

# Empiric Pulmonary Tuberculosis Treatment in Severe Burns & HIV



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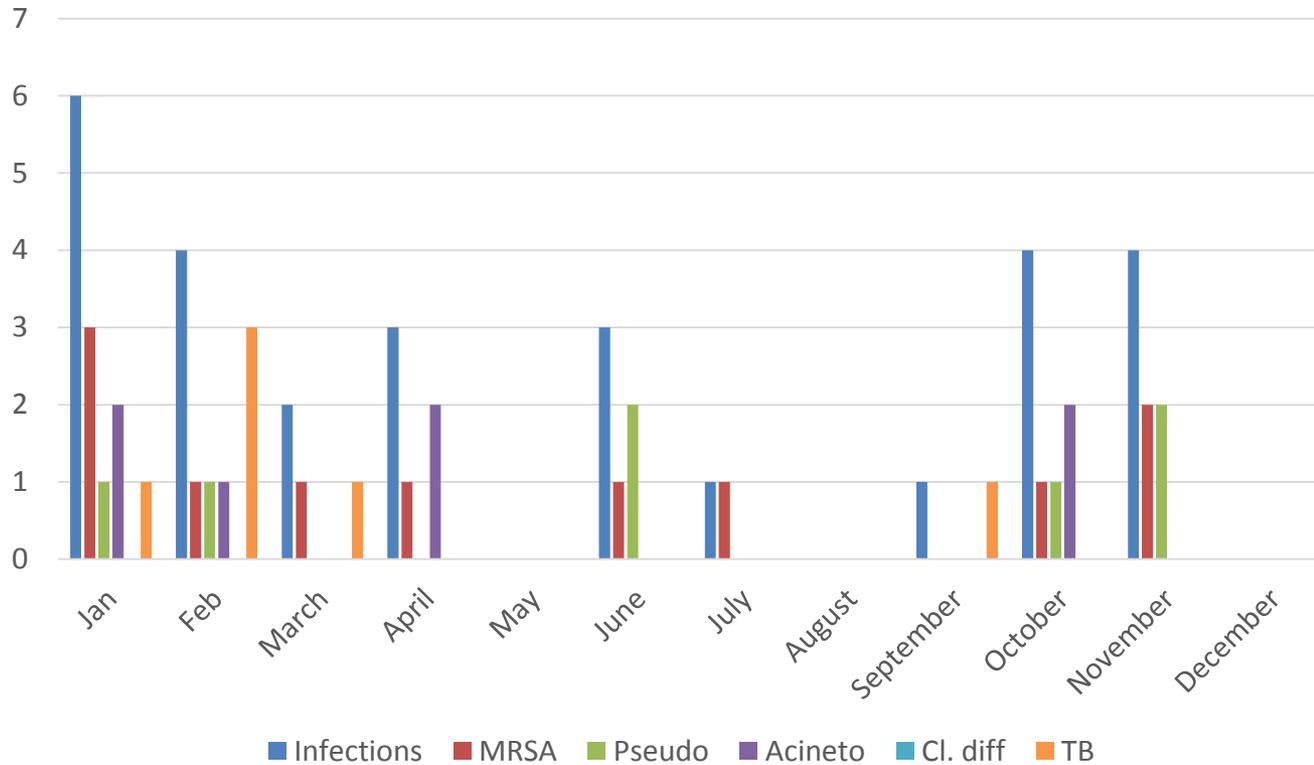
# Background

- Literature: mortality severe burns with AIDS is 100%
- *(Edge et al 2001; Chayle et al, 2011).*
- We have had 8 patients who survived a severe burns despite having HIV and underlying disease, and was ventilated for severe burn injuries.
- Empiric tuberculosis (TB) treatment based on the clinical evidence of reactivation of pulmonary tuberculosis (PTB) despite no laboratory evidence (gene-expert test negative, negative sputum and tracheal aspirate cultures).
- Common pattern of ventilation & when started on empiric TB treatment - rapid effective results.
- Common pattern: severe burns & inhalation & difficult to get off ventilators

