

**OFFICE OF PUBLIC HEALTH REGION 1
& WETMORE TB CLINIC AND LSU- UMC NEW ORLEANS
EXPERIENCE**

THE TOP 10 SPECIFIC CLINICAL ISSUES OTHER THAN MTB & LTBI IN GENERAL ROUTINE

1. TST & IGRA TEST
2. TB/PREGNANCY
3. TB /HIV
4. TB/DM
5. TB /RHEUM/EYE Clinic
6. EXTRAPULM
7. DISSEMINATED
8. IGRA IN CHILDREN
9. TB /DRUG LEVELS
10. TB/NTM

This presentation will focus on some of these in the context of T-Spot TB Test with
Observations and Perspectives related to above

Introduction, Background, Disclosures

Asalamolaikum

- Juzar Ali, MD, FRCP(C) FCCP
- Klein Professor of Clinical Medicine
- Section of Pulmonary/Critical Care & Allergy/Immunology
- LOUISIANA STATE UNIVERSITY Health Sciences Center, New Orleans
- LSU Health & Network Clinics *****
- Director, LSUHSC-Wetmore Office of Public Health
- TB Clinics & Clinic for Mycobacterial Diseases, *****
- University Medical Center, New Orleans
- Faculty, School of Nursing
- LSUHSC and School of Public Health & Tropical Medicine
- TULANE UNIVERSITY

- Consultant to Oxford Immunotec



Modified Public Health CLASSIFICATION *

- 0 No Exposure; Not Infected
- 1 Exposure; Not Infected
- 2 Infected; No Active Disease
- 3 Active Disease Pulmonary and or Extra-Pulmonary
- 4 Old Disease or “UDA”
- 5 Under Evaluation for Active TB
(suspicion of TB)

- 6 “TB wannabes”/Atypical/FMAN (NTM)
- 7 “TB Look Alikes”
- 8. Co-morbidities
- 9 Exposed Contacts

- **2a INCIPIENT DISEASE (IP)**
Determined by RNA seq
PCR and other biomarkers*
ATS 197/9 May 2018

- * **2b SUB-CLINICAL (SC)**

“To Be or Not To Be” *

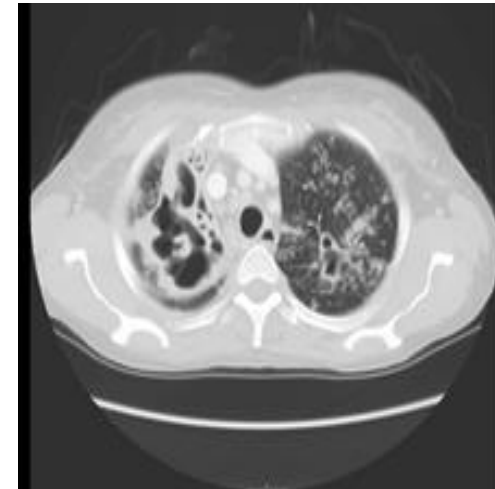
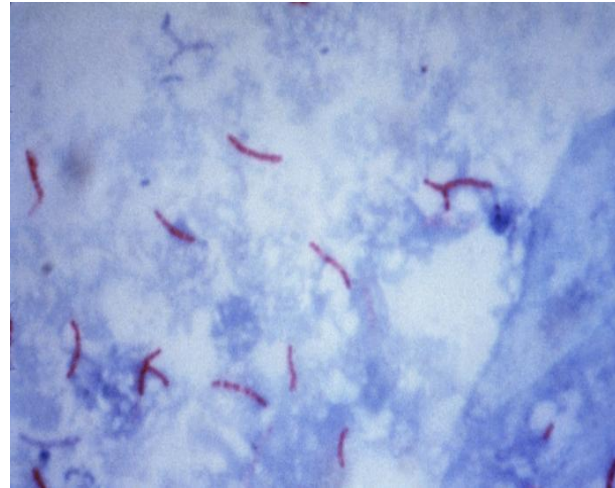
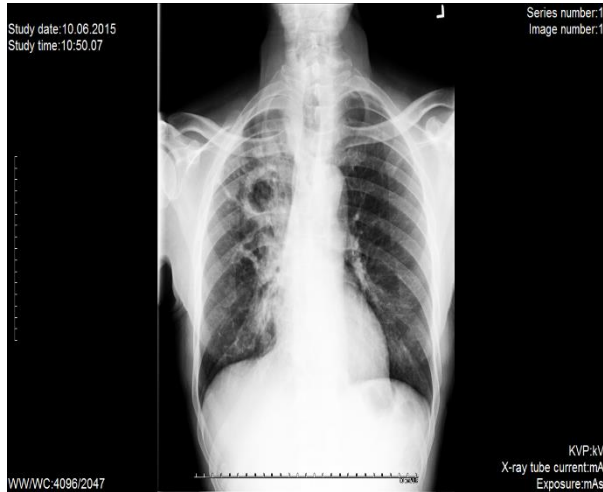
Risk, Pre-TEST likelihood; Symptoms, Signs, Images, Micro (Smear, NAAT, Culture, Gen Probe, Final Culture), Tissue Dx

w or w/o TST/IGRA

Looks like a duck, walks like a duck, must be...



...BUT IS IT?

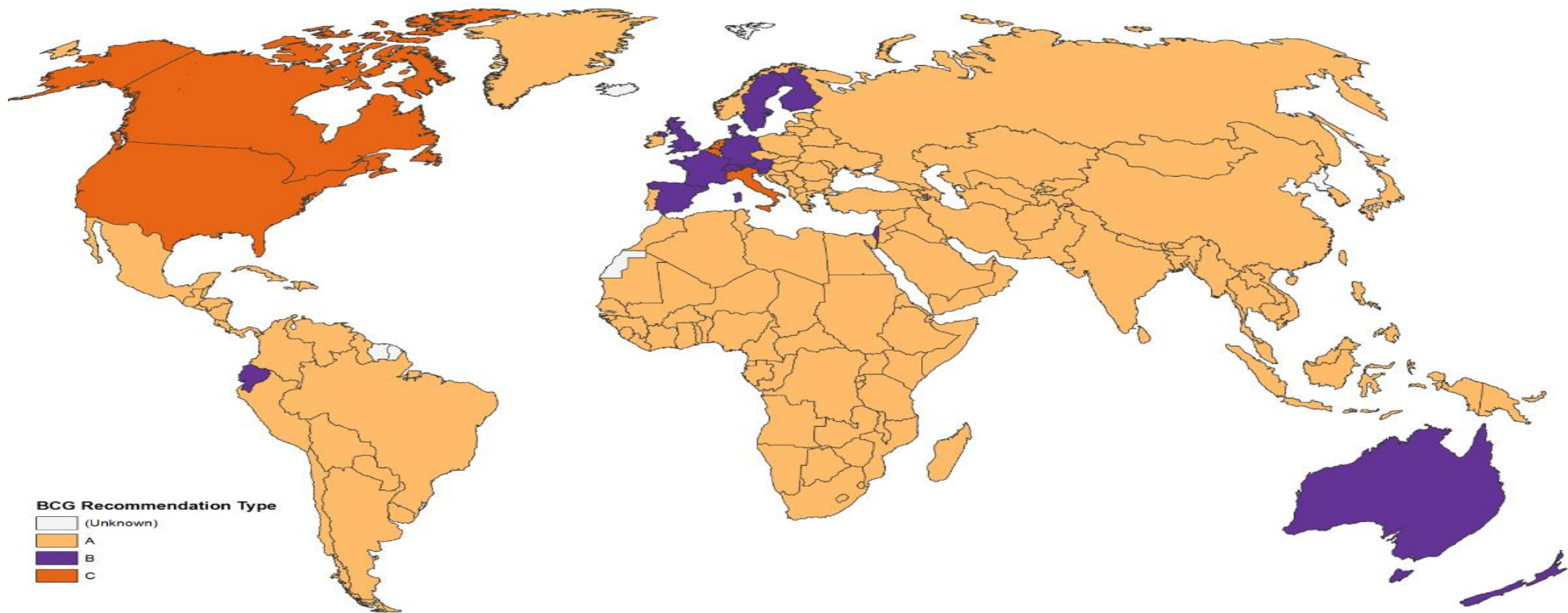


* 3 variables

BCG – Does that matter?

NTM - Is that important?

Where there is no culture data, what is the differential and what could be the action plan



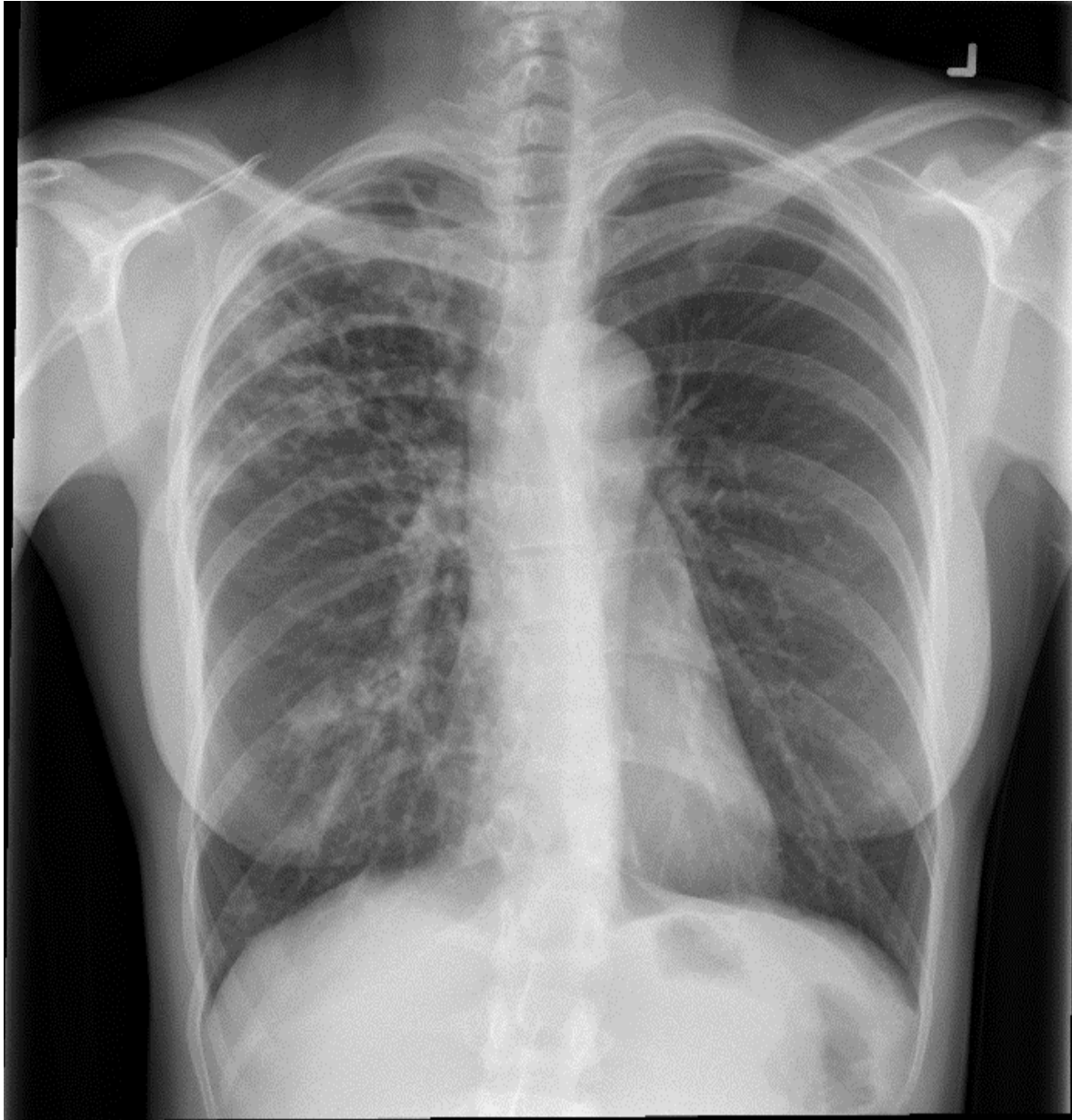
BCG - is it a big factor ?

