

Xpert Consensus Statement Part 2 Practical Implementation

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Disclosures

- No affiliation or financial relationship with any of the tests or companies mentioned in this presentation
- This presentation does not necessarily represent the official position of the US Centers for Disease Control and Prevention

Removing Patients from A.I.I.

- Traditionally used 3 sputum smears collected early morning
 - Took a long time: average 5-7 days in isolation
 - Not sensitive 50-60%
 - Not specific 70-90% (depending on NTM and TB prevalence)

Problems with Isolation

- Limited number of A.I.I. rooms
- Systemic review showed patients in isolation tend to:
 - Be seen less by HCWs
 - Have an 8 fold increase in adverse effects
 - Have a negative perspective of their care*
 - Delay in getting the proper procedure performed

*Abad et. al. J of Hosp Infection 2010:97

FDA News Release

New data shows test can help physicians remove patients with suspected TB from isolation earlier

Morbidity and Mortality Weekly Report

Revised Device Labeling for the Cepheid Xpert MTB/RIF Assay for Detecting *Mycobacterium tuberculosis*

Division of Microbiology Devices, Office of In Vitro Diagnostics and Radiological Health, Center for Devices and Radiological Health, Food and Drug Administration

Xpert and A.I.I. Labelling Change:

- Improved sensitivity and specificity of NAA versus sputum AFB smear
 - Compared to 2 or 3 AFB specimens, 1 Xpert identified 97% all smear and culture-positive and 2 Xpert 100%
 - Negative NAA from 1 or 2 sputum predictive of 2 or 3 AFB smears being negative
 - Cost savings by reducing time in A.I.I. and length of hospital stay

* Luetkemeyer, *et al.* ACTG and TBTC. Clin Infect Dis. epub 2/2/2016

FDA Approval of Xpert for A.I.I.

Either **one** or **two** sputum specimens can be used as an **alternative** to examination of serial acid-fast stained sputum smears to aid in the decision to discontinue A.I.I. for patients with suspected pulmonary TB



Consensus statement on the use of
Cepheid Xpert MTB/RIF[®] assay in making
decisions to discontinue airborne infection
isolation in healthcare settings

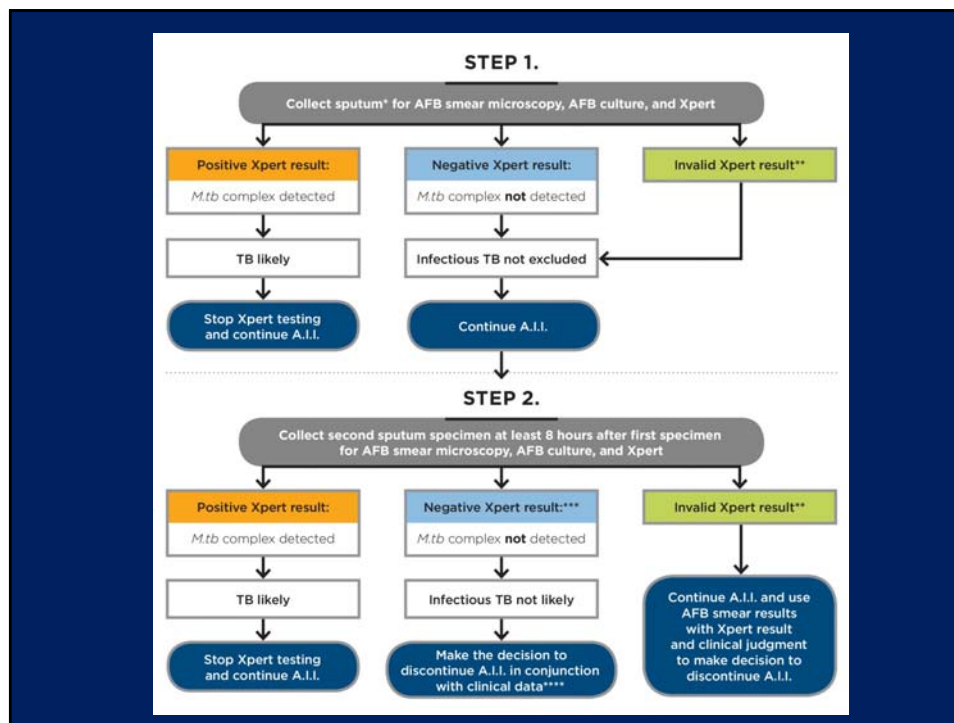
Purpose:

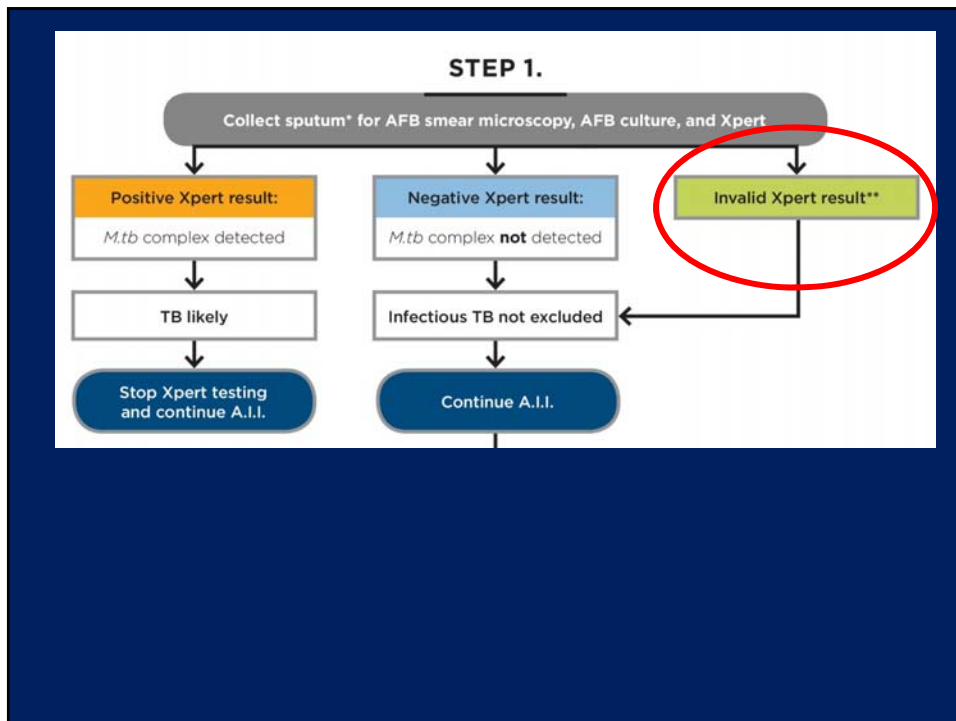
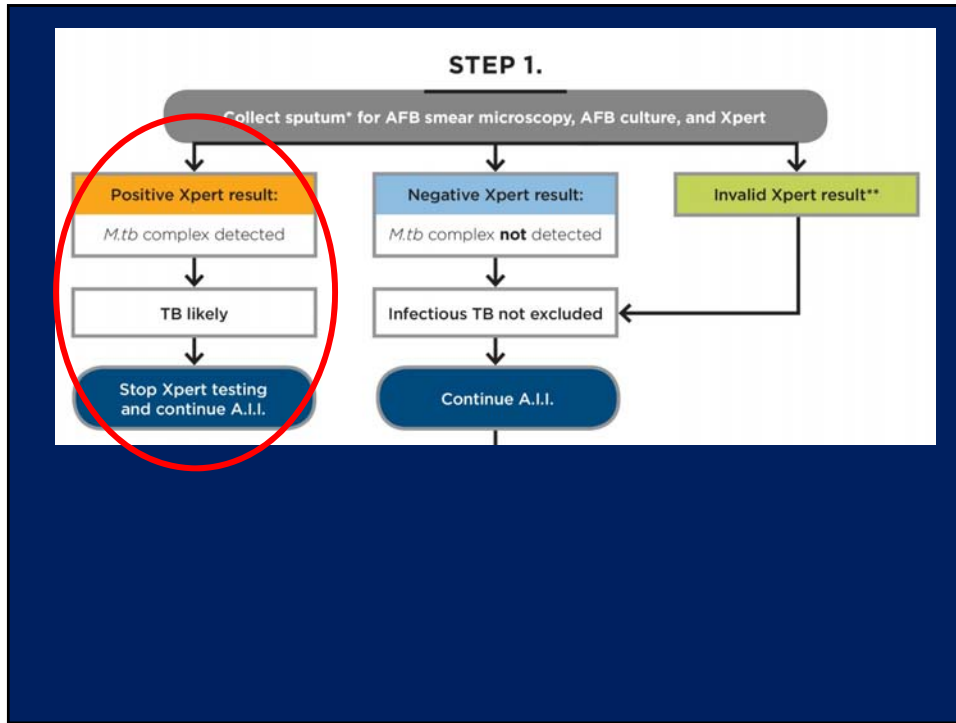
To provide guidance on the use of the Xpert to discontinue airborne infection isolation (A.I.I.) for persons with suspected, infectious pulmonary tuberculosis (TB)

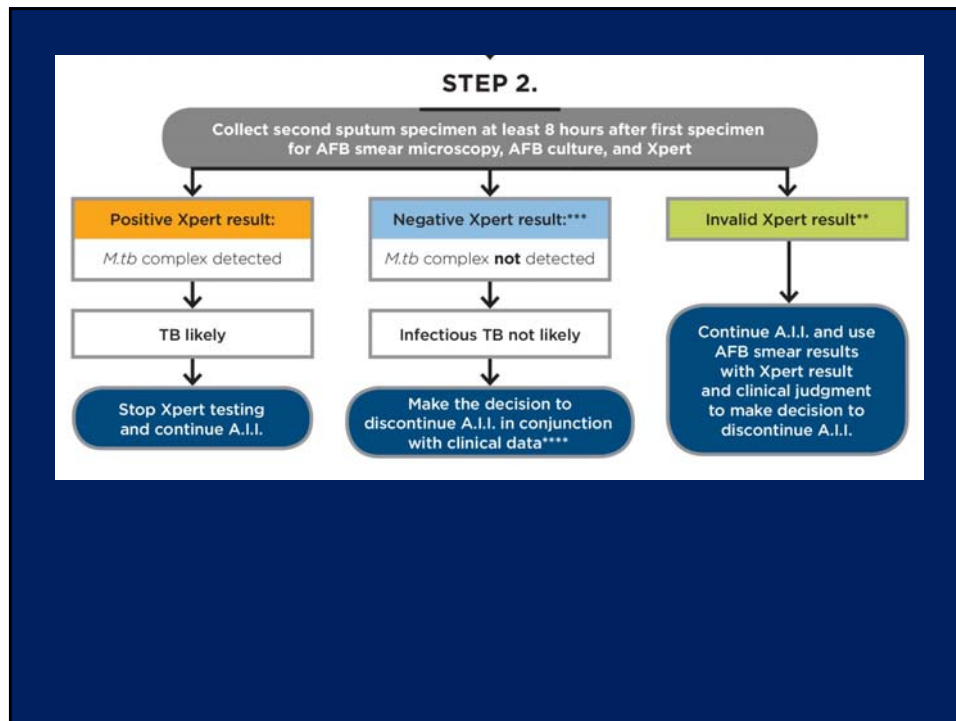
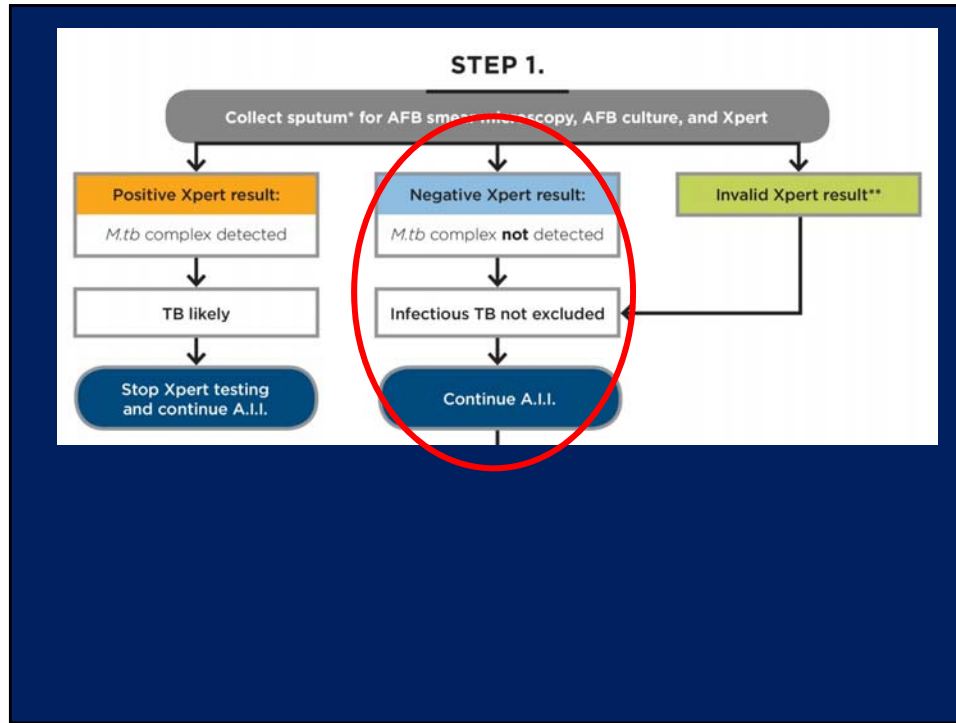
Consensus Statement