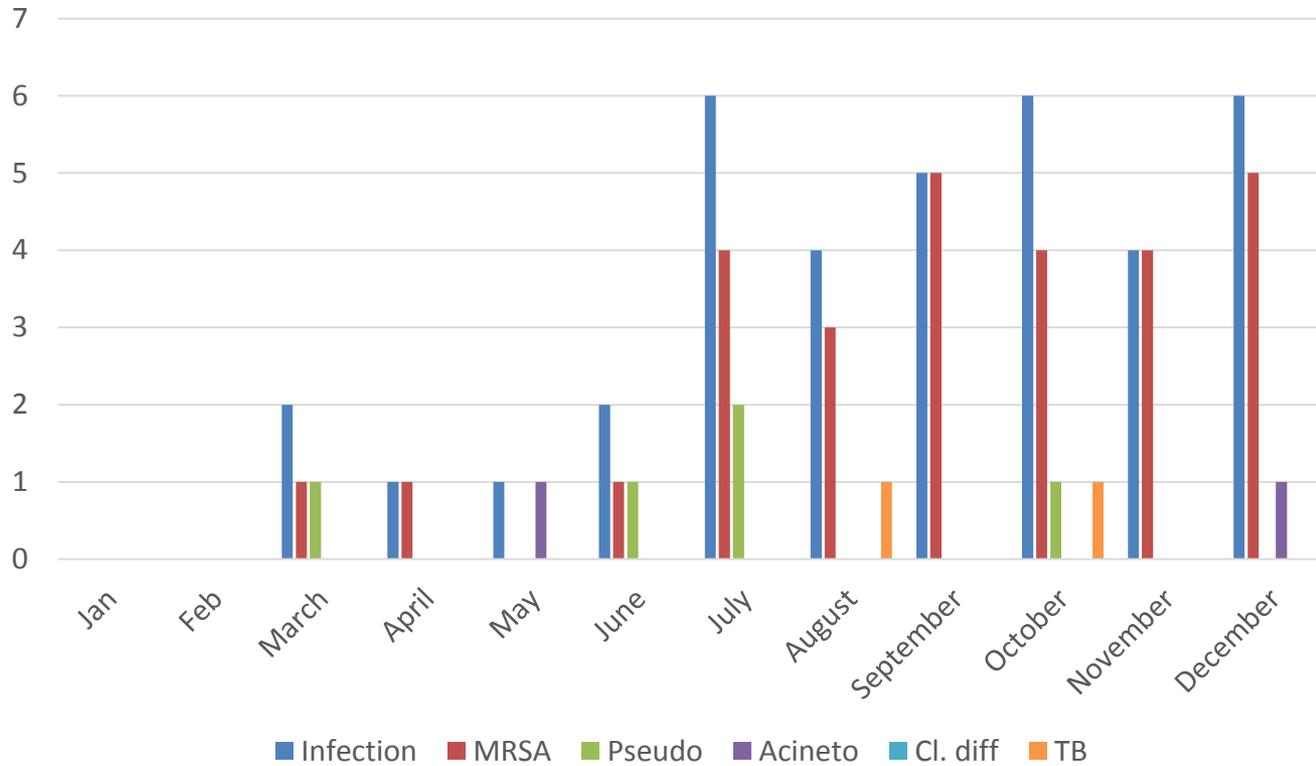
# Meta-analysis severe burns & HIV

AUTHORS, YEAR	COUNRTY	MORTALITY	MORBIDITY	ADULTS/KIDS
Edge et al, 2001	South Africa	No difference +/-; <b>except Aids</b> <b>100% mortality</b>	More infections Not statistically significant	Adults only
James et al, 2003	Malawi	↑ associated with sepsis	Equal infection rates	Adults & Kids
Sjoberg et al, 2004	Zimbabwe	No difference	Unknown	Unknown
Chayle et al, 2011	Uganda	↑ <b>if AIDS +</b>	Unknown	Adults & Kids
Sheyo, 2012	Zambia	No difference	↑ infections statistically +	Adults & Kids
Cloake et al, 2017	UK - South Africa	↑ mortality	↑ infections	Adults