BCG Recommendation Type

- (Unknown)
- A. Country currently has universal BCG vaccination program
- B. Country used to but currently does not have universal BCG program
- C. Country never had universal BCG vaccination programs

Broadly Speaking

- As a Pneumonia of an undetermined etiology with its varying differential
- As a AFB smear positive only
- As a Biopsy of Granulomatous Inflammation of Undetermined etiology in LN, Abdominal, EP, Pleural
- As a lymphocytic exudate only in Pleural Effusion
- As a part of contact screening
- Immune Compromised states: Non- HIV Diabetics
- Immune Compromised states: Non-HIV Non-Diabetics
- Immune compromised states: Non- HIV Non-Diabetics on Biologics with referral from Rheum/Eye/Skin Specialists



The start of the story in a clinic encounter

Broad Radiological Differential

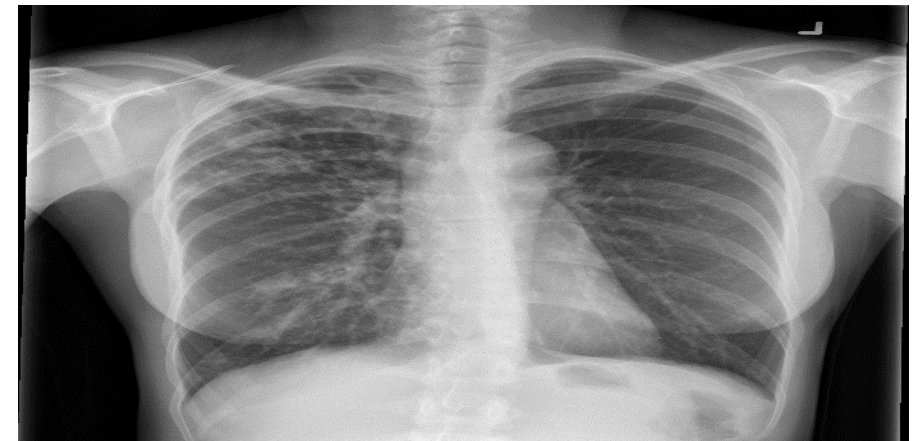
- 1.
- 2.
- 3.
4. Plus plus

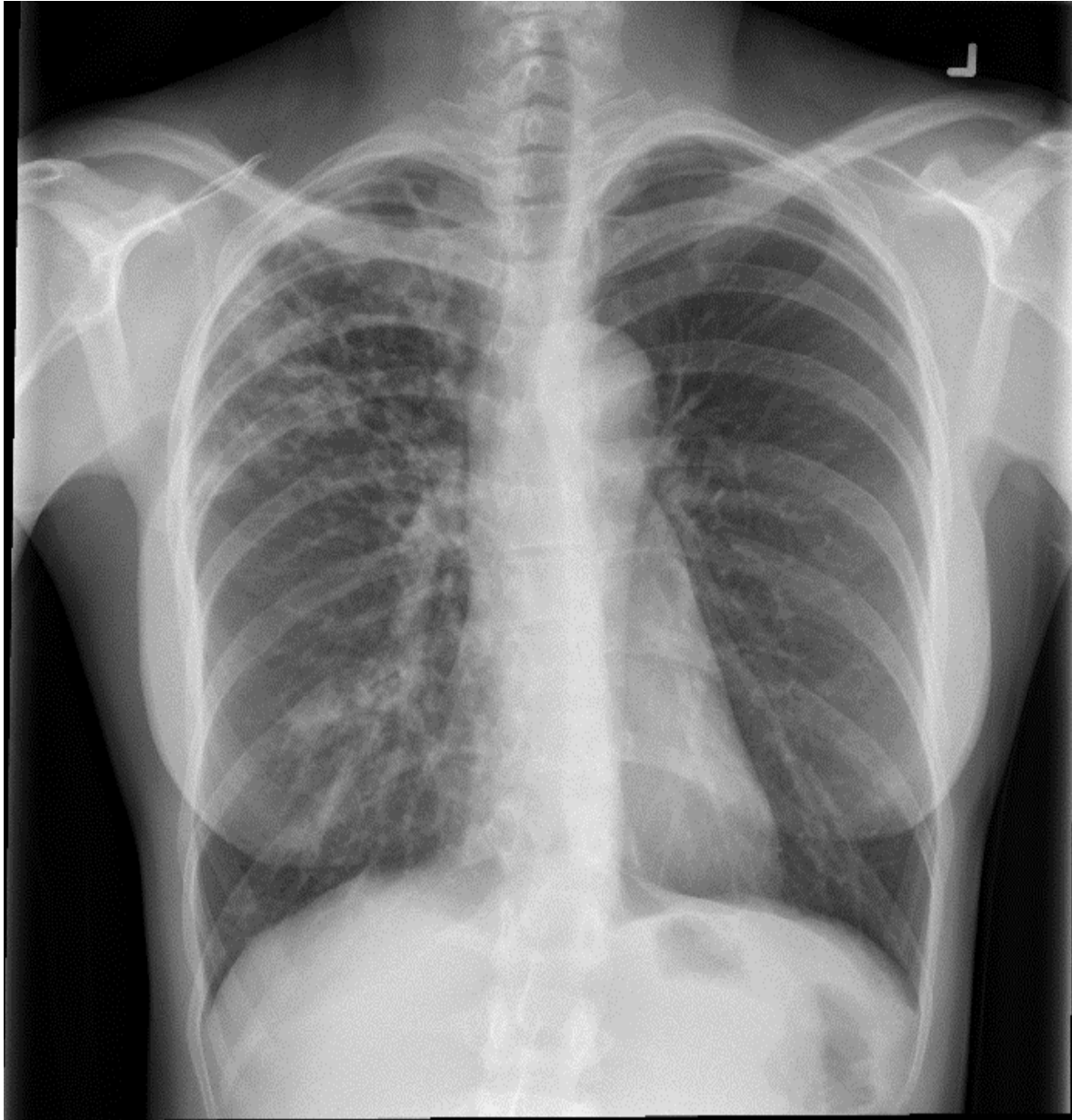
Mgm Strategies variable

1,2,3,4,....

MF, In this case...

- This patient , 30 year old , G4 P2 presented to the OB clinic for her pre-natal visit;
- TST done : 25 mm ,
- She was totally asymptomatic except for minimal shortness of breath; had no history of contact with any TB patient personally or professionally; Claimed had a negative TST 8 years ago
- CXR : just shown in previous slide →
- 3 sputum tests of 6 were positive for AFB





Going Back to this

Broad Radiological Differential

- 1.
- 2.
- 3.
4. Plus plus plus

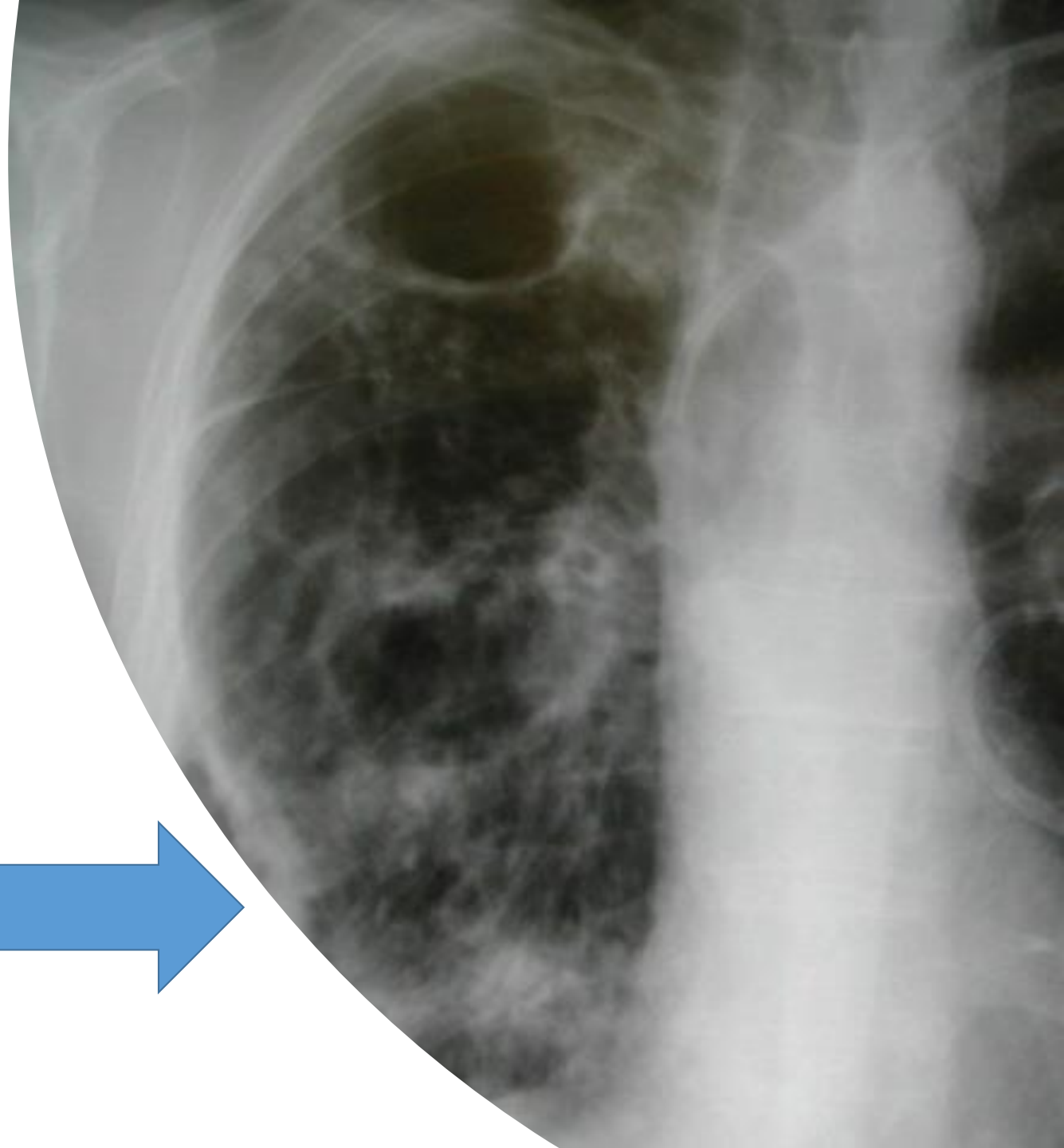
Mgm Strategies

1,2,3,4,....

