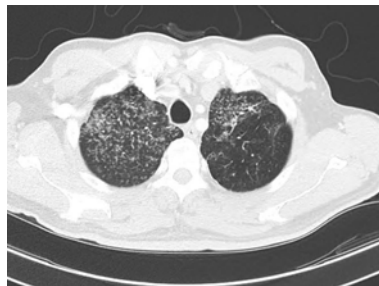
- 131.2 lb (baseline 167 lb) 99.6° F
- Vision 20/25 in both eyes, color blind
- Mild conjunctival injection Right eye
- Dry crackles anteriorly, Right > Left
- Right knee mildly boggy and swollen, not warm

- **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

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Chest imaging at start of treatment



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

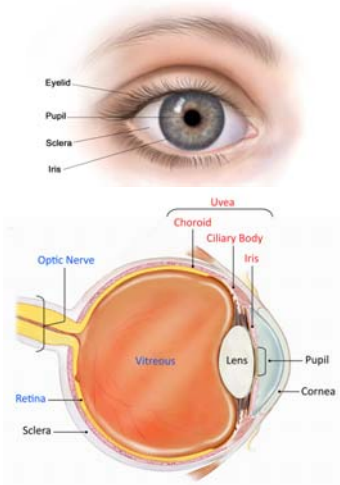
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Back to our question

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

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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/>

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Ocular tuberculosis masquerading as a tumor

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

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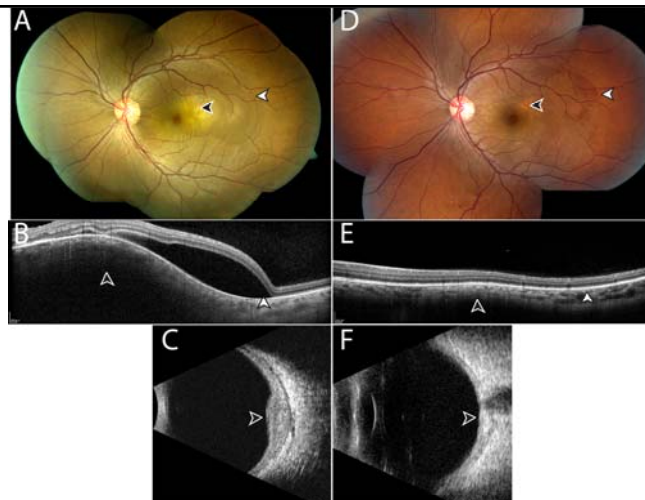
Case

- 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

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APPENDIX. Multimodal imaging of ocular tuberculosis before and after treatment.
 (A) On presentation, ocular examination of the left eye revealed a macular amelanotic choroidal mass (black arrowhead), with associated subretinal fluid (white arrowhead). (B) Optical coherence tomography (OCT) revealed a homogenous, hyporeflective choroidal lesion (black arrowhead) with overlying subretinal fluid (white arrowhead). (C) B-scan ultrasonography showed an acoustically-solid choroidal mass (black arrowhead). (D-F) Four-months after initiation of anti-TB therapy, fundus examination (D), OCT (E) and ultrasonography (F) revealed complete regression of the choroidal tuberculoma (black arrowheads, D-F) and associated subretinal fluid (white arrowheads, D, E).

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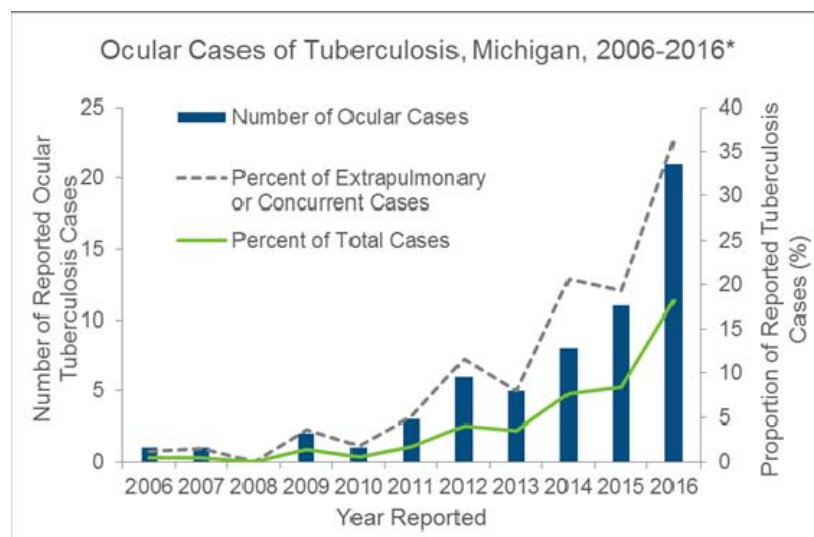
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How does TB get to the eye?