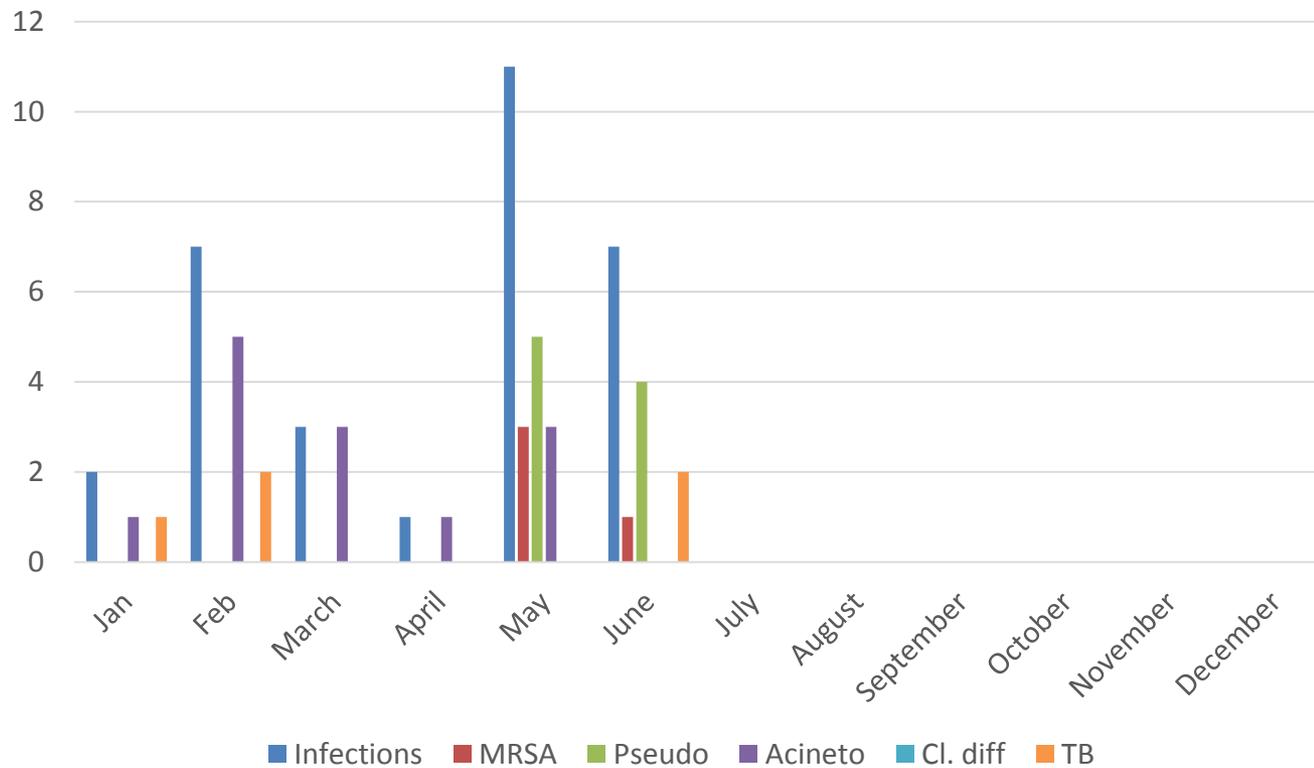
# Bacterial Profiles TBH BICU 2013



# Total Infections Recorded 2014

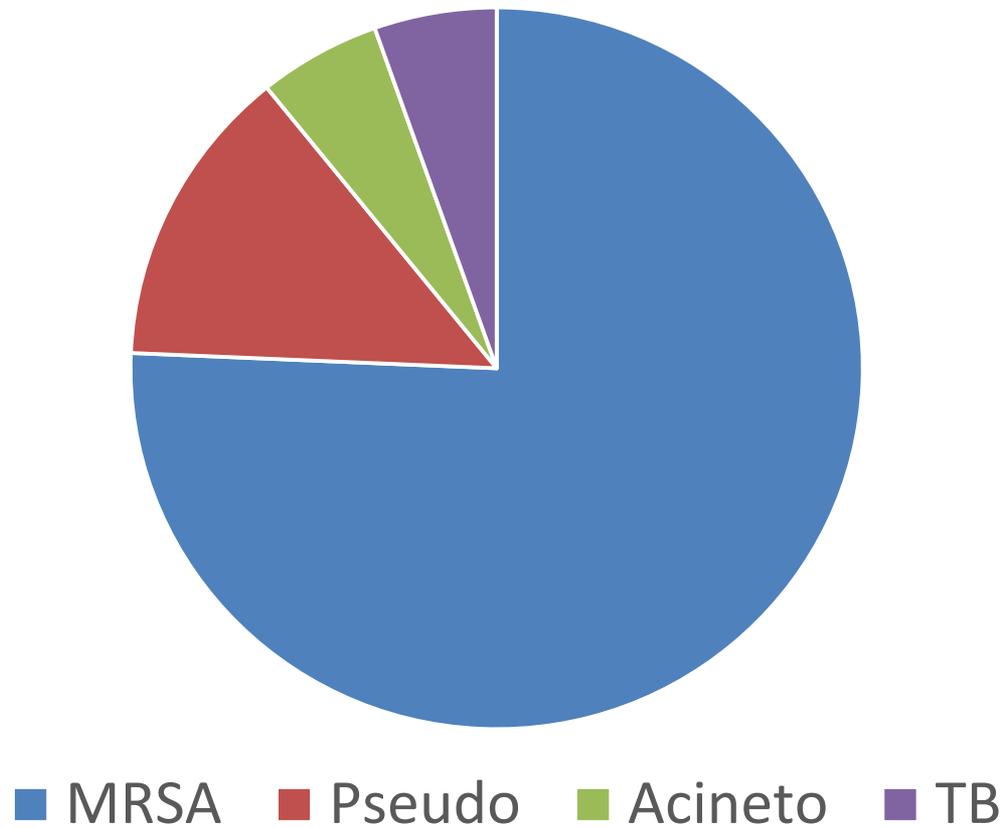