In this case

- T-Spot test was negative
- Culture turned out to be MAC
- Rx changed
- Good response
- But this could have turned out to be ??

- In another instance.....Not so



REFERRAL OR ENCOUNTER PATTERNS and related challenges

- Scenario with Culture Growth of MTB.....No issues per se/clear cut
- Culture TB Unknown.....Options
- Culture Growth of NTM.....Complex decision making
- TST positivity..... What to make of it ?
- T-Spot / IGRA positivity..... Importance and Rx timing
- Discordance between TST and IGRA Confusing /needs review
- Distinction between Invalid/Indeterminate/Borderline IGRA...Important
- Borderline resultsRepeat testing helps
- Latent TB.....As per “traffic light plan”

No cross-reactivity to BCG and most NTMs

Tuberculosis Complex	Antigens		Environmental Strains	Antigens	
	ESAT-6	CFP 10		ESAT-6	CFP 10
<i>M. tuberculosis</i>	+	+	<i>M. abscessus</i>	-	-
<i>M. africanum</i>	+	+	<i>M. avium</i>	-	-
<i>M. bovis</i>	+	+	<i>M. branderi</i>	-	-
BCG substrain			<i>M. celatum</i>	-	-
gothenburg	-	-	<i>M. chelonae</i>	-	-
moreau	-	-	<i>M. fortuitum</i>	-	-
tice	-	-	<i>M. goodii</i>	+	+
tokyo	-	-	<i>M. intracellulare</i>	-	-
danish	-	-	<i>M. kansasii</i>	+	+
glaxo	-	-	<i>M. malmoense</i>	-	-
montreal	-	-	<i>M. marinum</i>	+	+
pasteur	-	-	<i>M. neoaurum</i>	-	-
			<i>M. scrofulaceum</i>	-	-
			<i>M. smegmatis</i>	-	-
			<i>M. szulgai</i>	+	+
			<i>M. terrae</i>	-	-
			<i>M. vaccae</i>	-	-
			<i>M. xenopii</i>	-	-

ESAT-6 Early Secreted Antigenic Target
CFP-10 Culture Filter Protein

JA note: except **"KMSG"**

EM / 1157798



- 50 year old woman , Background Dx COPD /Chronic Bronchitis evaluated for symptoms consistent with acute exacerbation ;
QuantiFERON Gold Indeterminate ; referred to Wetmore
- Diagnosed with MTB in December 4, based on AFB smear positive
NAAT positive Gen Probe Rif resistant , initially started on RIPE Rx
- But T spot negative
- CDC-confirmation later: No MTB DNA amplification; X-pert NAAT negative; Initial result termed as false positive
- Culture MAC positive x 4

SS 12/21/1975 1265638

- RUL cavitary lesion in a ex smoker , chronic cough
- IR Rx: AFB smear positive
- T spot negative
- Started RIPE till we get the culture back
- Culture negative
- Then subjected to Open Bx: Granulomatous Caseating Inflammation
- MAC on excised specimen
- Decision options: Anti MAC Rx /No RIPE/ No Rx

FO 04/20/1951 ; 1156845

- CXR: RUL Cavitory disease
- AFB Smear positive
- T spot positive
- Rx As TB
- But then MTB negative
- M Kansasii
- Rx modified

EP 1349601

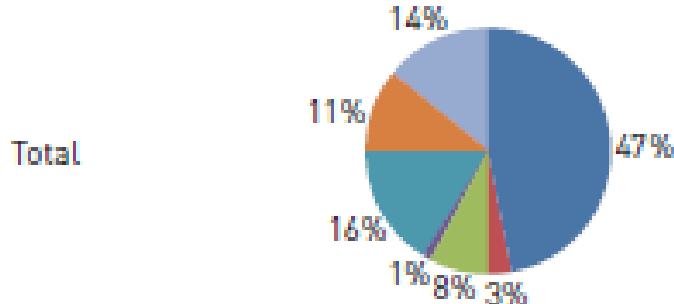
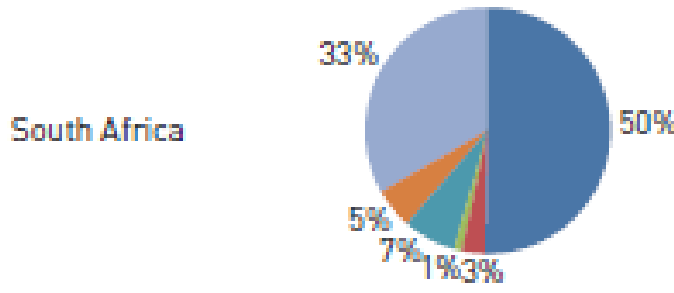
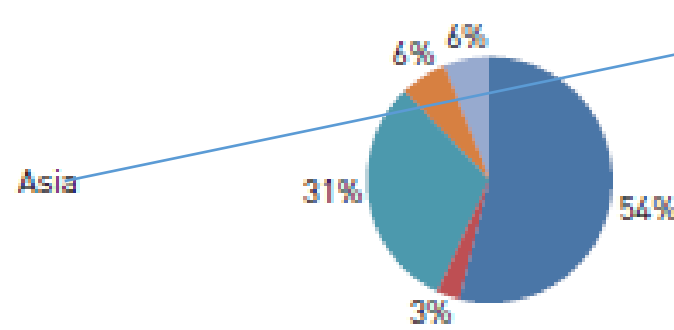
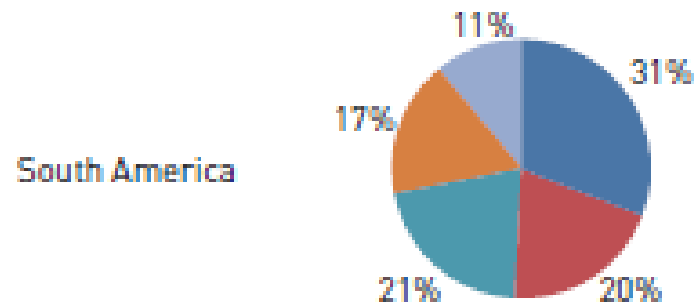
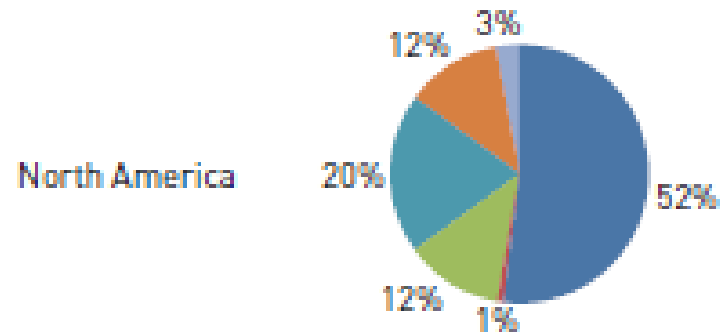
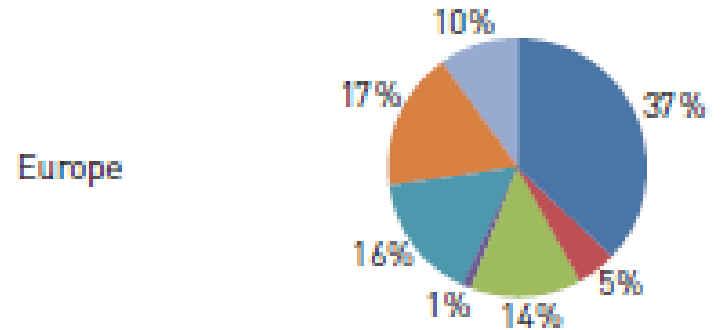
- Immigrant from Philippines brought documents with
- CXR : read as “consistent with TB”
- Culture negative for MTB but Culture positive for NTM
- CXR here in clinic, New Orleans negative
- Cultures for TB negative
- T spot negative here
- Cleared from Immigration and PH perspective

Worldwide NTM Distribution (Respiratory)

AKUH Study isolated from 25955 specimens
BMC Inf Dis 2013

Imran Ahmed, K Jabeen and Rumina Hasan

NTM in ME AA Velayati et al Int J Myco 2015



Distribution of NTM

- MAC
- M. kansasii*
- M. xenopi*
- M. mageritense*
- RGM
- M. goodii*
- other SGM

The “other mycobacteria” Who cares?*

Based on 2003 – 2007 Medicare data

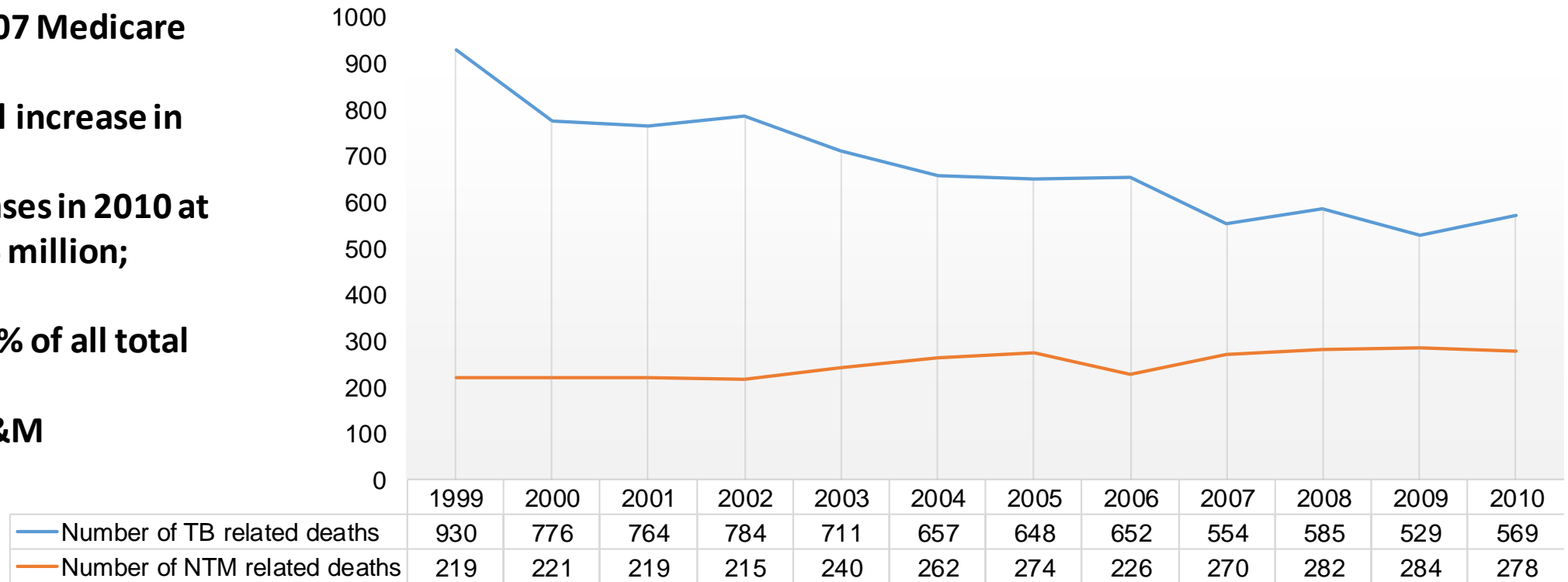
Projected 8% annual increase in prevalence

Estimated 86,244 cases in 2010 at an annual cost \$815 million;

87% inpatient

Medication cost: 76% of all total cost

Increased risk of M&M



**** maybe we should**

“The Hidden Reservoir of TB”

- Smear negative cases: 13-22% of cohort can acquire disease from smear negative contacts¹
- *“Verily Thou do DOTS but Doth do DOSE too ?”*
- Incomplete or Erratic Contact tracing and mixed results
- Undocumented immigrants/migrants/transient mobile population groups with prolonged symptoms with poor access to health care²
- Low index of suspicion when Specialists and Healthcare Workers (HCWs)* in the hospital have decreased awareness, with resultant missed or delayed diagnosis and treatment³
- *12 million HCWs in US⁴
- 10 million immunocompromised patients in US⁵

1. Tostmann A, Kik SV, Kalisvaart NA, et al. Tuberculosis Transmission by Patients with Smear-Negative Pulmonary Tuberculosis in a Large Cohort in The Netherlands. *Clin Infect Dis*. 2008;47(9):1135-1142.