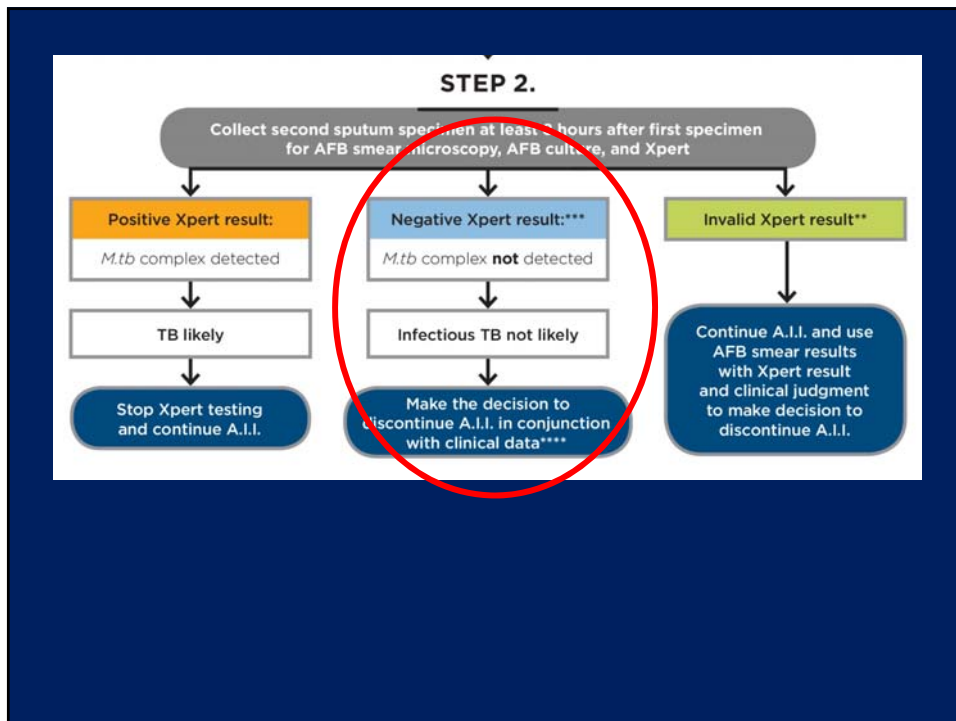
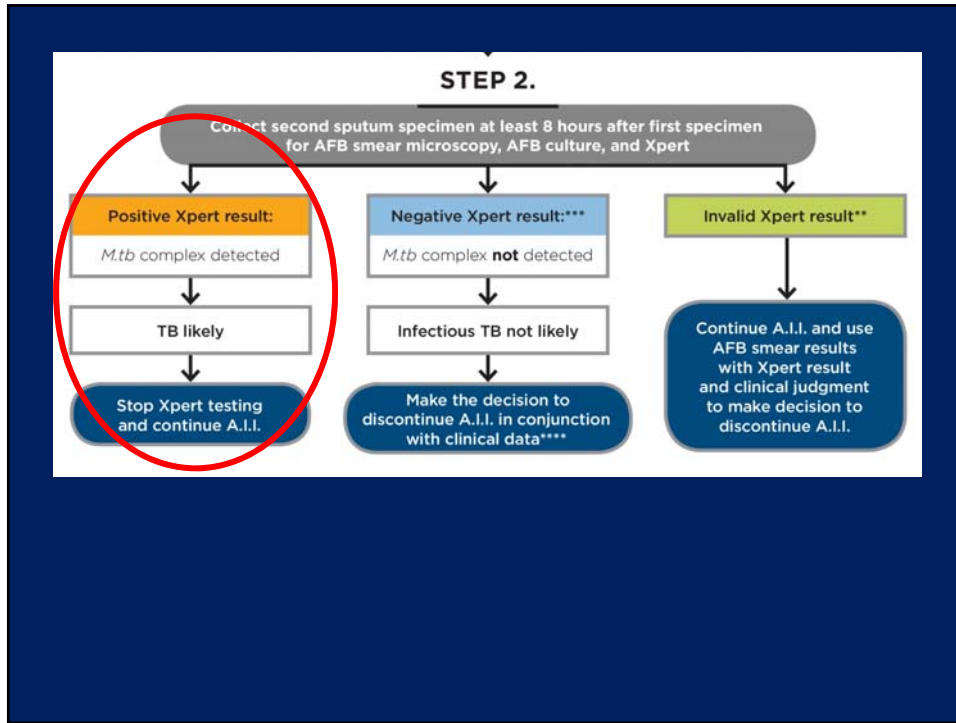
- **IS DOES NOT ADDRESS**
 - The diagnosis of TB
 - When a TB case/suspect can be released from the hospital
- **IT IS**
 - To help predict infectiousness
 - To help determine clinical appropriateness to be removed from isolation