# Total Infections Recorded 2015



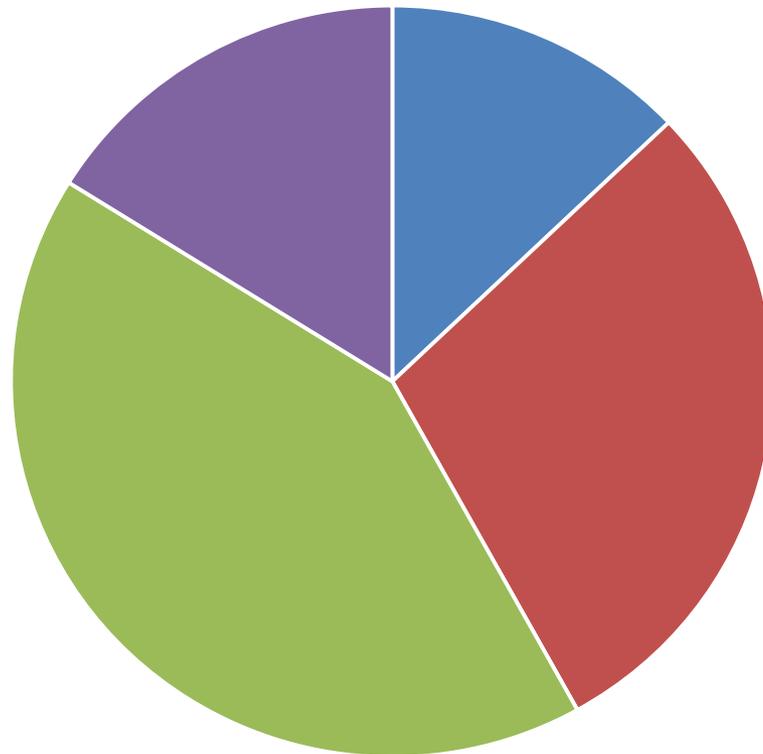
# Type of infections recorded 2014

Infection Type



# Type of infections recorded 2015