2. Achkar JM, Sherpa T, Cohen HW, Holzman RS. Differences in Clinical Presentation among Persons with Pulmonary Tuberculosis: A Comparison of Documented and Undocumented Foreign-born to US-born Persons. *Clin Infect Dis*. 2008;47(10):1277-1283.

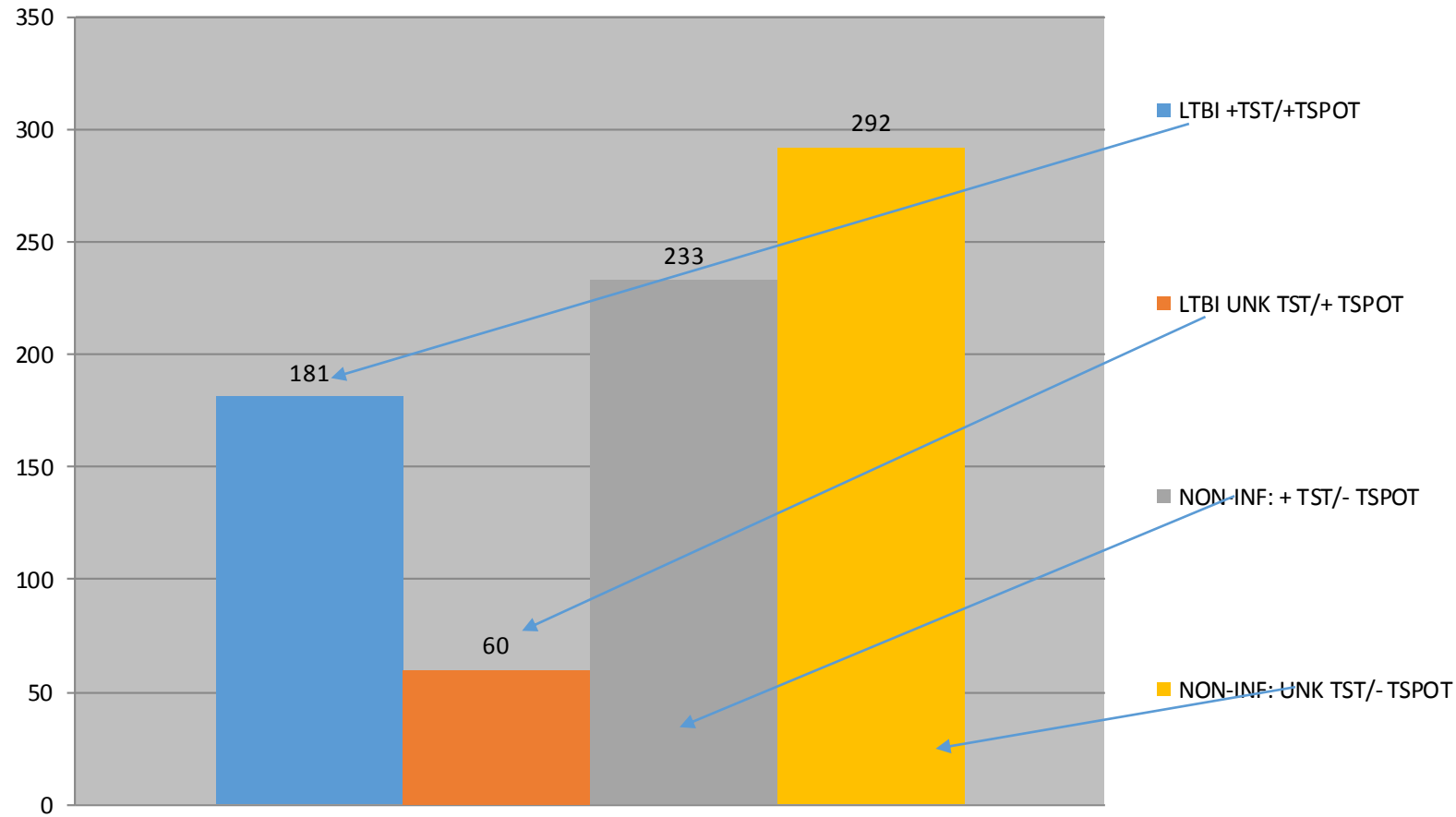
3. Chen T-C, Lu P-L, Lin W-R, et al. Diagnosis and Treatment of Pulmonary Tuberculosis in Hospitalized Patients Are Affected by Physician Specialty and Experience: *The American Journal of the Medical Sciences*. 2010;340(5):367-372.

4. May 2014 Occupational Profiles. Retrieved May 3 2015, from http://www.bls.gov/oes/current/oes_stru.htm

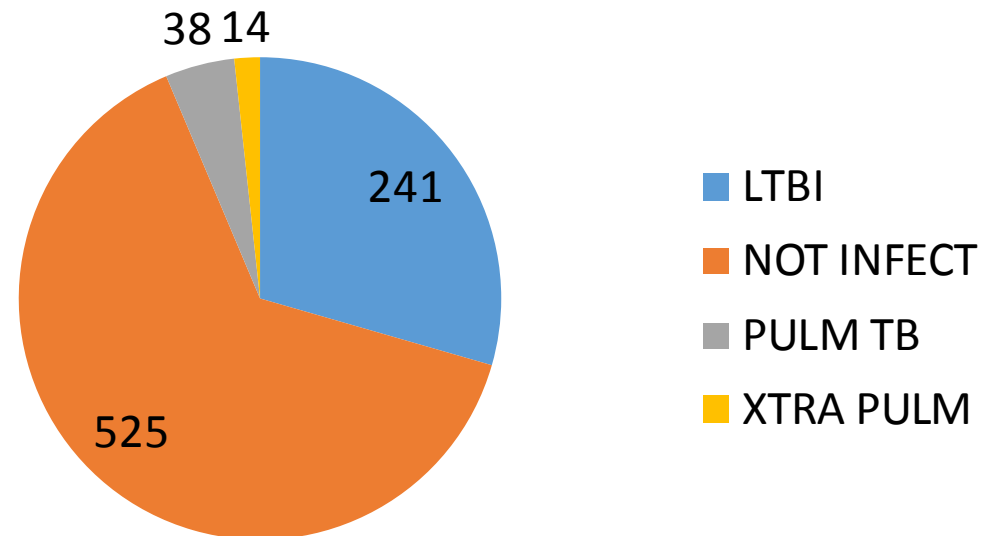
5. Redelman-Sidi G, Sepkowitz KA. IFN-gamma release assays in the diagnosis of latent tuberculosis infection among immunocompromised adults. *Am J Respir Crit Care Med*. 2013;188(4):422-431.

Tuberculin Skin Test vs T-Spot

4/2010-12/2012 Total Pts = 878



**T-SPOT TESTING: END DIAGNOSIS TOTAL
TESTED = 878 with positive TST at
Wetmore TB clinic 2010-2012 data**



Section : Contacts



13-years of Tuberculosis Outbreak in the St. Bernard Parish, Louisiana

Mirani G¹, MD, Ghaffar A², MD, Sharif J², BDS, MPH, Brown C³, Noel T³, DeGraw C⁴, Schieffelin J¹, MD, Silio M¹, MD, Ali J⁵, MBBS (MD), FRCP(C), FCCP

¹Tulane University Health Sciences Center, ²Tulane University School of Public Health & Tropical Medicine, ³Wetmore TB Clinic, ⁴Louisiana Office of Public Health, ⁵LSU Health Care Network Clinics & Interim LSU Hospital, New Orleans, Louisiana



Background and Significance

According to CDC Data and Statistics, tuberculosis (TB) is one of the world's deadliest diseases with 9 million people around the world becoming sick in 2011, and 1.4 million TB-related deaths worldwide (1). In 2012, a total of 9,951 new tuberculosis cases were reported in the United States (2). Louisiana was ranked 10th in terms of TB case rates in the year 2011. 149 cases were reported in the state of Louisiana in the year 2012, with a case rate of 3.3/100,000 (3). The goal of the Tuberculosis Control Program in Louisiana is to ultimately eliminate tuberculosis in the state.

Introduction

The Louisiana TB Control Program operates via nine different regions comprising of various parishes. Region 1 TB Program in New Orleans includes Orleans, Jefferson, Plaquemines, and St. Bernard Parishes. At the Region 1 TB Clinic, extensive contact investigations have occurred over the last 13 years involving the same cluster of individuals from the St. Bernard Parish (See Figure 1 for case rate comparison). Recognizing and containing TB outbreaks is an important step towards TB elimination.

Objectives

1. To investigate cases of TB in this cluster of individuals and link them epidemiologically
2. To describe afflictions in the contact cluster
3. To explain reasons for recurrence of the outbreak
4. To learn mechanisms of tuberculosis outbreak in a family and a community setting
5. To apply those learning points to contain tuberculosis in Louisiana by requesting and applying resources from available organizations

Methods

The study was approved by the Tulane University Medical Center IRB as well as the Louisiana Department of Health and Hospitals in November 2014. Patient consent was not required as only decoded information was obtained for public health investigation purposes. The subject population consisted of the family members and their contacts between the years 2000 and 2013. Information on demographics, diagnosis, risk factors, and treatment was collected via reviewing medical records and interviewing the involved personnel at the Region 1 TB Clinic. A family tree and maps were created based on the zip-codes of their residence. The information on genotype of the isolate was reviewed when available.

