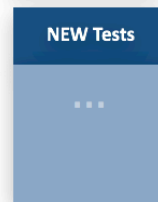
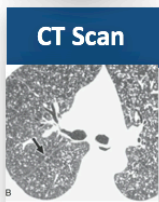
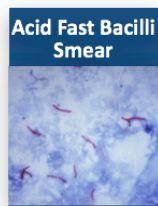
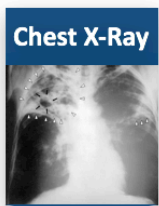


Diagnostics of Tuberculosis

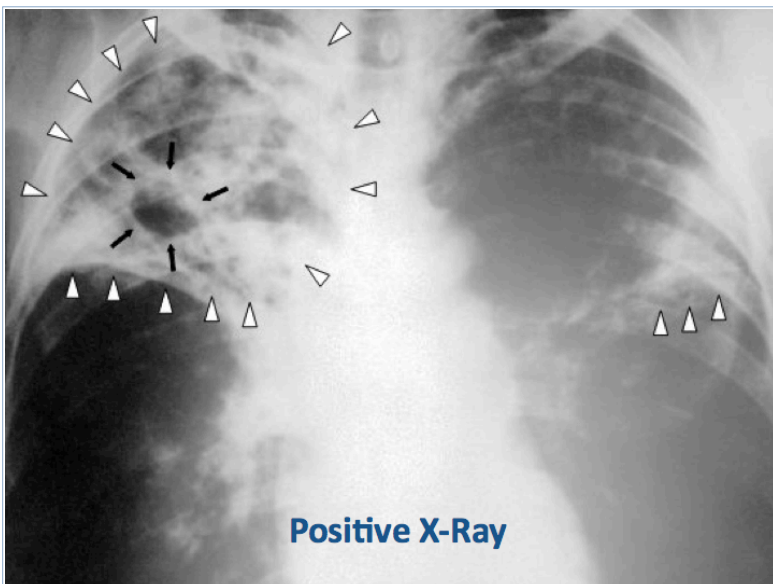
Jerrold J. Ellner, MD
Boston University School of Medicine
March 2013

Boston University
School of Medicine

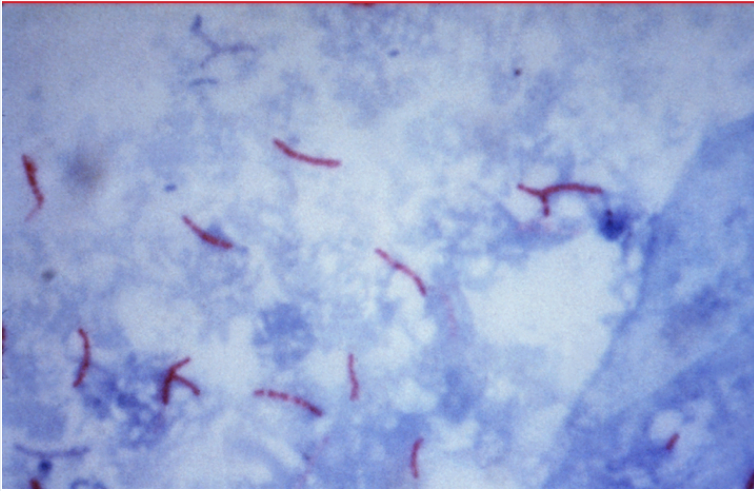
Overview of diagnostic tools for detecting tuberculosis



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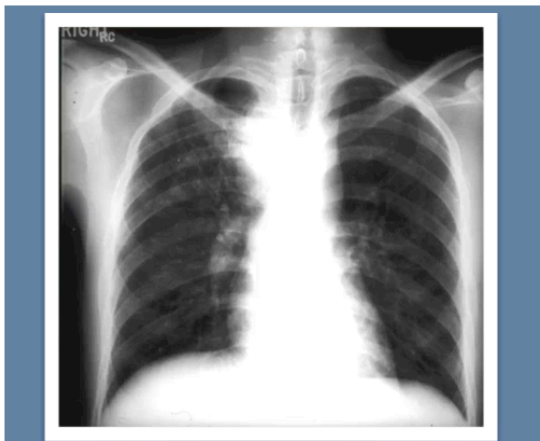
Positive Acid Fast Bacilli Smear (AFB Smear)