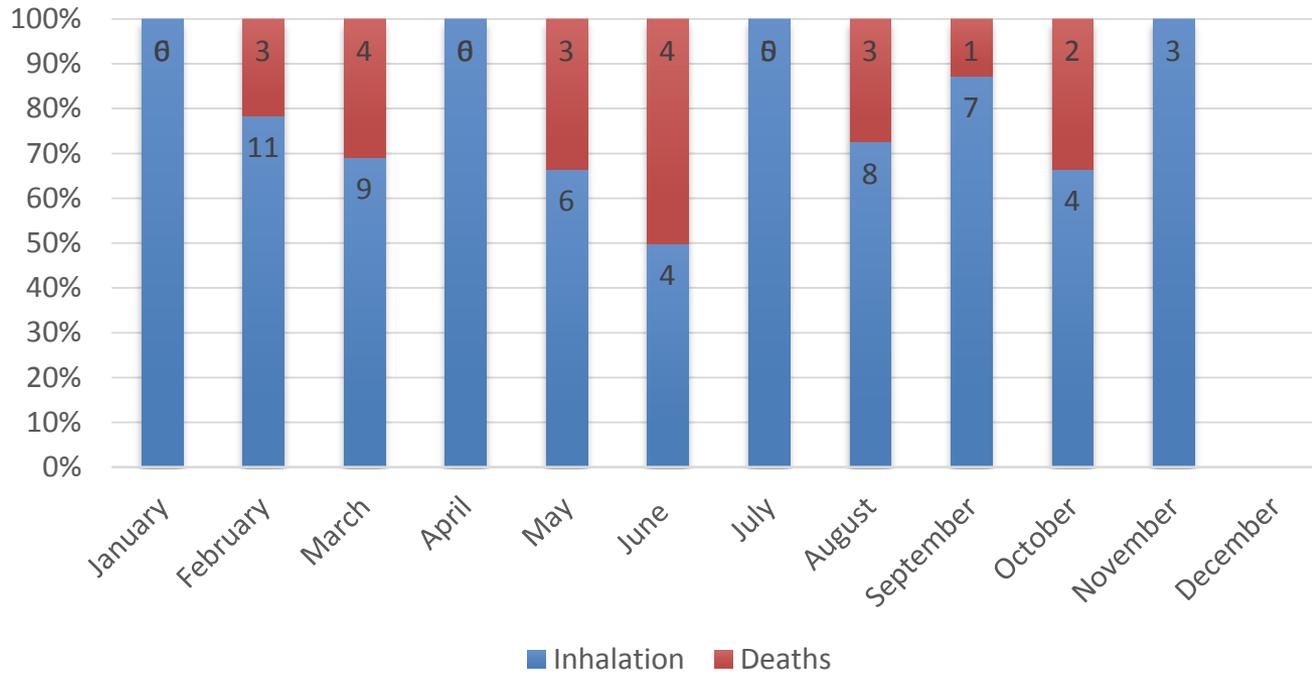
Infection Type



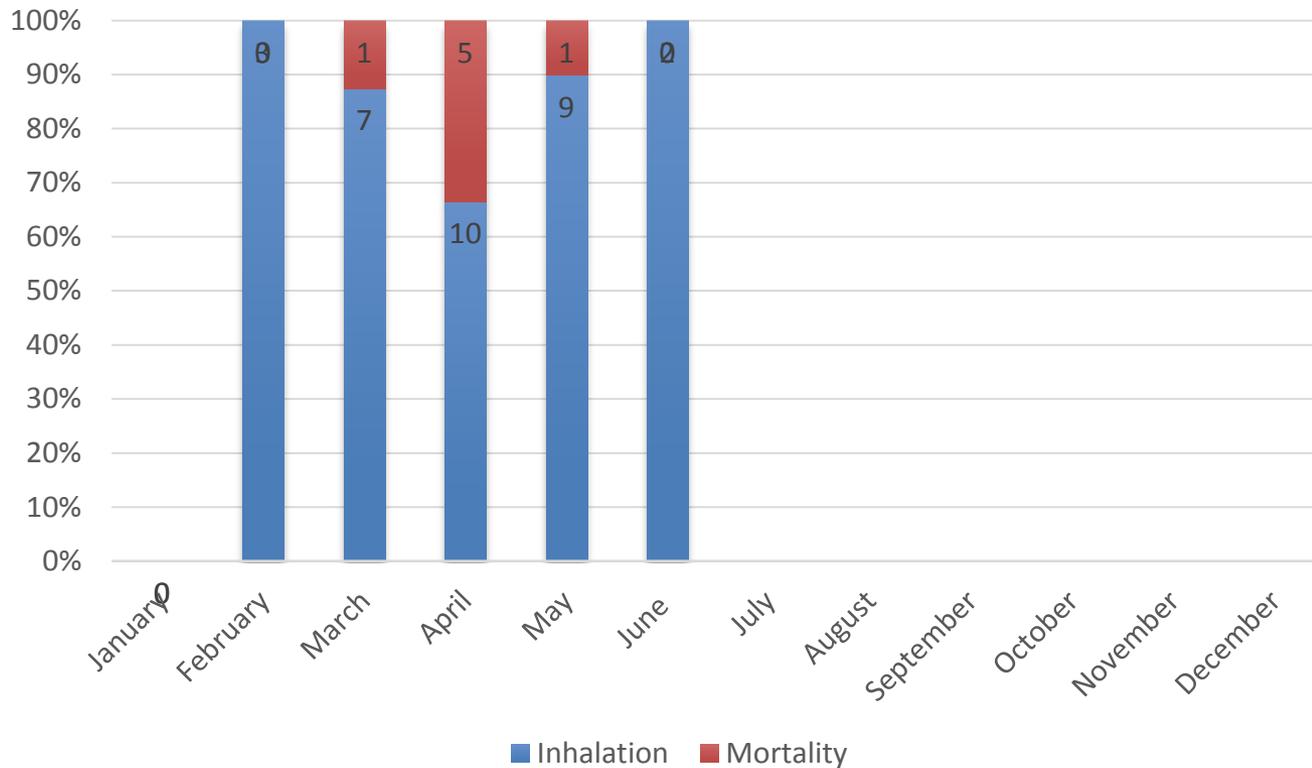
■ MRSA ■ Pseudo ■ Acineto ■ TB

# Mortality in patients who suffered inhalation