*Presenting Author, contact information: gmirani@tulane.edu

Figure 1 TB Case Rates per 100,000 Population

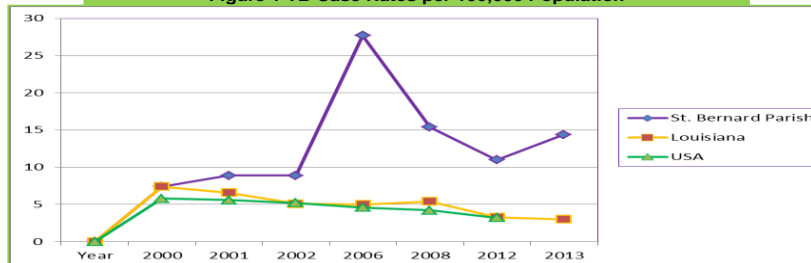
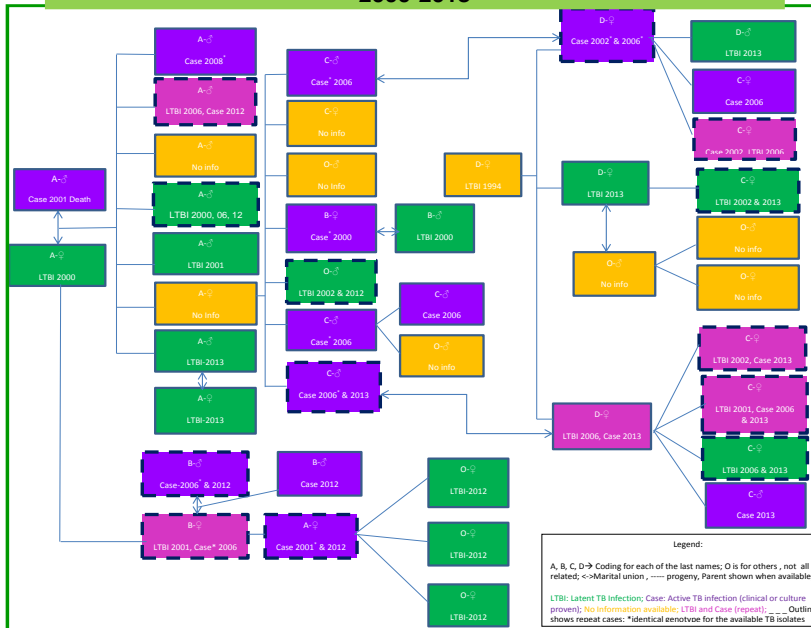


Figure 2. Family Tree Outlining Relationships and TB infections 2000-2013



Results

69 cases were reviewed (47 adults, 22 children) as of April 2014. All the 37 (17 males, 20 females) individuals were otherwise healthy (HIV negative), of white race, and US born with no travel history outside of the USA. The family tree and mapping data outlined four families with involvement of four generations, residing in the St. Bernard Parish (See Figure 2). Smoking history was reported in 19 and drug use was reported in 3 individuals. Out of 69 cases, 30 were reported as latent tuberculosis infection (LTBI), 11 as having no infection, and 4 remained unknown (See Table 1). 50% of LTBI patients completed age-appropriate treatment. 24 were active cases of TB, including 6 cases of children. 23 out of 24 individuals completed appropriate treatment for active TB infection with directly observed therapy (DOT). One individual migrated to another region towards the end of the therapy. There were 12 subjects who had a repeat treatment either as a latent TB or an active case. Of those repeat cases, 5 patients had active TB twice and they were treated with appropriate TB therapy with DOT each time. 17 out of 18 (1 diagnosed at death) TB strains isolated from adult active pulmonary cases were all pan-sensitive. The genotypes of the collected strains were identical from the years 2000 (n=3), 2006 (n=5), and 2008 (n=1).

Table 1 Number of TB Infections by Year and Treatment Completion Data

The year of outbreak	2000	2001	2002	2006	2008	2012	2013
Case	2 (C)	1 (C)	2 (C)	9 (8 C/1 NC)	1 (C)	4 (C)	5 (C)
LTBI	6 (1 C/4 NC/1 NA)	4 (2 C/2 NC)	5 (C)	5 (3 C/2 NC)	0	5 (2 C/3 NC)	5 (2 C/3 NC)
No Infection	1	0	1	2	0	2	5
Unknown	0	2	0	1	0	1	0
Total=	2/9 (5)	1/7 (6)	2/8 (6)	9**/17 (7)	1/1 (2)	4/12 (4)	5/15 (6)

(*) Total number of cases in St. Bernard Parish, LA that year; ** 2 from Region 9; C-Appropriate Treatment Completed, NC-Treatment not completed, NA-No information available

Conclusions

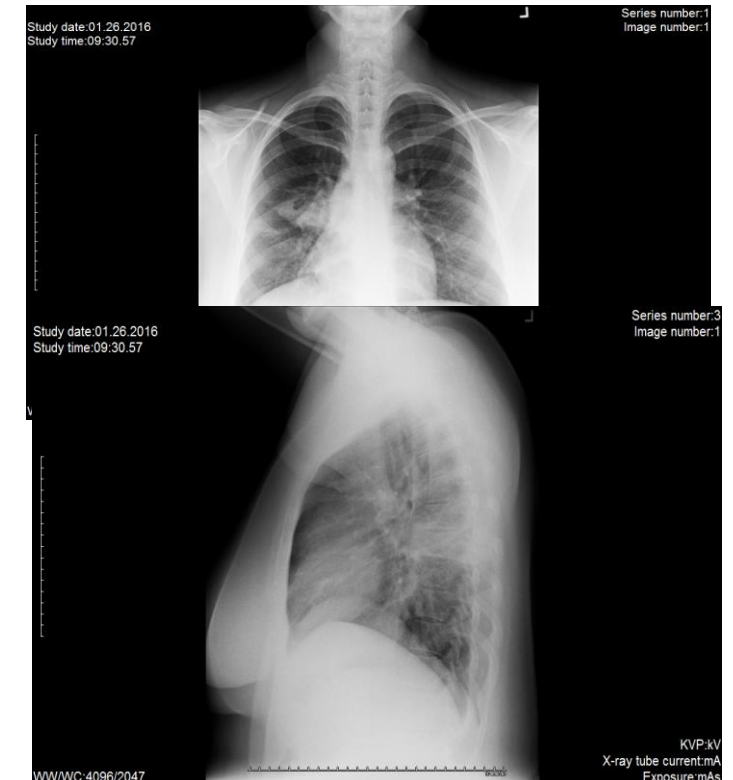
We are reporting the largest outbreak of tuberculosis, spanning over 13 years, in the St. Bernard Parish in the state of Louisiana. The next part of the project would involve searching for etiologies for persistence of TB in this cluster of individuals by tracing their migration, work and social activities more closely.

References

1. Centers for Disease Control and Prevention Division of Tuberculosis Elimination (DTBE) Atlanta, GA. CDC Tuberculosis Data and Statistics. Accessed August 12, 2013. Page last reviewed September 1, 2012. <http://www.cdc.gov/tb/data/>
2. Miranmontes R, Pratt R, Price SF, and Navin TR. Trends in Tuberculosis—United States, 2012. CDC MMWR Weekly 2013, 62(11): 201-205.
3. Louisiana TB Control Manual available on Department of Health and Hospitals, State of Louisiana website. <http://www.dhs.louisiana.gov/assets/oph/Center-PHCH/Center-PHCH-LouisianaTuberculosisManual06-2012.pdf> Accessed August 12, 2013. Last Reviewed June 27, 2012.

DA 995022 ...The story HA patient

- Index case HA : MTB;
- Contact DA screening done; IGRA negative; issues with clinical follow-up...until now
- In the Interim DA was dx as DM, started on metformin, Erratic follow-up; Apparently stopped Rx/DM uncontrolled
- Now, months later, admitted with dx of pneumonia; Rx non-TB BS antibiotics
- CXR: cavitary disease RLL sup segment, LUL nodular disease
- IGRA (T-SPOT.® *TB* positive), smear negative, culture pending
- RBS 388 at POC at Wetmore; No PCP, Difficult to start Insulin
- Rx as suspect TB; RIPE based on above data

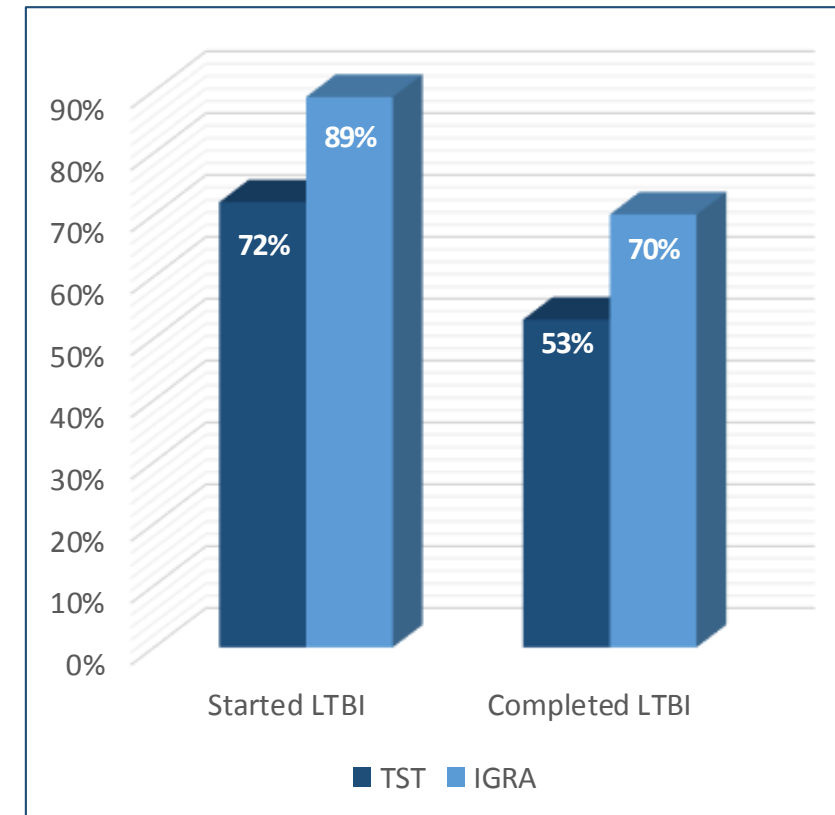
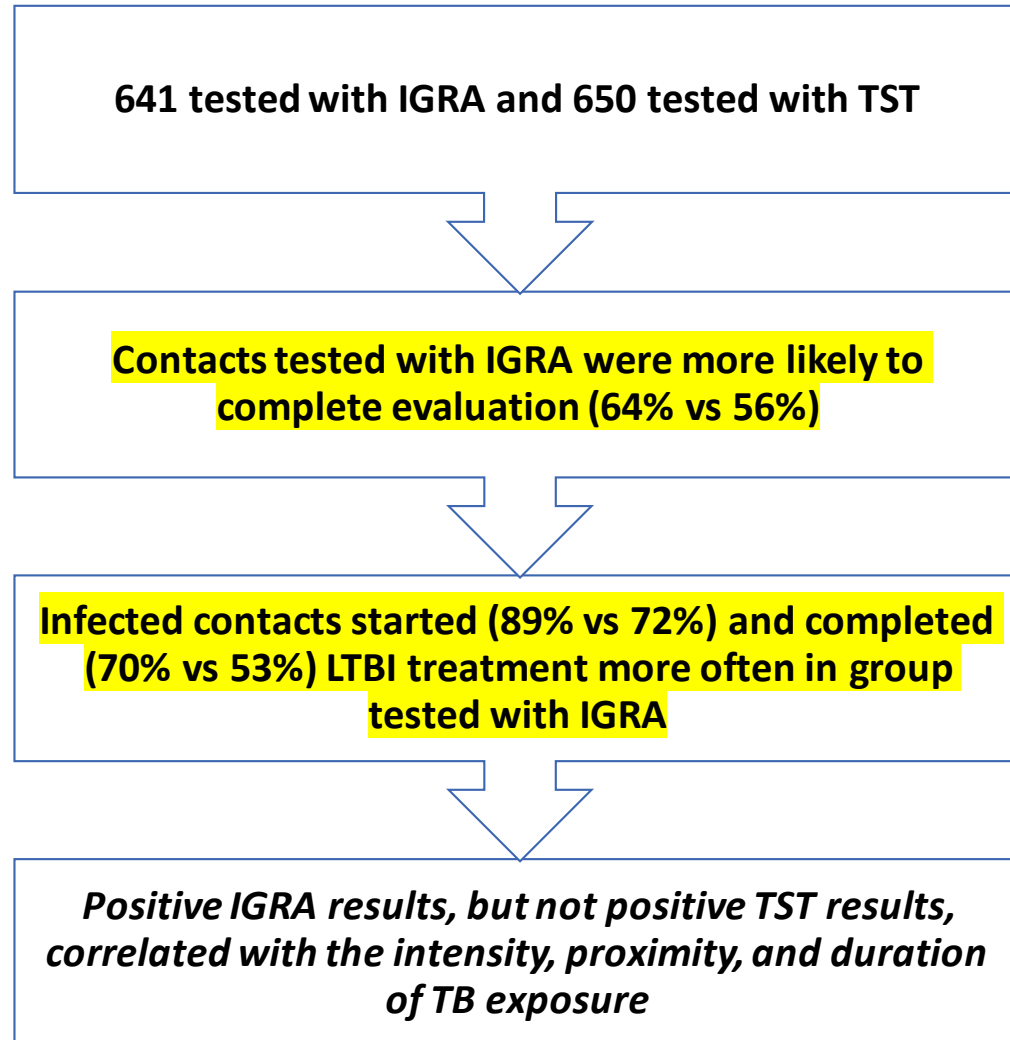


