Case Study
TB Intensive Workshop
Oct. 5, 2012

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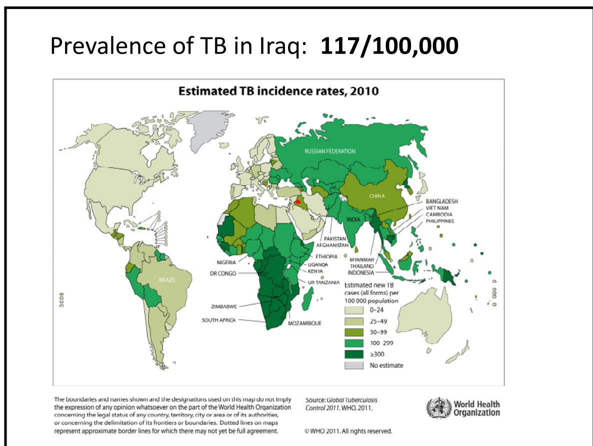
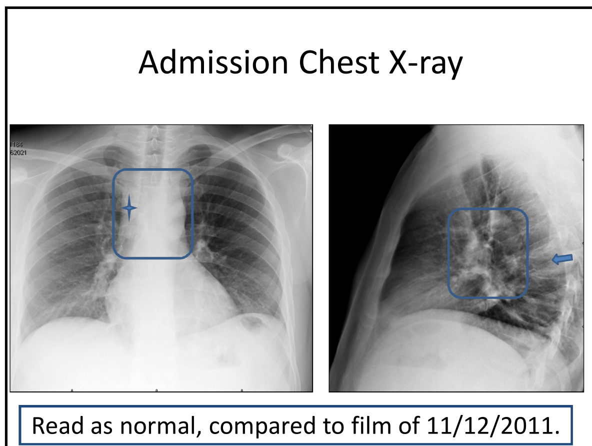
Fever of Unknown Origin

- 43 year old man from Baghdad, living with his wife & 2 school-age sons
- October, 2011 – fevers, loss of appetite, 35# weight loss, fatigue, night sweats
  - Visited multiple hospitals
  - EGD & colonoscopy, PSA
- January 31 - February 13, 2012 – admitted to hospital with a diagnosis of FUO
  - Fevers 38.5 – 39.5 C

Prevalence of TB in Iraq: **117/100,000**

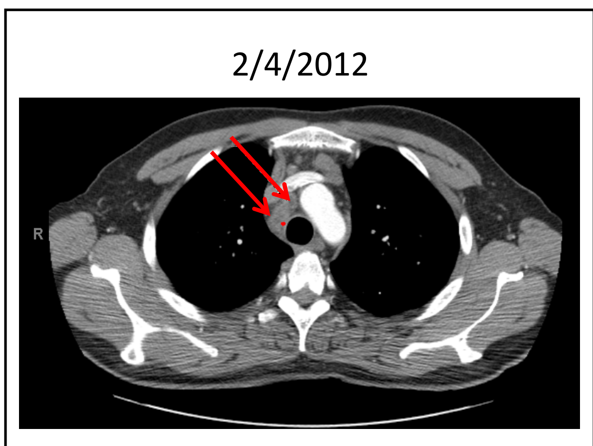


Admission Chest X-ray



Read as normal, compared to film of 11/12/2011.

2/4/2012



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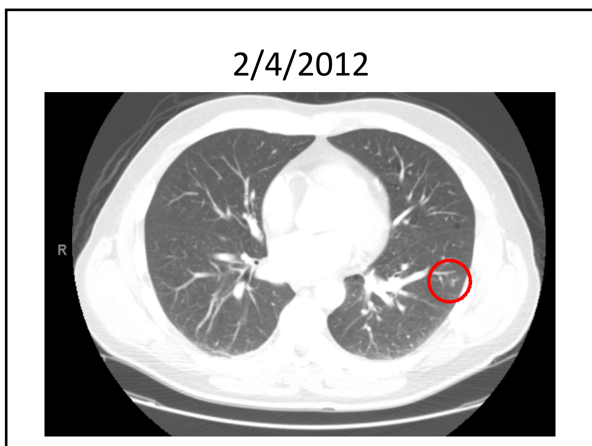