in 2014

Chart Title



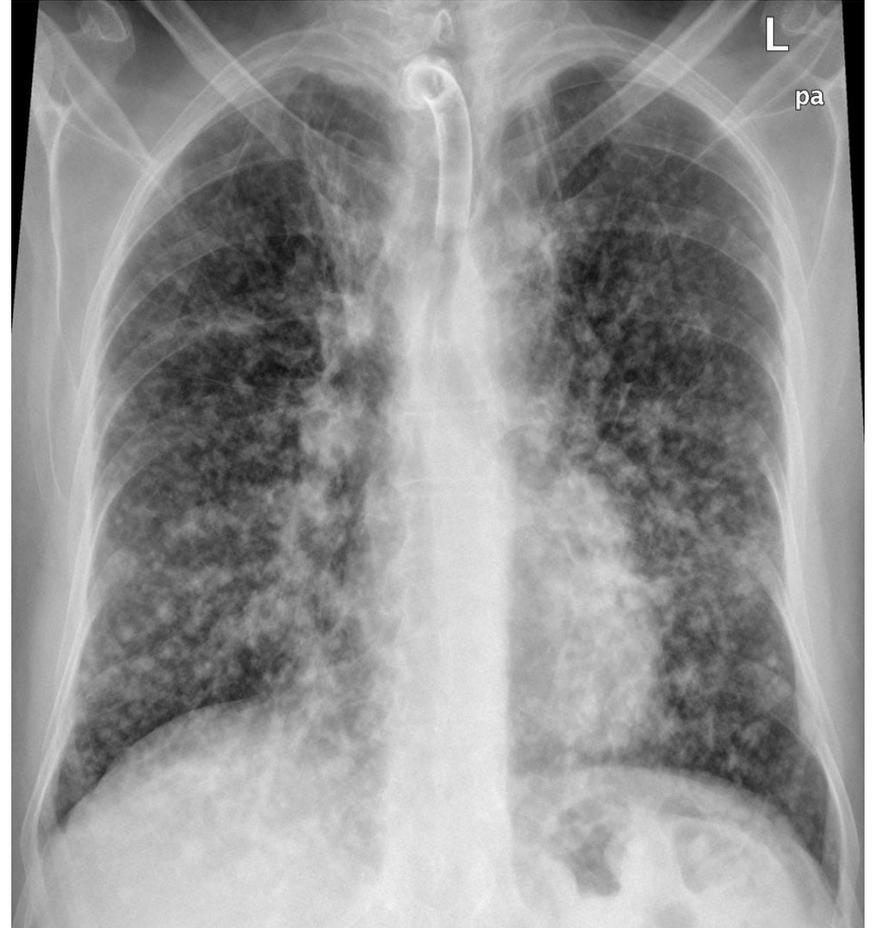
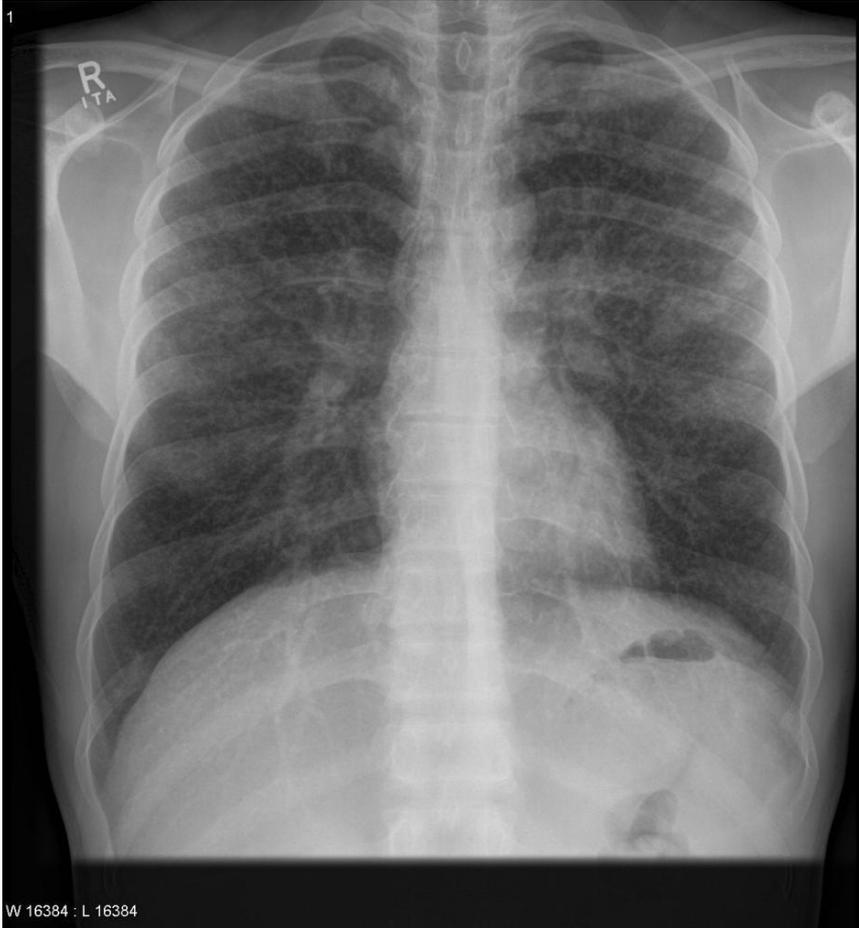
# Mortality in patients who suffered inhalation 2015