Sputum AFB Smear

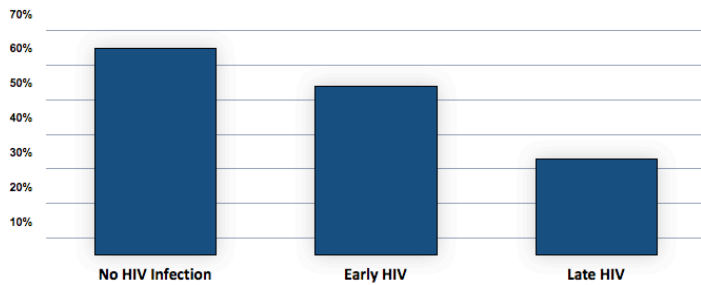
- ▀ Requires 1000 - 10,000 AFB/mL
- ▀ At least 2 smear should be
- ▀ Fluorescence microscopy increases sensitivity 10%
- ▀ Concentration or sedimentation increases sensitivity 15-20%

HIV co-infection complicates diagnosis



HIV co-infection decreases AFB Smear sensitivity

AFB Smear Positivity in TB patients



*Similar for "classic" RUL infiltrate

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LED microscopy (Fluorescent light-emitting diode microscopy)

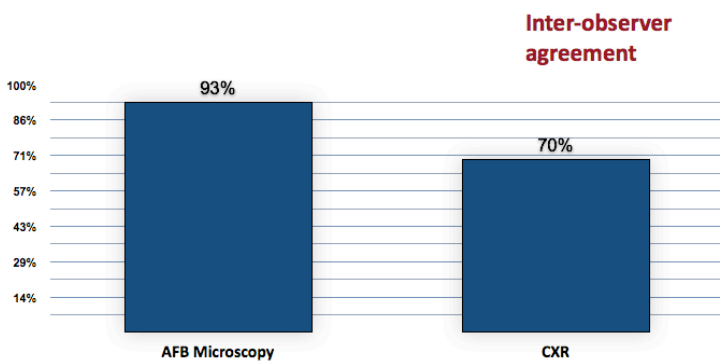
Endorsed by WHO in 2009:

- ✓ "LED microscopy to be phased in as an alternative for conventional ZN light microscopy in both high- and low-volume laboratories.



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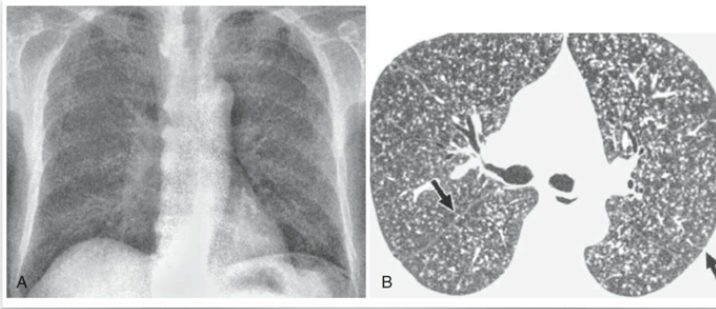
Interpretation AFB Smear vs. Chest X-Ray (CRX)



Toman, pg 17, 54

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CT scan for detecting TB



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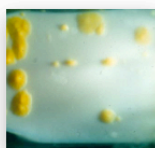
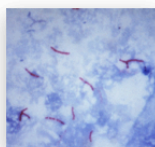
Mycobacterial Cultures

- Used to **confirm** diagnosis of TB
- Culture all specimens, even if smear negative
- Growth in 1-2 weeks on liquid media (MGIT) vs. 4-8 weeks on solid media



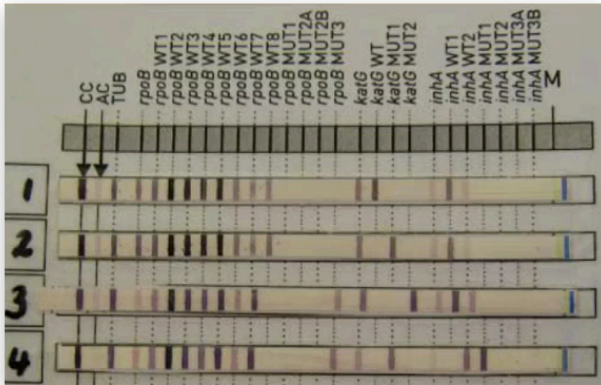
Why do we need new diagnostics?