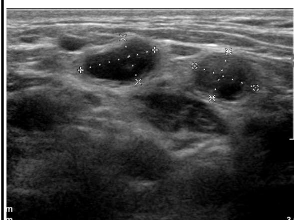
Radiologist Report

- Multiple lymph nodes with central low attenuation (necrotic)
- 2 mm nodule lingula
- Tree-in-bud opacity LLL

Testing

- TSH, ANA, RF, CCP, ANCA, ENA, ESR 48, CRP, EBV / CMV, Brucella Ag, fungal serology, urine histoplasmosis Ag.
- TST 25 mm induration
- QFT + (TB Antigen – nil >10)
- Sputum AFB negative on 2/8, 2/9, 2/10
  - Placed in AII 2/8-2/13

2/8 Needle Aspirate Supraclavicular LN



- Necrotizing Granulomas
- AFB negative

Questions

- Would you have taken him out of AII after receiving the results of the AFB smears?
- Should he be referred to the local health department?

More Questions

- Which is his diagnosis now?
  - A. Tuberculosis
  - B. Latent TB infection
  - C. Tuberculosis suspect
  - D. Tuberculosis has been ruled out
- Should you give him prescriptions for any TB medicine with a follow-up appointment in your (or ID) clinic?

Referred to the Health Department

- What would you do now?
  - A. Start INH, Rifampin, PZA, Ethambutol
  - B. Collect sputum for mycobacteria
  - C. Label him “TB Suspect”
  - D. All of the above

What Happened Next

- 2/14 – Seen in health department
- 2/14, 2/15 & 2/16 - 3 sputum samples collected
  - All 3 were AFB smear negative
- INH, Rifampin, PZA, EMB started
- Question: can he return to work in a factory?

Next

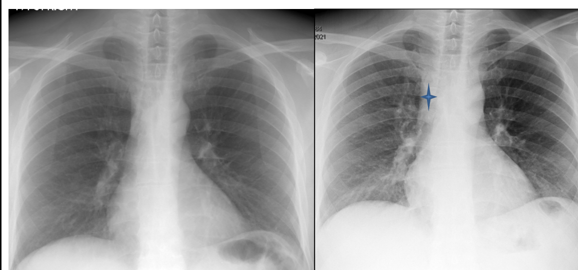
- He was kept on home isolation
- 3/9 – 1/3 sputum samples collected in the health department were reported culture + for MTB
- 3/21 – Drug susceptibility tests were complete – no resistance

TB Suspects Likely to Have TB & Confirmed Cases: When Can They Be Considered to Be Non-infectious?

- All of the following conditions are met:
  - Adequate treatment for 2 weeks or longer
  - Improved symptoms
  - 3 consecutive negative sputum smears from sputum collected in 8-24 hour intervals (at least one early morning specimen)

NOTE: 3 sputums negative for AFB does not rule out TB and does not rule out the possibility that the patient is infectious.

8/17 The End



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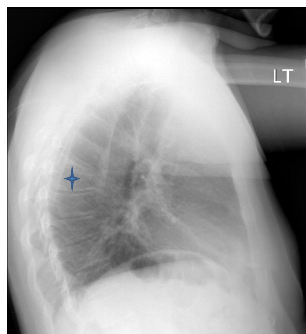

Community Collaboration in the Treatment of a Patient with Active TB Disease

Pain in the Knee

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HOPI:

CC: Knee pain

- **51 yo, US born, AA male with h/o left knee pain for 3 years**
- **h/o trauma 2001-Left leg fracture**
- **Increased pain in last 3 years**
- **Diagnosed with rheumatoid arthritis in 2008**
  - **Minimal relief with oral pain medications**
  - **Started Humira 6 months ago, initial improvement of stiffness but now increased swelling and pain**
- **Pain relieved only for a few days after each steroid injections**