WHO 2018 Updated and Consolidated Guidelines

Pooled estimates of **risk for active TB among household contacts** stratified by age and baseline LTBI status as compared with the general population

Age (years)	LTBI-positive at baseline				Regardless of baseline LTBI status			
	Follow-up < 12 months		Follow-up < 24 months		Follow-up < 12 months		Follow-up < 24 months	
	No. of studies	Risk ratio	No. of studies	Risk ratio	No. of studies	Risk ratio	No. of studies	Risk ratio
General population	-	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)	-	1.0 (reference)
0–4		24.3 (0.73–811.0)	3	22.9 (7.7–68.6)	3	25.9 (16.9–39.7)	5	14.8 (9.8–22.3)
5–14	2	27.1 (17.5–54.1)	3	8.2 (2.3–29.4)	3	24.1 (16.9–34.4)	5	6.3 (2.9–13.7)
≥15	1	30.7 (17.5–54.1)	2	13.4 (9.5–18.8)	1	24.7 (14.2–43.0)	3	11.7 (7.6–18.0)

Diagnosis Acceptance in TB Contacts



Section : Non-HIV Immune compromised

US Immunocompromised Population

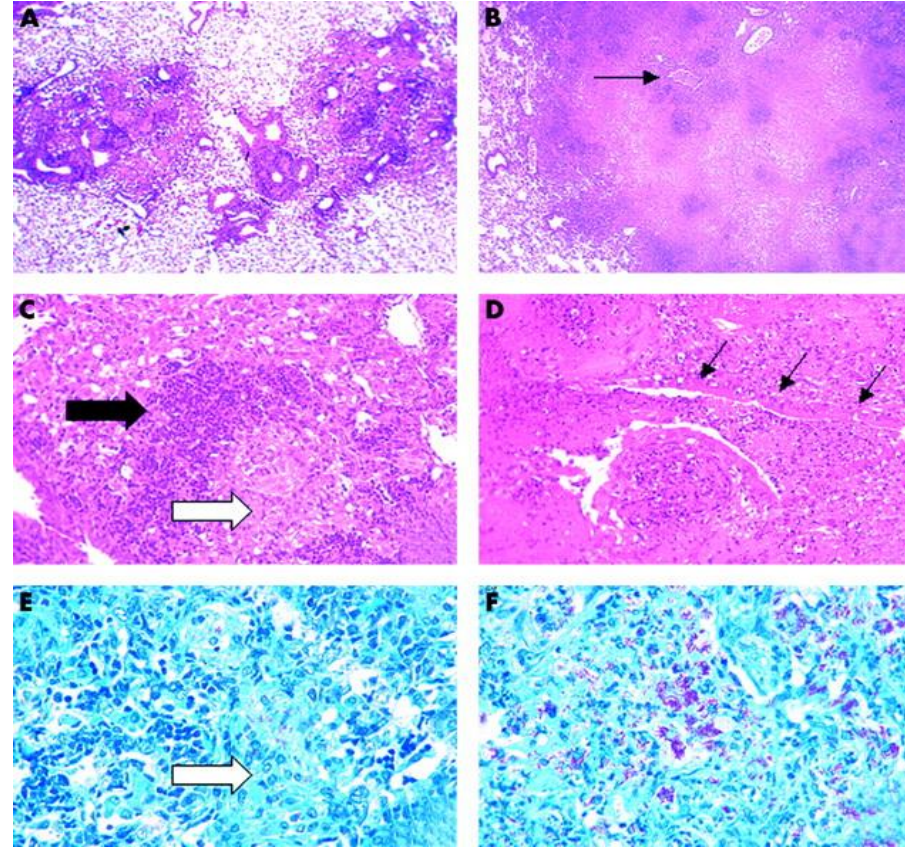
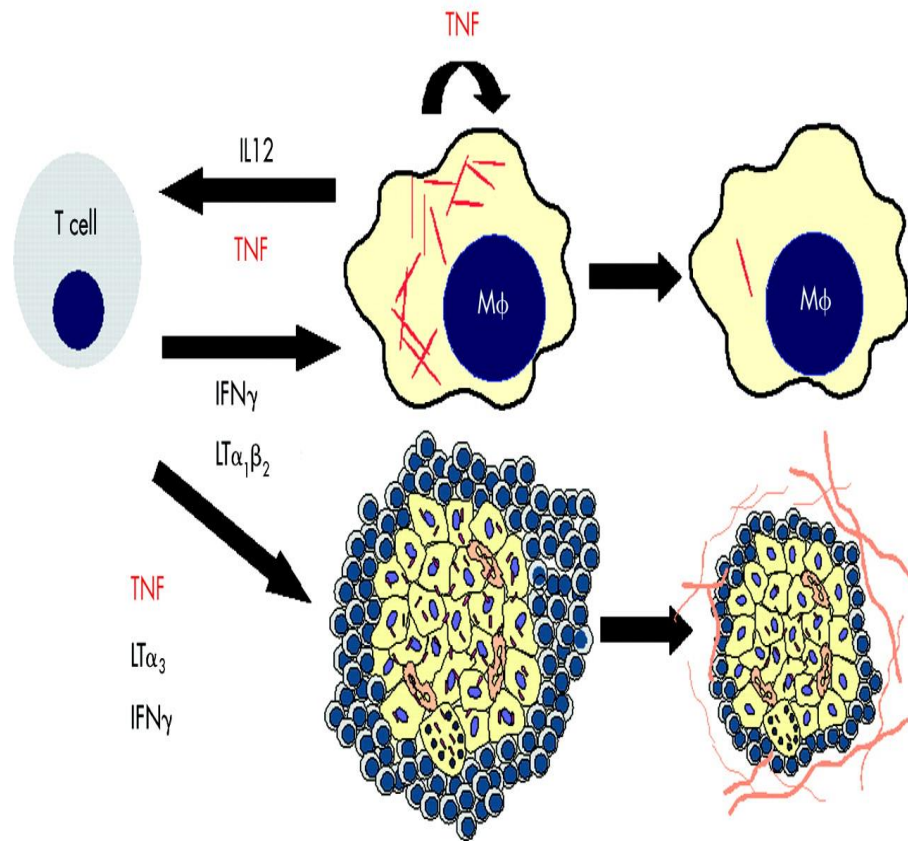
Condition	Estimated # of US Persons Living with Condition
HIV infection	1.2 million
Rheumatoid arthritis	1.5 million
Inflammatory bowel disease	1.1 million
Systemic lupus erythematosus	320,000
Systemic sclerosis	49,000
Spondyloarthropathies	2.4 million
Vasculitis	1.0 million
End-stage renal disease	0.87 million
Hematologic malignancies	1.0 million
Solid organ transplant candidates	120,000
Total	10 million

JA Note: something's missing!!

Double Jeopardy
(Disease and Rx)

Tumor Necrosis Factor – Alpha

Macrophage to Inflammation to Granuloma



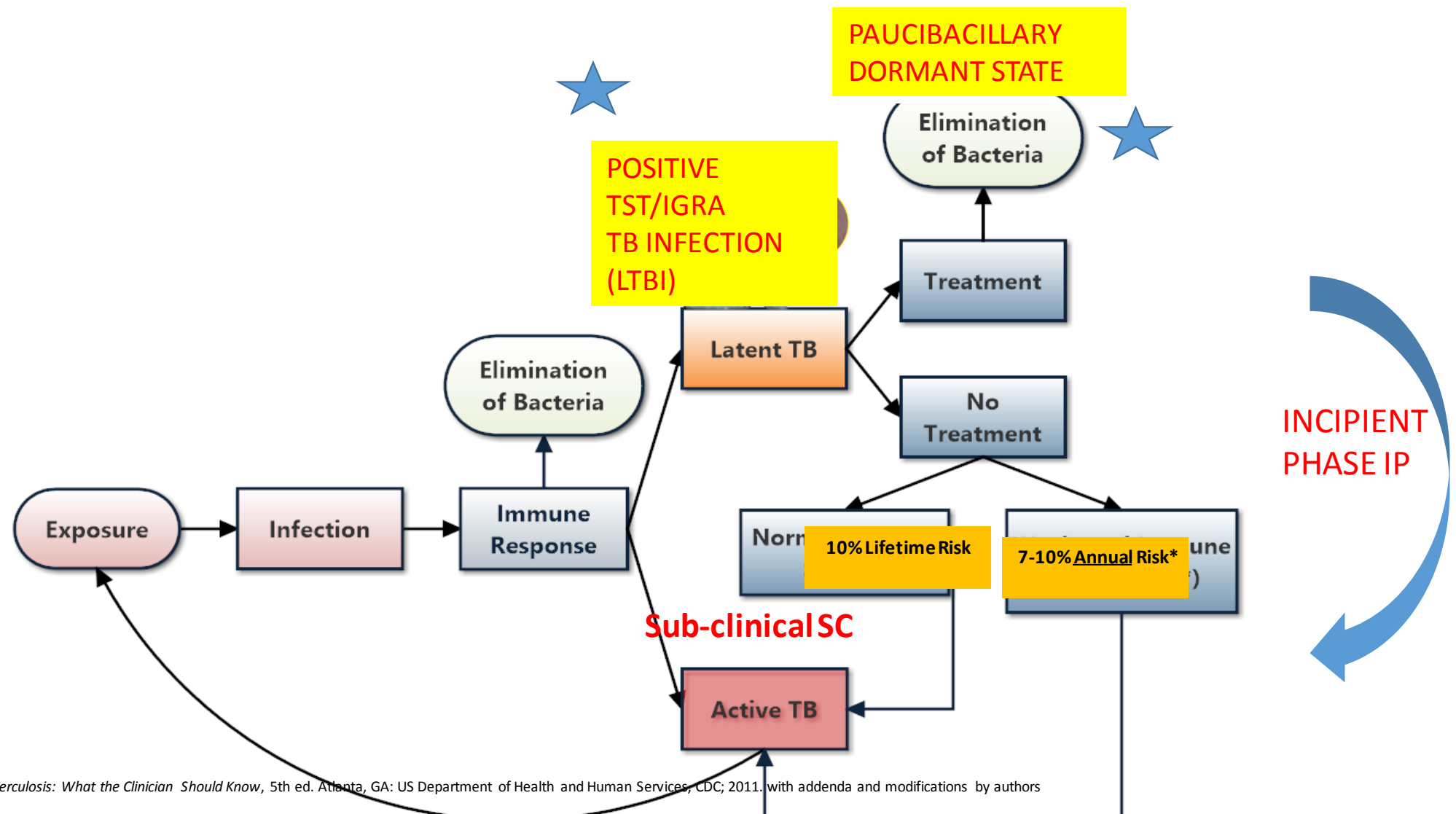
“TNF is involved at multiple steps in antibacterial and inflammatory responses to *M. tuberculosis* infection. It is a macrophage activating cytokine and is necessary for the sustained recruitment of inflammatory cells into granulomatous lesions. It is produced by macrophages and T cells, and it strongly synergises with interferon- γ in containing tuberculous infection by inducing bacterial killing and granuloma development.”