- **Sputum AFB smear** technically **difficult** and **insensitive**
- Culture (6-8 weeks) and drug susceptibility testing is expensive, slow, and not useful in routine decision-making



New Diagnostic Tools (I)

Hain Genotype MTBDR_{plus}

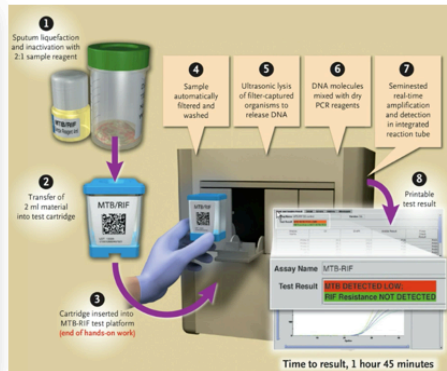


M. Barnard et al. AJRCCM, 2008

New Diagnostic Tools (II)

Diagnosis of Active TB - Genexpert

- ✓ One sample - 98% smear pos. and smear neg.
- ✓ Specificity - 99%; Sensitivity MDR-TB - 97%



New Diagnostic Tools (III)

Prototypes of Point-of-Care Devices

- ➔ Nucleic acid amplification test (NAAT)



Better tools needed (I)

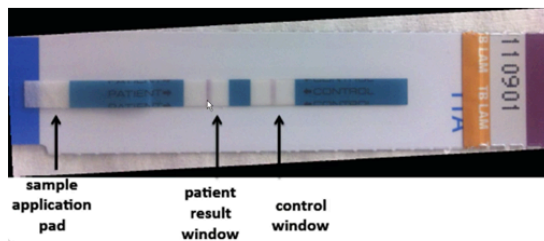
Rapid diagnostic for TB-HIV

- More smear neg PTB, extra-pulmonary TB
- High case fatality
- Need rapid ARTs

Dip stick test (LAM)

“Determine TB-LAM” lateral flow assay (Alere)

- uses Determine testing platform
- no sample processing, results in 25 minutes
- Analytical sensitivity reported to be 0.25 ng/ml
- Reporting scale: no band, band of intensity 1+ to 5+



Rapid Diagnostics TB-HIV

“Determine TB-LAM” lateral flow assay (Alere)

- Xpert sensitivity: 62%
- LAM sensitivity: 45%
- LAM + Xpert sensitivity: 79%

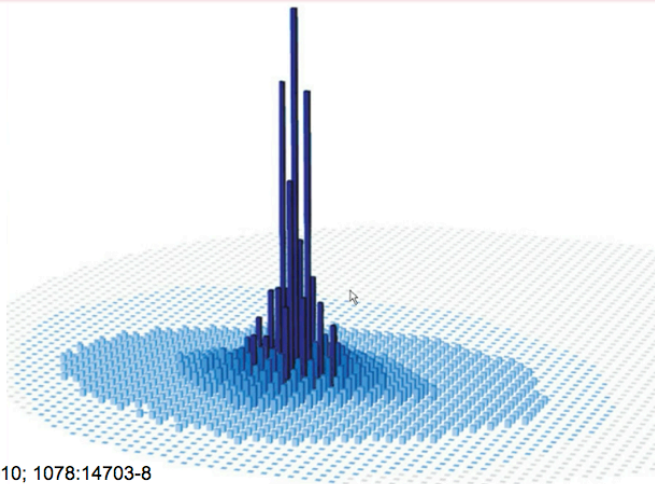
Screening Test = "Triage Test"

- ➔ 5% prev smear pos TB in "suspects"
- ➔ Screening test 85-100% sens
- ➔ Spec > 50%, cost < 50%

Better tools needed (II)

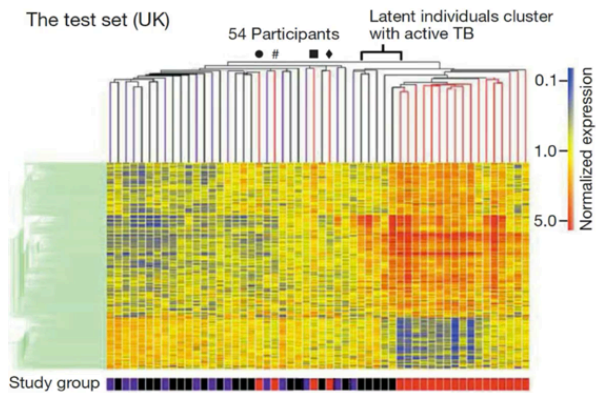
- ✓ Rapid diagnostic for MDR, XDR, TDR-TB
 - ➔ Second generation Xpert Cartridges
- ✓ Diagnostic for extra-pulmonary TB
- ✓ Diagnostic for pediatric TB
- ✓ Latent TB Infection (LTBI) at risk of progression to TB

The Host Immunoproteome



PNAS 2010; 1078:14703-8

393 Transcripts TB v LTBI v HC



Berry, *Nature*, 2010

Better tools needed (III)

MOST CRITICALLY:

- ✓ Point of Care NAAT
- ✓ Screening test
- ✓ Diagnostic for activity for Latent TB Infection

Thank you!