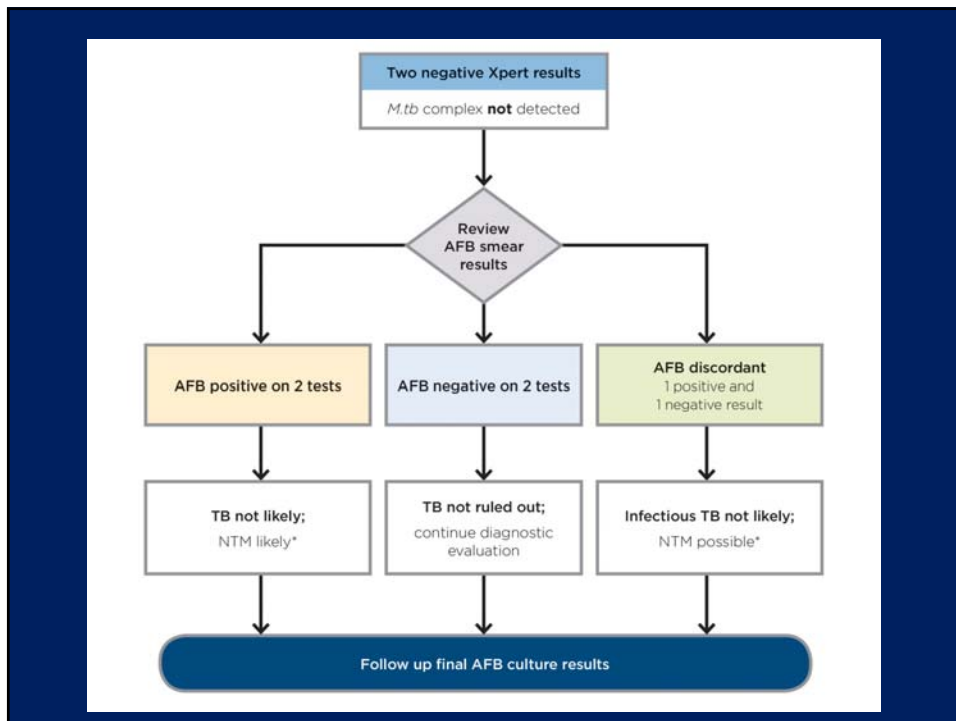
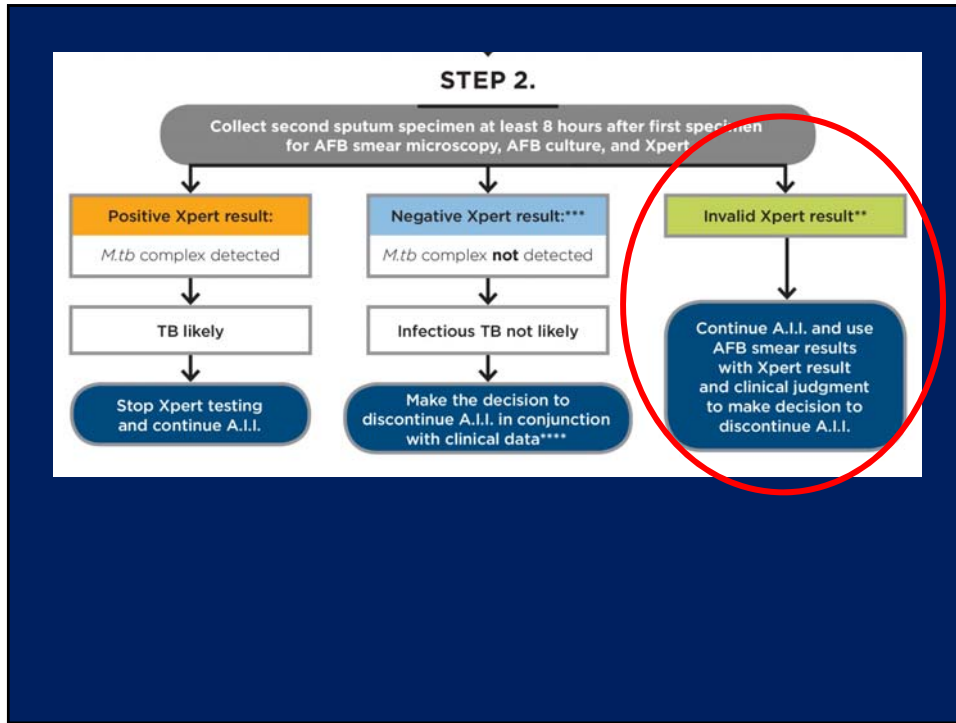
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GeneXpert: Examples From the Field

Dr. Regina McDade
TB Clinical Care Coordinator
Department of Infection
Prevention and Control
Jackson Health System
Miami, FL



Office of TB Control

- Established as a result of Nosocomial outbreak of MDR TB
- Partnership with health department team onsite
- TB Control Nurse hired in 1993
- TB beeper coverage 24 hours/7 days a week
- Microbiology lab
- TB subcommittee



Airborne Infection Isolation Policy

- Implemented at ER Triage or point of entry
- Clinical suspicion of TB
- Employees authorized to isolate a patient pending physician evaluation
- Automatic A.I.I. isolation when a sputum or gastric washing is ordered for AFB in patients with suspected/known TB



Infection-Control Surveillance

- Training and Education for Jackson Health System
- Biannual TB Control/ Employee Health Office Report to Infection Control Committee
- Baseline employee TST testing
- Serial Employee TST testing based on risk assessment
- Serial screening for signs or symptoms of TB
- Respiratory Protection Program



When to Call Tuberculosis Control

- Concern regarding proper isolation
 - Possible or known exposures
 - Information regarding past treatment
 - Case management of TB patient
- Tuberculosis Control Contact Numbers
Office: 305-585-6629
Pager: 305-314-2881

Jackson-PROTECT

Jackson
HEALTH SYSTEM
Miracles made daily.

Discontinuation of A.I.I.

- Current
 - Physician order three AFB smear & culture, induced sputum as needed
 - Three negative sputum AFB smears collected 8-24 hours apart with one early morning specimen required to discontinue A.I.I.
- Change in practice
 - Physician order two induced sputum AFB smears, culture, and two GeneXpert
 - Two negative induced sputum GeneXpert collected at least 8 hours apart (preferably with one early morning sputum) to discontinue A.I.I.

Jackson-PROTECT

Jackson
HEALTH SYSTEM
Miracles made daily.