More History

PMHx
- Anxiety
- Depression
- L femur fracture 2001 s/p ORIF
- Rheumatoid Arthritis -2008
- Stab injury RUQ

NKDA

Medications
- Vistaril
- Duloxetine (Cymbalta)
- Trazodone
- Prednisone
- Adalimumab (Humira)

ROS: musculoskeletal pain

Social Hx
- Some college education
- Military x 6 years
- +Tobacco x 30 yrs
- +ETOH abuse in past, now ~4 beers/ week
- Occasional marijuna
- No h/o incarceration
- No travel outside US

PE

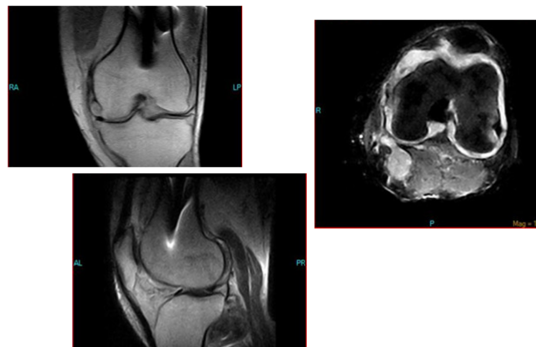
- T96.5, P88, BP 132/90, Wt 205#
- Ambulates with cane and walks with a limp
- Left Knee - marked swelling with significant effusion and some synovial hypertrophy
- No instability of knee to valgus or varus stress
- Negative anterior drawer sign and Lachman tests

Radiology

Knee X-ray
- End of medulary rod with mild arthritic changes

MRI
- Tear in medial meniscus and moderate tri-compartment arthritis
- Knee effusion with Baker's cyst

MRI Knee



Orthopedic Surgery

- **Scheduled for arthroscopy with synovectomy, meniscectomy and chondroplasty of the knee**
- **Should this fail, will need total knee replacement**
- **Intra-op**
  - **Fluid cloudy**
  - **Sent fluid for aerobic, anaerobic, AND AFB**
  - **Pathology**

Diagnosis?

Mycobacterium tuberculosis

Patient Referred to the TB clinic-1

- What does the TB clinic need to do?
- Patient diagnosed with extrapulmonary TB but needs to evaluated for pulmonary TB
  - Isolation
  - Medical evaluation
  - CXR
  - Sputum
  - Treatment

Patient Referred to the TB clinic - 2

- Identified missed opportunity
  - 2001, PPD positive 22mm
  - Refused LTBI treatment
- Social worker consultation

More Social History

- At the start of TB treatment, pt was in the process of being evicted from his home
- Residing in a home for clients with mental health issues
- →Shelter
- Shelter assisted him with housing - didn't like the area and returned to shelter
- →Housing found

Community Partners

Columbus Homeless Shelters & Services For The Needy

1. Homeless Shelter
- **Provide safe housing for clients**
- **Help clients relocate and find housing**
- **Homeless clinics and treatment centers resources**
- **Dental Clinic**
- **Many shelters also provide services such as alcohol and drug rehab treatment along with clinics.**

Community Partners

2. *The P.E.E.R. Center*

- drop-in wellness, recovery and support center. Operational since January 2007

- mission is to provide *a safe place where individuals receive respect, encouragement, and hope that supports and strengthens their recovery in mental health, addictions and trauma*

Columbus TB Task Force

- Meet quarterly at Columbus Public Health
- Community representation
  - Homeless shelters
  - Jail, prison
  - Schools
  - Hospitals
  - Immigration/Refugee Agencies
  - Community organizations
    - Ethiopian Tewanhedo Scial Services
    - Somali Community Association of Ohio
    - Somali Women and Children's Alliance