Pathway of Pathogenesis in Non-Immune Compromised Patients with a Connection and yet a disconnect between Infection, Immune response and ... Incipient /Sub-Clinical ? /Active Disease



- **INHALATION**
- Macrophage phagocytosis
- Shedding and macrophage turnover
- Alveolar Dendritic Cell migration to regional LN
- MTB Antigens ESAT-6; CFP-10 with CD4/CD8 interaction differentiate into INF-G, TNF, TH1 or cytotoxic Tc1 cells respectively IL 17, 21, 22 **IMMUNOLOGICAL RESPONSE REFLECTED BY IGRA TESTING (PROS & CON)**
- *DTH Reaction-positive TST with Intragranuloma necrosis called Ghon Complex* **SKIN TEST RESPONSE (TST) ADV/DisADV**
- **Note:** Ghon Complex is not necessarily limited to lung) **PATHOLOGY**
- Post Primary IL-4 IL-13 TH 2 response with central caseation **SEQUELLA TO BACTERIOLOGICAL AFFECT**
- **Thus Granulomas are Dynamic Lesions with Continuous Turnover and Variable Bacillary Activity or Disease Activity or Dormancy Organized granuloma /Bacillary burden ratio!**
- ****NO CLINICAL ACTIVITY and SIGNS HENCE CALLED “LATENT TB”**
- **** LTBI: LATENT TB INFECTION OR IS IT BETTER UNDERSTOOD AS LASTING TB IMMUNITY**
.....And then dormant/incipient/active phase ?

TB Infection Flow Chart (adapted)



American College of Rheumatology Recommendations (2015)

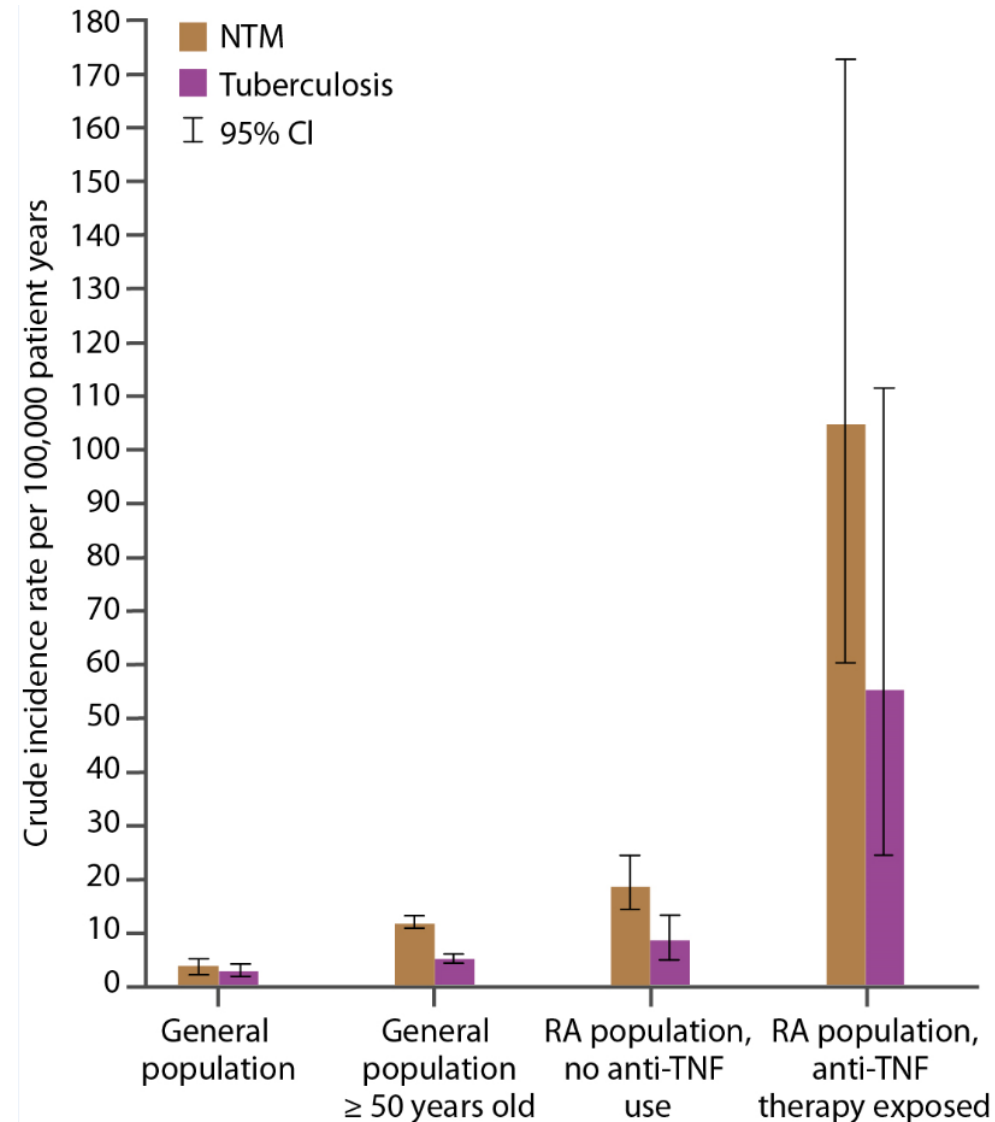


Recommendations for TB screening in patients being considered for or receiving biologics

- **All patients** being considered for **biologics or tofacitinib**, regardless of the **presence of risk factors**, should be screened with an IGRA or the TST
(JA: Consider prevalence of NTM in cohort) / BE AWARE OF DEVELOPMENT OF SARCOID LIKE GRANULOMAS WITH USE OF BIOLOGICS
- **IGRA recommended** over the TST in patients who have previously received a **BCG vaccination**, due to the **high false-positive test rates for TST**

Tuberculosis and nontuberculous mycobacteria in the general population and in patients with rheumatoid arthritis

Crude incidence rates of TB and NTM disease observed in the general population and in patients with rheumatoid arthritis in a large northern California health maintenance organization 2000 to 2008..

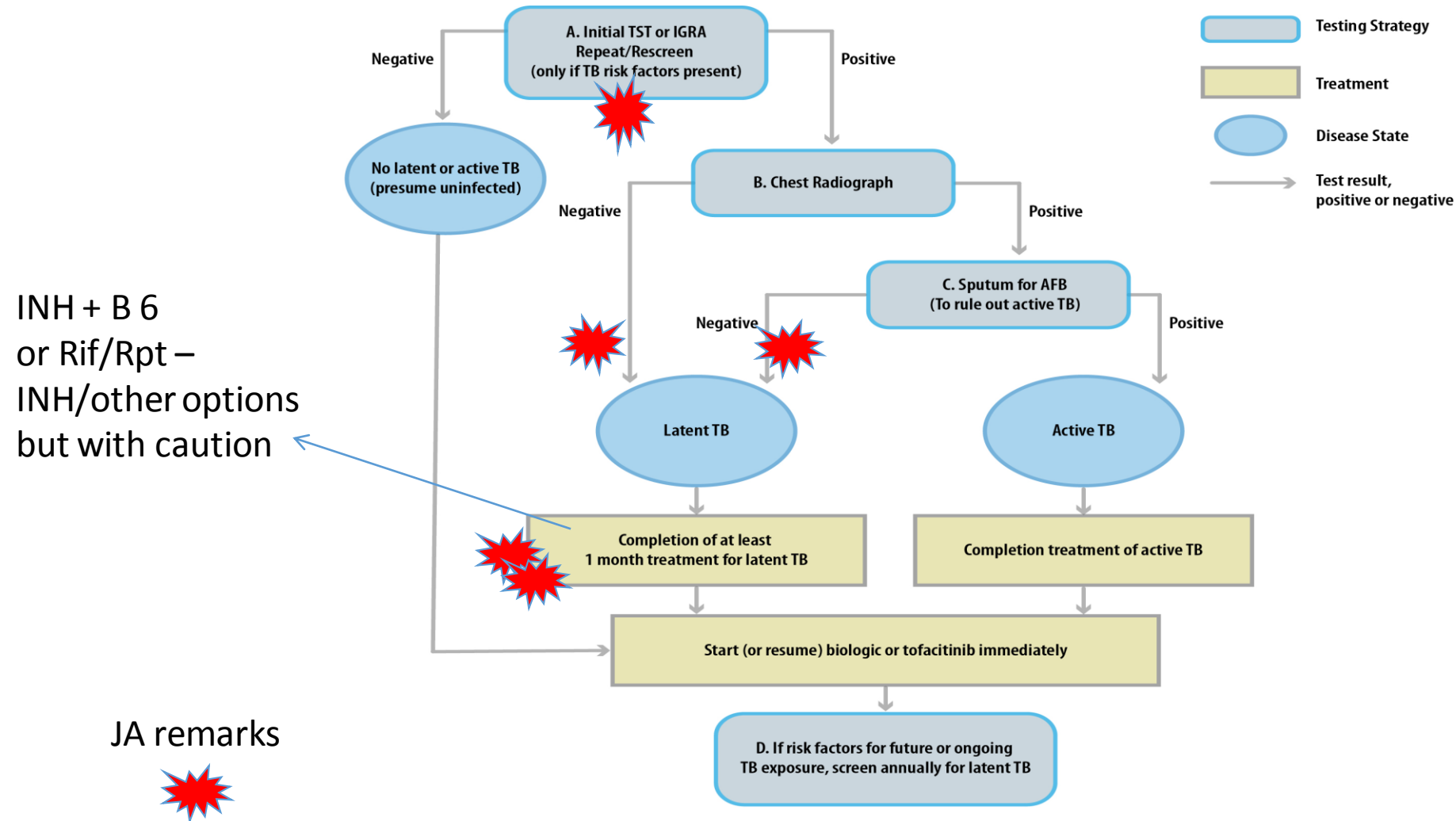


Comparison of T-SPOT.*TB* and TST Test Sensitivity and Specificity in Rheumatic Disease Patients

- 311 subjects with rheumatic disease or probable rheumatic disease
 - 83.9% BCG-vaccinated
 - 256 patients (82.3%) on glucocorticoid or immunosuppressant therapy
 - 28 patients (9.0%) clinically diagnosed with TB disease
 - overall positivity rates
 - TST test 37.8% (42/111)
 - T-SPOT.*TB* test 14.2% (44/311)

	T-SPOT. <i>TB</i> test n/N (%)	TST n/N (%)
Sensitivity	92.9% (26/28)	81.8% (9/11)
Specificity	93.6% (265/283)	67.0% (67/100)
“As a new immunoassay for TB diagnosis, the sensitivity and specificity of [T-SPOT.<i>TB</i> test] is higher than TST. It is of great importance in the diagnosis of active or latent TB infection in rheumatic disease patients.”		