Update on Change in Practice

- Meetings held with Infection Prevention & Control, Infectious Disease, Pulmonary, Microbiology Lab, IT, Nursing, Respiratory Therapy, and Department of Health
- Microbiology lab will process twice a day
- A.I.I. Policy change presented to Infection Control Committee, voted and accepted

- IT order bundle
 - A.I.I.
 - Order sputum for AFB smear, culture, and GeneXpert X 2
 - Respiratory Therapy induce sputum
- IT Go-Live date is pending

Evaluation

- Appropriate A.I.I. bed utilization
- Decrease ER admission
- Decrease LOS
- Cost Effective
- Continue to monitor TB exposure incidents
- Continue to monitor employee TST Conversions

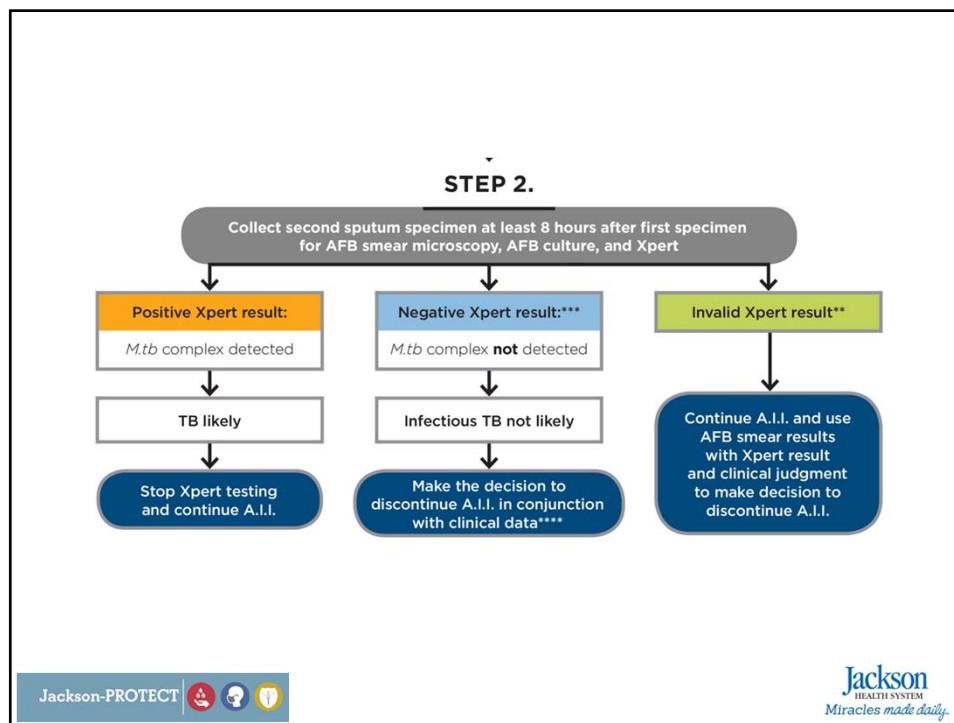


Case Presentation

- A 60 year old Haitian female present with a cough for 8 days and night sweats. Reported that at age 17 she was treated for TB in Haiti for 1 year, medication regimen unknown, physician told her she was cleared of disease.
- PMH: Hypertension, Hypothyroidism, Hyperlipidemia, Polymyalgia Rheumatica (diagnosed 1 year, on steroid therapy).
- Social History: Moved to US from Haiti 13 years ago. Lives with adult son and employed as a housekeeper.



- Abnormal CXR
- Orders for A.I.I. , Sputum for AFB smear and culture X 3, culture (current practice)
- 1st sputum AFB smear negative, culture pending
- GenXpert X 2 ordered (change in practice)
- 1st sputum AFB smear positive, GenXpert **MTB complex not detected**, culture rapid grower (mycobacterium ID pending)
- 2nd sputum AFB smear positive, GenXpert **MTB complex not detected**, culture rapid grower (mycobacterium ID pending)
- A.I.I. discontinued



Case Presentation

- A 62 year old male inmate complain of cough for 2 weeks. Denies fever, night sweats, weight loss, etc
- Abnormal CXR
- PMH: Arrest date 4/29/16, TST performed was positive. History of positive TST 8 years ago and stated he was treated with INH & Vit B6 while in prison.
- Admitted to A.I.I. cell to rule out TB
- Physician ordered two induced sputum for AFB smear, culture and GenXpert
- Specimen transported to JMH Microbiology lab
- 1st sputum collected - **MTB complex not detected**
- 2nd sputum collected - **MTB complex not detected**
- A.I.I. discontinued



References

Centers for Disease Control and Prevention.
Guidelines for Preventing the Transmission of
Mycobacterium tuberculosis in Healthcare Settings,
2005. MMWR 2005; 54(No. RR-17).

National Tuberculosis Controllers Association (2016).
*Consensus Statement on the use of Cepheid Xpert
MTB/RIF Assay in Making Decisions to Discontinue
Airborne Infection Isolation in Healthcare Settings*,
Atlanta, GA.



Implementation of Real Time Xpert in the Hospital: Local Program Experience

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San Francisco Tuberculosis Clinic, Zuckerberg San Francisco General Hospital and Trauma Center
July 27, 2016

Healthy People 2020/NTIP Targets for NAAT: SF Public Health Laboratory

Baseline 2010 Number (%)	2012	2013	2014	NTIP/HP2020
9	35	26 (67%)	37 (77%)	75%

National goal is to have confirmation of TB diagnosis by NAAT within 48 hours in > 75% of specimens that are ultimately determined to be Mtb positive

{ 2 }

Real time TB NAAT testing at the former SFGH (now ZSFG): February 2015

Introducing Xpert MTB/RIF Testing for Active Pulmonary TB at SFGH

Supported by Caring Wisely 2.0

What: Molecular testing of sputum for TB using GeneXpert MTB/RIF (Xpert, under lab test code MTBX) real-time PCR, a new assay with better sensitivity, specificity, & turn-around time than serial sputum AFB smear microscopy

Why: To improve ED flow and reduce inpatient duration of respiratory isolation for patients undergoing evaluation for pulmonary TB by replacing serial sputum AFB smear microscopy with an Xpert-based isolation triage rule

Where: Emergency Department and Inpatient Family Medicine & Internal Medicine Services