- 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

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**Detroit Metro Airport
Spring of 2017
Arrived from Yemen, sick**

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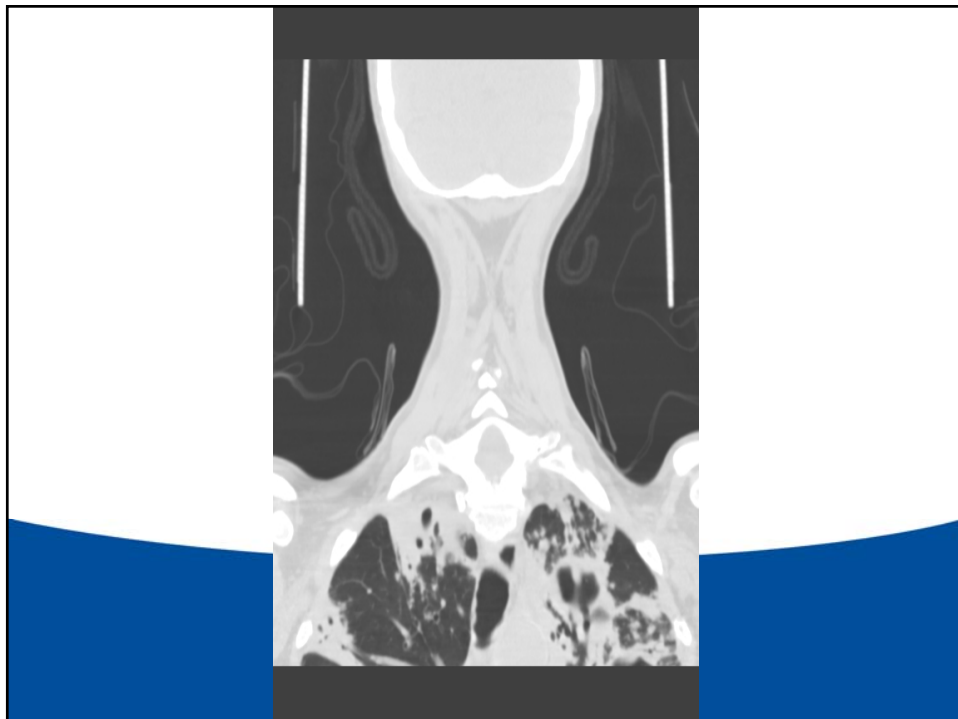
CT Scans April 2017

- *“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”*

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Final diagnosis

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

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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%	

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Iseman et al. A Clinicians Guide to Tuberculosis, 2000

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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).

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Peritoneal TB

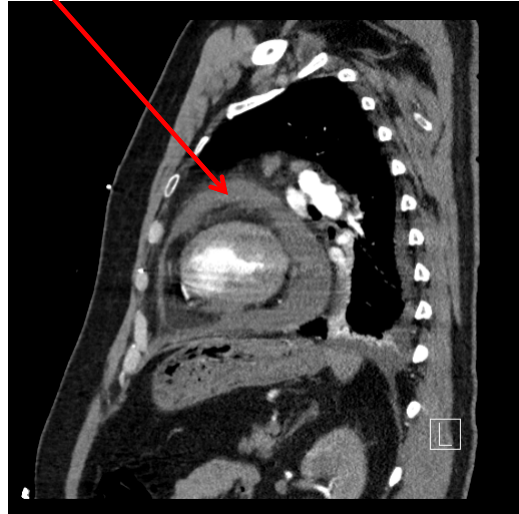
Finding	%
Abdominal pain	60%
Abdominal swelling	53-100%
Weight loss	50-90%
Fever	45-100%
Concomitant respiratory TB	30-53%

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Iseman et al. A Clinicians Guide to Tuberculosis, 2000. p182

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Pericardial TB



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Pericardial TB

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

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A Clinician's Guide to Tuberculosis
Michael D. Iseman MD 2000

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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).