TB SCREENING IN RHEUM PTS ON BIOLOGICS



Adapted from Singh, JA, Saag, KG, Bridges, SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis & Rheumatology*. 2015;68(1):1–26 doi:10.1002/art.39480

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JC 5/19/1985 / 1302673

- 33 year old man, Hx Crohn's Disease* on Azathioprine and TNF Blocker; * Hx colonic perforation/partial colectomy
- Cavitory lesion on Chest x-ray;
- Hx TST positive when back in Pakistan
- IGRA negative x 2 T spot negative**
- BAL negative x1
- BAL positive MTB the second time around when evaluated a year later for increase in pulmonary symptoms

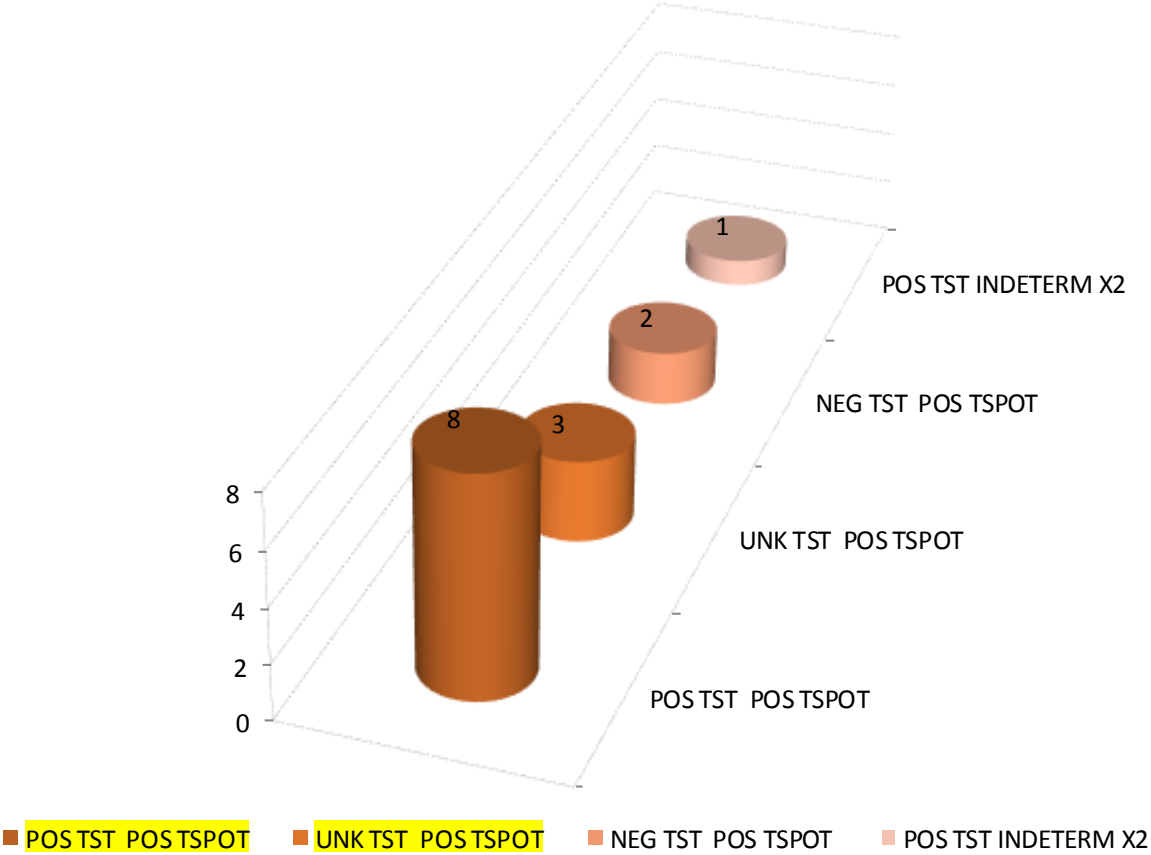
Discussion points

- IGRA negativity in Active TB/ Maybe as high as 12 %
Associated with Old age, Underweight, HIV, EP TB
(Ref: Nguyen et al Em Inf Dis vol 24 #3 march 2018)

Understanding a GRANULOMA without a culture confirmation

Section : Abdominal/GI

TST vs T-SPOT: RESULT SCENARIOS
EXTRA-PULMONARY TB 14 PTS TESTED
WETMORE CLINIC DATA



171304289 03/21/1993/1002362302 ZM

- 25 year old man, originally from Pakistan , admitted October /Nov 2017 with abdominal /GI symptoms, clinical dx of sepsis
- Extensive work up and Rx for 1. Abd abscesses/ESBL/Gram-negative infection/cholangitis/
- Negative for EH, Brucella ,Schistosomiasis/Tularemia
- Hepatic abscesses requiring partial hepatic lobectomy
- Continued symptoms
- AFB smear and culture on all initial specimens negative
- T spot Borderline 0,1,5 >20 !!

And then finally....

- T spot positive done by us POSITIVE : 0 11 18 20
- Hepatic resection finally grew MTB
- Clinical Response through in and out patient follow up : Very good with some interim S/E

T-SPOT.TB Test Borderline Category

- Establishing test cut-off
 - test result data from known active TB patients and low risk patients plotted to determine optimal test cut-off point for T-SPOT.TB test
 - effect of different cut-off points on test sensitivity and specificity determined and a cut-off of 6 spots chosen to provide maximum specificity and optimal sensitivity
- **Borderline (equivocal) results**
 - represented by ± 1 spot from the cut-off of 6 spots (5-7 spots)
 - are valid, clinically interpretable, and should be followed up
 - indicate a clinical judgment should be made which includes patient history, and retesting of the patient is recommended, using a new sample
- **A study of US healthcare workers**
 - **79.8% of borderline test results resolved as positive or negative upon retesting (n = 465 pairs)**
 - **23% retesting as positive, suggesting that the borderline is useful in maintaining test sensitivity and specificity**

NJ 181264233

- 28 year old ; no risk factors per se, non-HIV
- Diffuse Mediastinal and Abd Lymphadenopathy
- Usual Differential/ No Bx , No Culture
- T-spot positive ; Decision to treat as TB while work up continued
- Significant side effects with meds; poor tolerance , very unhappy with Rx
- Stopped Rx , did not follow up till she developed increased fever
- Granulomatous Inflammation on lymph node Bx
- Later: M TB by Bx ; pan sensitive

Section : Pleural

RG 07/17.1980 171293910

- PLEURAL EFFUSION , LYMPHOCYTIC EXUDATIVE
- T spot positive : 50 , 50
- Rx as TB
- MTB on culture later

SH; 08/22/1981

- Immigrant from New Guinea
- History of contact
- L chest pain; L pleural effusion; Lymphocytic exudate
- TST negative; T-Spot positive
- LUL cavitory lesion on CT seen later
- No immediate TB Rx ; Delay in dx about 6 weeks
- Later Bronchoscopy results MTB on culture

Section : Renal /Urology

DD 181311268 /02/01/1962

Ex Marine

Extensive travel

Hx Fungal infection during Katrina

Evaluated for painless hematuria

Work up included Urine c/s and AFB c/s

M TB pan sensitive

- T spot positive

PH 31110043566 AV patient

- Diabetic, controlled
- Initial IGRA negative
- Hematuria: Urology follow-up
- L kidney atrophic seen on CT
- Subsequently IGRA (T-SPOT.[®] TB) positive
- Urine: MTB on culture subsequently
- RIPE; intolerant to PZA with increased Uric Acid
- 9 months Rx: Repeat urine negative
- Further urology follow-up
- Diabetes under control
- Dual follow-up emphasized

Section : Ortho/Potts

PG 181334360

- 60 year old woman, health care worker ; Past Hx of LTBI Dx based on Positive Skin test ; apparently started on LTBI Rx but unsure if that was completed
- Recent development of back swelling , constitutional symptoms
- Dx : epidural abscess /bacterial Osteomyelitis with MRSA Rx ; Subsequent grew 1 colony of MTB!! Unclear of significance of this
- Rx on the basis of this and positive T spot
- Later confirmed MTB by culture positive in other specimens

Section: Cervical nodes

AG 181340137 12/16/1982

- Cervical Lymph nodes swelling
- LN Bx Granulomatous Inflammation
- HIV
- Cardiomyopathy
- T-spot positive 50 ,50
- Rx for TB

Story 78

MS 3110043552

- 45 year old
- Recent immigrant from Philippines
- Cervical Ln bx: Granulomatous inflammation
- T spot – positive
- Started on RIPE as TB lymphadenitis
- IGRA helped !!

LAR 1 of 3

- 57 yr. old female, originally from Honduras, last visited her home country in 2000, referred from a community clinic
- HIV negative, TST 13 mm, T-SPOT.*TB* test positive
- Cervical lymph node swelling with biopsy showed caseating granuloma (with rare multinucleated giant cells) which was culture negative
- Sputum x 3 positive for MAC, *M. terrae*, MAIS (*Mycobacterium avium-intracellulare-scrofulaceum*) complex
- Chest X-ray and CT scan negative
- Differential:
 - A. MAC lymph nodes and MAC pulmonary disease w/LTBI
 - B. Lymph node TB with MAC colonization

LAR 2 of 2

- We opted to treat as TB with subsequent surveillance for NTM/MAC
- Take Home Point: Extrapulmonary TB by available criteria despite culture negativity

Section: Eye clinic referrals

Case 7 MWS

- 57 yr. old male with rapidly decreasing visual acuity diagnosed with **serpiginous chorioretinitis and posterior choroiditis**, placed on steroids and immunosuppressive drugs and referred to Wetmore with **positive T-SPOT.TB.**
- Extensive work up including HIV-neg; ACE15; ANA-neg; HLA-B27-neg; RF-neg; MPO-nml; PR3-nml; Hep Panel-neg;
- His pulmonary exam was negative, no lymphadenopathy palpable, with normal CXR; no clinical features of sarcoidosis
- **No culture/Bx/PCR available**
- Cause?

continued....

MWS Case 7 continued...

- Wide Differential Diagnosis

- TB**
- Other with Latent TB
- NTM? *M. szulgai*? !!
- *!! Interesting*

** Bansal R, et al. *Ophthalmology* 2015;S0161-6420(14)01115-4

- *We opted to start treatment as TB with RIP and Clarithromycin*

MF 1129801 3/11/1981

- Referred from the Opth Clinic : Dx Pan uveitis
- IGRA positive
- Negative CXR
- No Pulm Symptoms

Discussion

- Conundrum of Non specific Rx of Eye symptoms with multiple causes and differential
- IGRA / T spot differential may be helpful

SUMMARY

- Understanding the apparent disconnect and transition from infection to disease
- Phasic progression from exposure to inhalation through immunology to mycobacterial disease
- Tests focus on various phases
- Using the compendium of these tests as appropriate
- Of course : Global Clinical Sense

Questions / Comments / Opinions / Feedback

JALI@LSUHSC.EDU

*Wus Salam : Thank you for your kind attention
Juzar Ali ,New Orleans*