When: Monday-Friday 7:30am → 7pm: 3-hour turn-around time from receipt of Xpert sputum sample in lab

Nights/Weekends: Turn-around time as after-hours staffing allows

Who: Possible active pulmonary TB at risk of spreading TB in hospital or community requiring admission for *EITHER*:

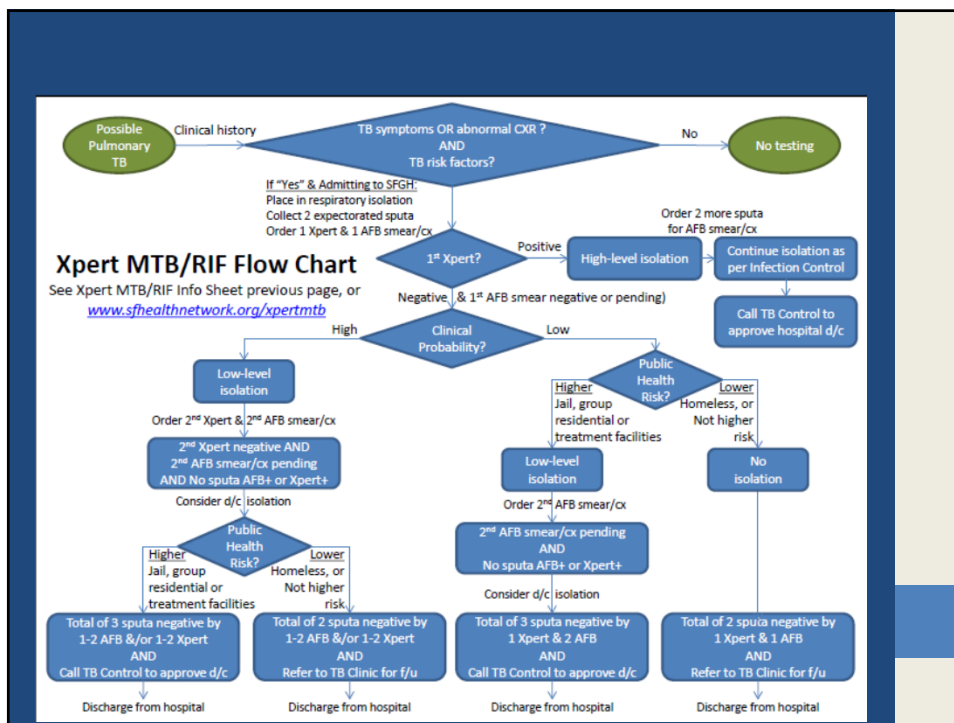
- 1) **Clinical requirement:** Admitting for inpatient care for any reason & also needing evaluation for active TB due to:
 - a. TB symptoms (e.g. cough ≥2 weeks), *OR* Radiological findings suggesting TB (e.g. abnormal CXR), *AND*
 - b. TB exposure risk factor or history (e.g. contact to TB case, immunosuppressed including HIV+, homeless, foreign-born, incarcerated, positive tuberculin skin test (TST) or Quantiferon), *OR*
- 2) **Public health requirement:** Not allowed to enter congregate living facility until evaluated for TB transmission risk:
 - a. Higher public health risk
 - i. Group residential or treatment facilities (e.g. LHH, SNF, drug rehab, inpt psych, dialysis, respite)
 - ii. Jail
 - b. Lower public health risk: Homeless (lower b/c of shelter TB screening); SRO residents

SFGH and SFDPH partnership

- SFGH
 - Combination of pulmonary and emergency medicine teams with lead pulmonologist and lead emergency medicine physician
 - ED needed to create mechanism for collecting induced sputa safely
 - Sputum induction tents
 - Training staff to collect sputa
 - SFGH laboratory
 - Staffing and training to process Xpert specimens during business hours and after hours
 - Creation of order set in EHR
 - Education of house staff
 - 24/7 pager for questions
 - Educational Flyer (criteria, how to collect sputa, algorithm)
 - Data collection/analysis, reagents funded by internal grant

SFGH and SFDPH partnership

- SF TB Control program
 - Set policy for A.I.I. clearance from SFGH to the community and sensitive locations (SNF, corrections, dialysis, long term care, psych, homeless)
 - For those d/c'd from emergency department, accepted referral to be seen in TB clinic (walk in referral clinic)
 - Safety net for tracking patients d/c'd who may be higher risk than initially thought and need further evaluation
 - Public Health Laboratory experienced with Xpert test and had capacity and reagents to run confirmatory tests on specimens from hospital
 - Was "hands off" on A.I.I. criteria for within the hospital



Real time Xpert at SFGH had staying power

- Pilot was deemed successful and the hospital laboratory secured resources to continue real time NAAT after the pilot
- There was demand! Xpert real time pilot expanded in one day from availability only in the emergency department to the inpatient hospital floor
- There were early diagnoses of active TB made in the ED and hospital floor that helped get patients into A.I.I. and on medications faster
- A number of corrections patients were able to be evaluated in the ED alone and avoided admission to the hospital
- No major misses - when Xpert did not detect, clinical suspicion was so high, these patients were empirically treated