TB and TNF-alpha blockers

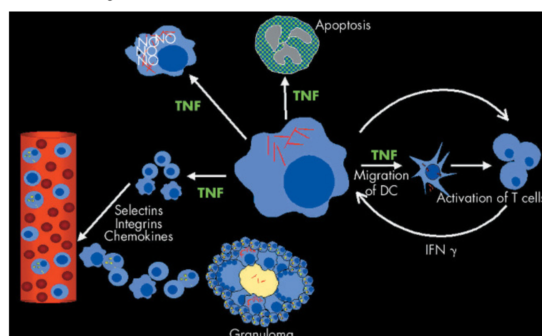
Heartland NationalTB Center
http://www.heartlandntbc.org/products/tumor_necrosis_factor.pdf

Tumor necrosis factor-alpha (TNF-α)

- Potent cytokine
- Mediates body's response to infection
- Promote inflammation and tissue destruction in immune mediated disease
- Important for granuloma formation

- TNF-α antagonists used to treat rheumatoid arthritis, Crohn's disease

Key Functions of TNF in TB



Ann Rheum Dis 2005;64:iv24–iv28

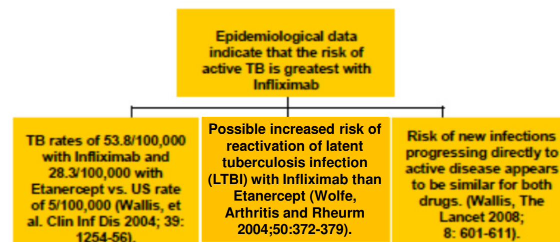
TNF-α antagonists used in the U.S.

Generic name	Brand name
Infliximab	Remicade
Adalimumab	Humira
Certolizumab	Cimzia
Golimumab	Simponi
Etanercept	Enbrel

Why do They Increase Risk of TB?

- Granuloma formation is crucial for containing and controlling TB infection
- In TB – these drugs
  - **inhibit** macrophage activation, recruitment of inflammatory cells, granuloma formation, and maintenance of granuloma
- Antibody against TNF-α causes increased susceptibility to *M. tuberculosis* in mice models

TNF-α antagonists – Increase Risk for TB disease



What Can be Done to Decrease the Risk of TB When Using these Agents?

- Carefully screen all candidates
  - Identify risk for TB exposure
  - Screen for LTBI, r/o active disease, treat for LTBI
- Educate patient about the risk of opportunistic infections
- Instruct patients to report symptoms of infections
- Fever, malaise, cough, local or generalized pain
- Onset of TB may be subtle, but can escalate and disseminate quickly
- CXR may be normal
  - CT scan for miliary infiltrates

What Additional Recommendations are there for LTBI Screening and Treatment?

- Repeat testing periodically for TB infection even if TST or IGRA is initially negative
- When can you start TNF-α blockers ?
  - After completion of LTBI treatment
    - (MMWR 2004:53)
  - After one month of LTBI therapy
    - (Furst Annals Rheum Dis 66 (suppl 3):ii2-22

What if a Patient who is on One of These Agents Develops TB?

- Evaluate for routine and opportunistic infection
  - CXR- if normal and patient has pulmonary symptoms→ Chest CT
  - Sputum smear and culture
- Stop TNF-α blockers until diagnosis is made
- Wait to restart TNF- α blockers
  - Until…
  - Until TB is treated and under control, cultures are negative, and patients are tolerating their TB medications

What is the Typical Course of TB Patients Taking these Agents?

- TB progresses rapidly
- Median duration of onset = 12 weeks after initiating TNF-α blockers in 57 patients
- TB more likely to be extrapulmonary and disseminated
  - 56% EP and 24% disseminated

Keane, NEJM 345(15):1098

How do you Monitor Patients on TNF-α blockers

- Monitored carefully for any signs or symptoms of active infections
  - mycobacteria, viral, fungal, bacterial, protozoan
- Immune reconstitution inflammatory syndrome (IRIS)
  - may occur when TNF-α blockers are stopped and TB therapy is started