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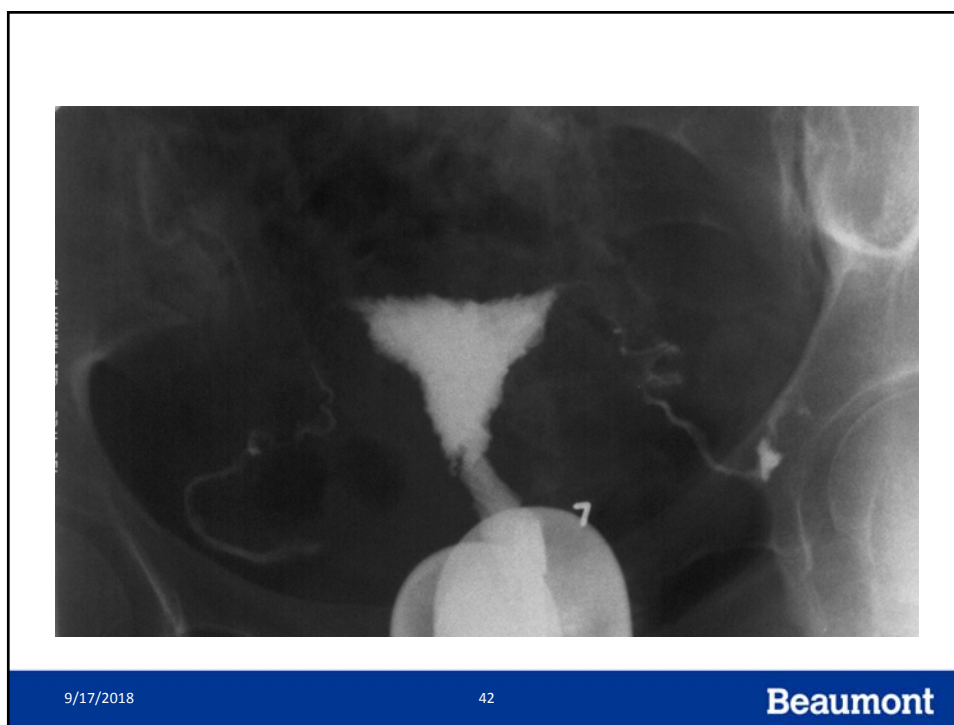
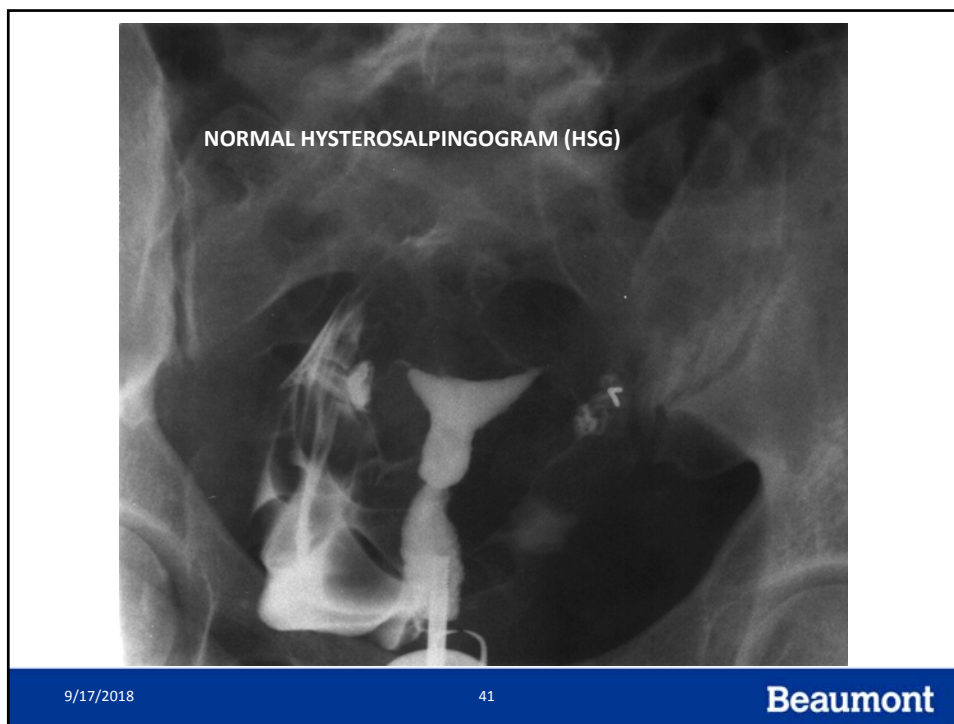
Genitourinary TB

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

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Uterine TB diagnosis

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

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Paradoxical reactions to TB treatment



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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

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Treatment of TB Disease

- 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.

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Duration of Extrapulmonary TB treatment

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

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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

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