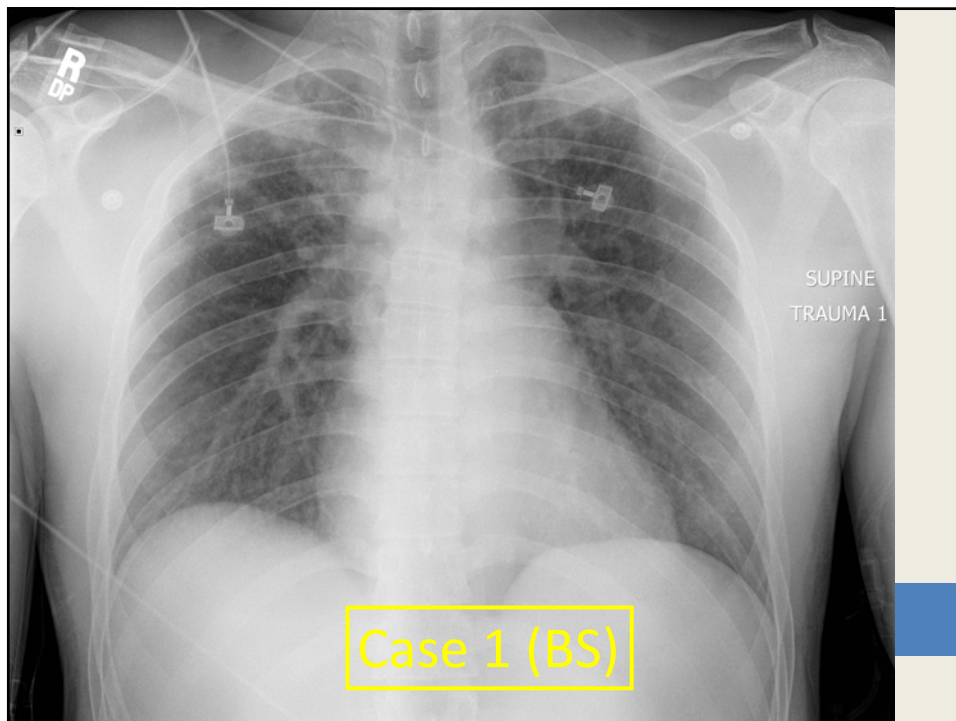
Lessons learned...

- Algorithm too complicated, i.e., had to consult it for each question!
- Forgot to include dialysis as a “special circumstance” in algorithm
- Initial group of tests were 10-20% “no test” because of poor specimen quality
- Direct specimens were less sensitive and did not have smear and culture results
- Testing in emergency department dramatically reduced after the attending who spearheaded the implementation left SFGH - need a point person or liaison

Case 1

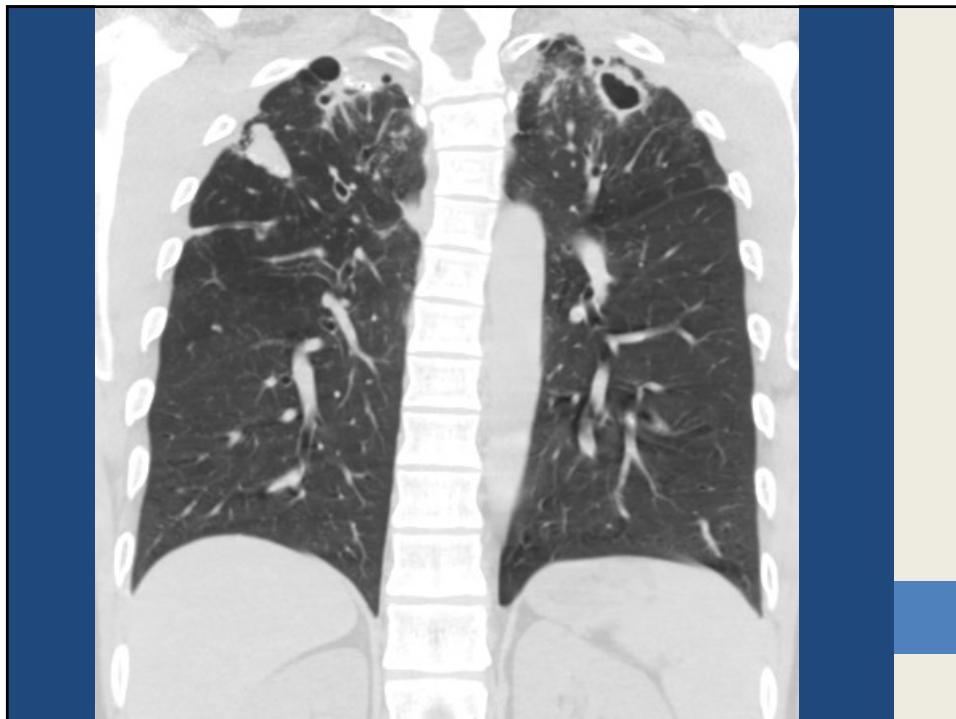
30 yo "pop up" inebriated bartender assaulted and found down on way home from work. Brought to ED.

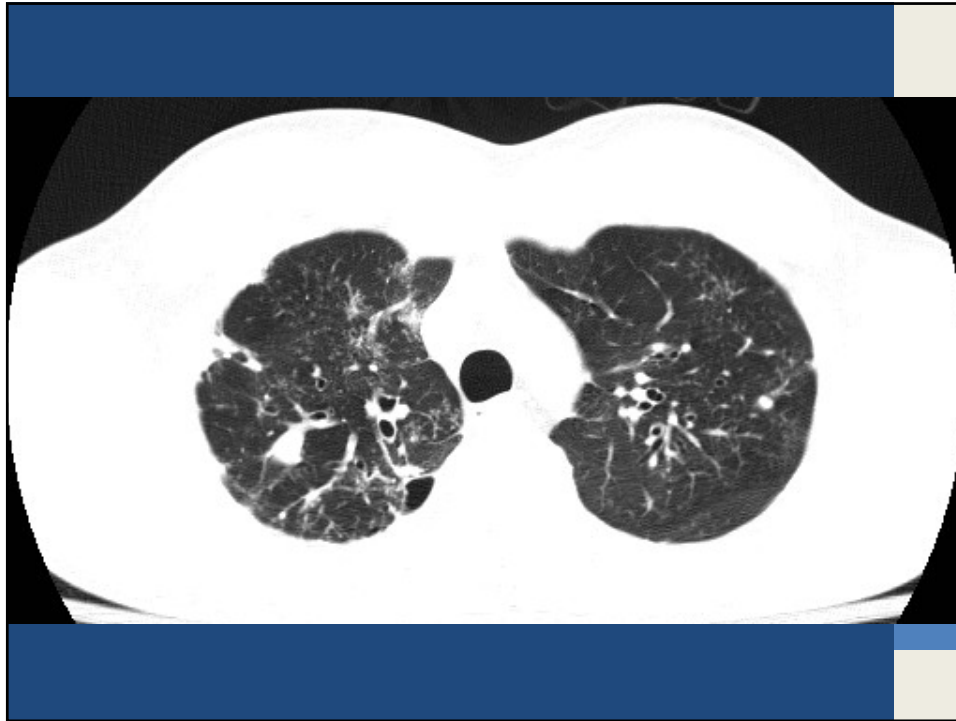
Everything taken - phone, wallet, keys. He wants to leave AMA.



Case 1

- Asymptomatic
- U.S. born, but recently returned from spending 8 years in Korea
- TB Control sends over DCI to talk to patient and set up follow up for empiric anti-TB treatment
- ED is running new “Xpert” point of care test for Mtb





Case 1: The False Negative

- Xpert is negative! (direct specimen)
- Patient has already been told he will be treated regardless of test result from ED by TB control...
- Patient goes home and returns to clinic the next day.
- AFB smear from ED is positive (rare)
- Xpert done on concentrate from AFB smear is positive for Mtb
- Infection Control says, "Are you sure you want to keep doing this?"

Case 2: Airline Travel Clearance

- 21 yo foreign born Asian out of state college student intern at a tech company in downtown SF
- Seen in urgent care for cough and has new cavitory CXR
- AFB smear positive in all three specimens (2+, 3+)
- Xpert negative on one specimen
- Initiated on anti-TB treatment

Case 2: Airline Travel Clearance

- Student internship is almost over and his housing will be unavailable in about a week - he needs clearance to fly back!
- We do not believe this is Mtb, and collect two more specimens and do Xpert testing on both of them (negative for Mtb)
- Call to local TB program where college resides to coordinate transfer to their jurisdiction.
 - Local program agrees this is not TB - we continue anti-TB treatment plus azithromycin
 - Student allowed to return to student on campus housing
 - Local TB program consultant happens to also be the college student health physician
- AFB culture grows out *M. kansasii*

Case 3

- 58 yo Asian man s/p treatment for Mtb five years prior returns with cough/fever x several weeks
- New cavitation on CXR - AFB collected, smear negative x 3
- Xpert on one specimen is positive for Mtb
- Initiated on anti-TB treatment plus moxifloxacin, as patient has poor dentition

Case 3: Another False Positive


- Patient undergoes reimaging (chest CT) after three weeks of treatment with some improvement
- AFB Cultures are negative x 3
- Given pace of improvement of cavity and evaluation by oral maxillofacial surgery finding need for complete tooth extraction, patient given diagnosis of anaerobic lung abscess
- Mtb from Xpert thought to be “dead bacteria”

The way forward...

- Consensus statement algorithm is user friendly and easily applied
- The clinician still needs to make decisions to initiate empiric treatment despite negative Xpert results in situations where the clinical suspicion for TB is high
- Continued evaluation of NAAT test performance and feedback to the users is necessary for maintaining good use of the test.

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 - Luke Davis, MD and Adithya Cattamanchi (pulmonary)
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 - Chris Keh, MD (Medical Director/acting TB Controller)



National Tuberculosis Controllers Association

CONSENSUS STATEMENT ON THE USE OF CEPHEID XPRT MTB/RIF[®] ASSAY IN MAKING DECISIONS TO DISCONTINUE AIRBORNE INFECTION ISOLATION IN HEALTHCARE SETTINGS

WORKING GROUP OF
THE NATIONAL TUBERCULOSIS CONTROLLERS ASSOCIATION
AND
THE ASSOCIATION OF PUBLIC HEALTH LABORATORIES,
AND
OTHERS

July, 2016

Nucleic Acid Amplification Testing and A.I.I. Decisions

- In February, 2015, the FDA approved a change in the package insert for the **GeneXpert** to reflect expanded claims related to A.I.I.*

Specifically:

... results using this assay on “either one or two sputum specimens” can be used as an alternative to examination of serial acid-fast stained sputum smears to aid in the decision to discontinue A.I.I. for patients with suspected pulmonary TB.

* CDC. MMWR, 2/26/2015



The Consensus Statement

- Concerns by APHL and NTCA leadership that various interpretations of this change will result in premature discharge from A.I.I. prompted the creation of this document
- Opportunity to improve on the process of patient evaluation for A.I.I. by optimizing the use of this novel technology
 - offers detailed guidance for clinicians, nurses, and hospital infection preventionists on the use of Xpert *in making A.I.I. decisions*



The Statement: What it is **NOT**

- This is **NOT** a diagnostic algorithm
 - sputum smears and cultures are essential for identification of the organism, drug susceptibility testing, and genotyping
- NAA testing ***should not be used to monitor response to treatment or to release a newly confirmed TB patient from A.I.I.***
- This statement is **NOT** an endorsement of Xpert or of any specific product
 - reflects new FDA approval of NAA technology that applies to the Cepheid *Xpert MTB/RIF*® system *only* and for this specific indication
- This is **NOT** a rationale for delaying the start of empiric treatment when TB is suspected



The Statement: What it *IS*

- A series of recommendations on how to interpret the GeneXpert MTB/RIF results
- A document
 - stressing the difference between diagnosis of TB and infectiousness of TB
 - providing easily followed instructions/protocols for sputum induction
 - containing a customizable flowchart for use in hospital policies and procedures manuals or as a decision-making tool
- A reminder of the importance of working with local public health TB program and the public health lab



Xpert and A.I.I. Labelling Change: Operational Considerations

- Communication and coordination between clinicians and patient service providers are essential
 - Dietary
 - Nursing
 - Respiratory Therapy
 - Medical providers
 - Laboratory
 - IT / reporting platforms
 - Institutional Infection Control
- Recognition of this process as independent of diagnostic protocol: Smears and cultures still must be obtained, followed-up



In The END, This Is Just The Beginning

- Data Collection and Analysis
 - Infection Control programs should collaborate with the TB Laboratory and public health to collect and analyze data to determine and evaluate the effectiveness of institutional methods used to determine discharge from A.I.I.
 - Periodic analysis of protocol performance should be used to improve and/or modify policies and procedures as needed



Help NTCA/APHL help you!

- As with any paradigm shift, early implementation experiences are important to document...
- Send questions, comments, success, challenges, highlights of internal assessments to ntca@tbcontrollers.org
 - NTCA/APHL will update statement as appropriate
 - NTCA/APHL will develop a frequently asked question (FAQ) document regarding implementation and post on website



Acknowledgments

The A.I.I. Working Group:

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Diana Nilsen	Susan Ray
Randall Reves	Barbara Russell
Max Salfinger	Caitlin Reed

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David Warshauer

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CDC:

Neha Shah	Jimmy Keller
Brian Baker	