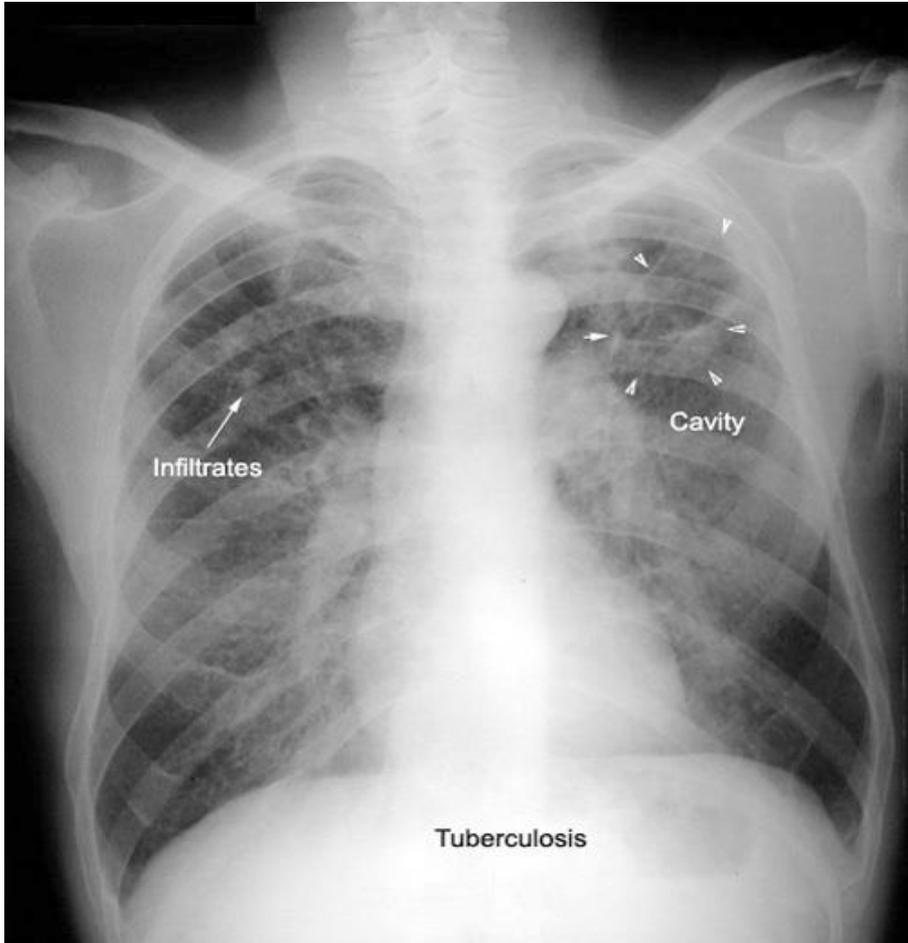
# X-ray Types

- Miliary PTB
- Focal cavities
- Pneumonia; cavities

# Miliary Tuberculosis



# Tuberculosis Cavitation's



# Pneumonia



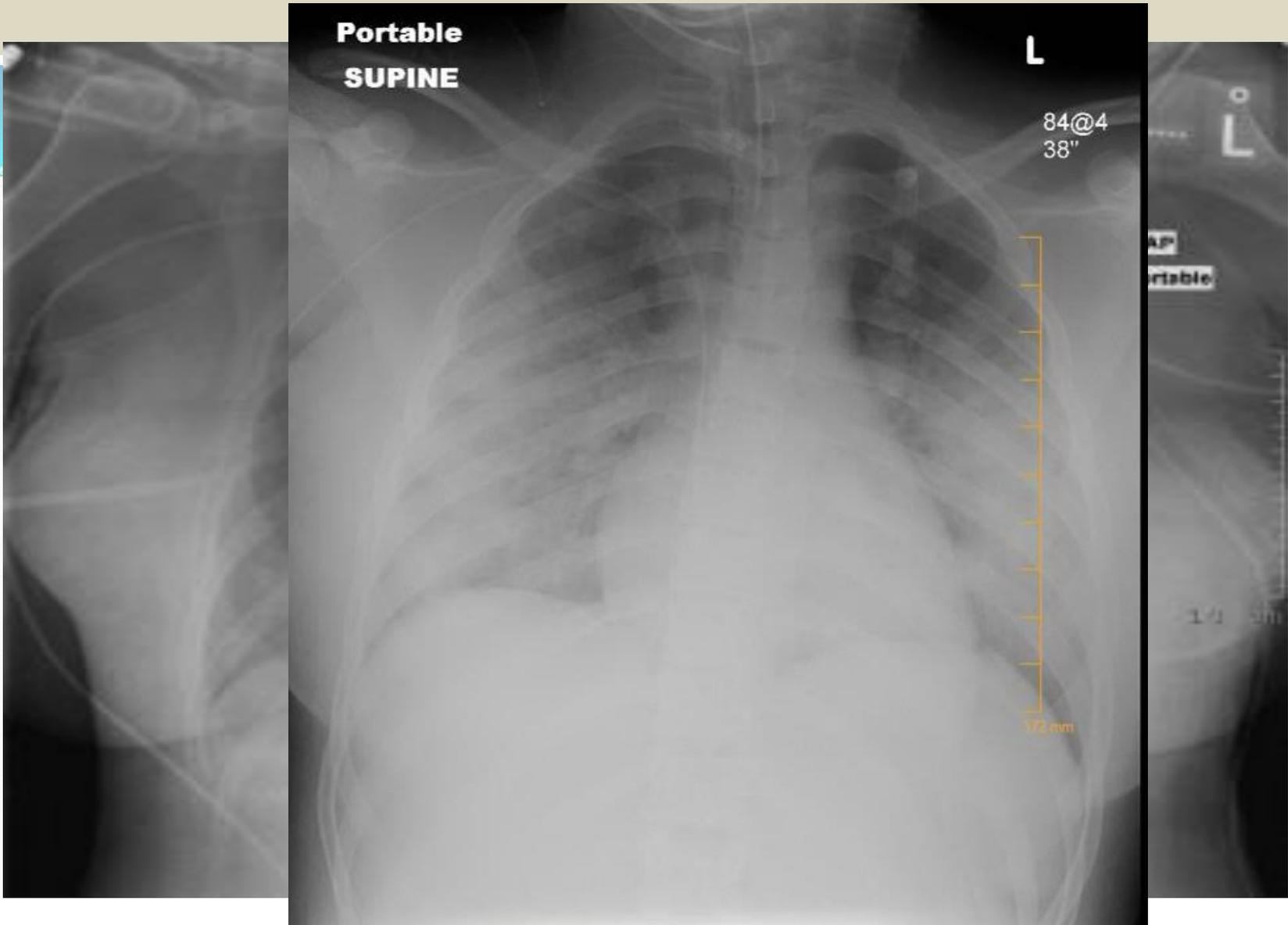
# Reactivation PTB

- Progressive secondary TB (reactivation of MTB) - apical cavity on CXR due to high V/Q ratio - usually for reactivation TB

# Aetiology of Cavities

- Cavity can be encountered in practically most lung diseases.
- Common diseases and their characteristics
- Primary Lung Cancer
  - Thick wall
  - Shaggy lumen
  - Eccentric cavitation
- Necrotizing Pneumonia
- Lung abscess
  - Gravity dependant segments
  - Thick wall
  - Air-fluid levels
- Tuberculosis
  - Superior segments
  - Infiltrate around
  - Bilateral
- Fungal infections
  - Aspergillus
    - Fungous ball
    - Sub acute invasive aspergillosis
- Metastatic disease
  - Thin walled (Squamous cell)
  - Thick wall (Adenoca)

# But how to know ?



# Failure to Extubate; re-intubation



# Results

- Common pattern
- On empiric TB treatment - with rapid effective results.

# Results: Common ICU Pattern

Inhalation  
Burn

Difficult  
Wean

Failed  
Extubation

Prolonged  
Ventilation

Lab test  
+/-; > = -

# Hirudo Medicinalis



# Discussion: Immunology in severe burns

- Postulate - immunosuppression - burn injury - reactivation of the PTB.



- Immune Response; Inflammatory R



- Pro-inflammatory Cytokines

# Immune Response in TB

Humoral IR

Cellular IR

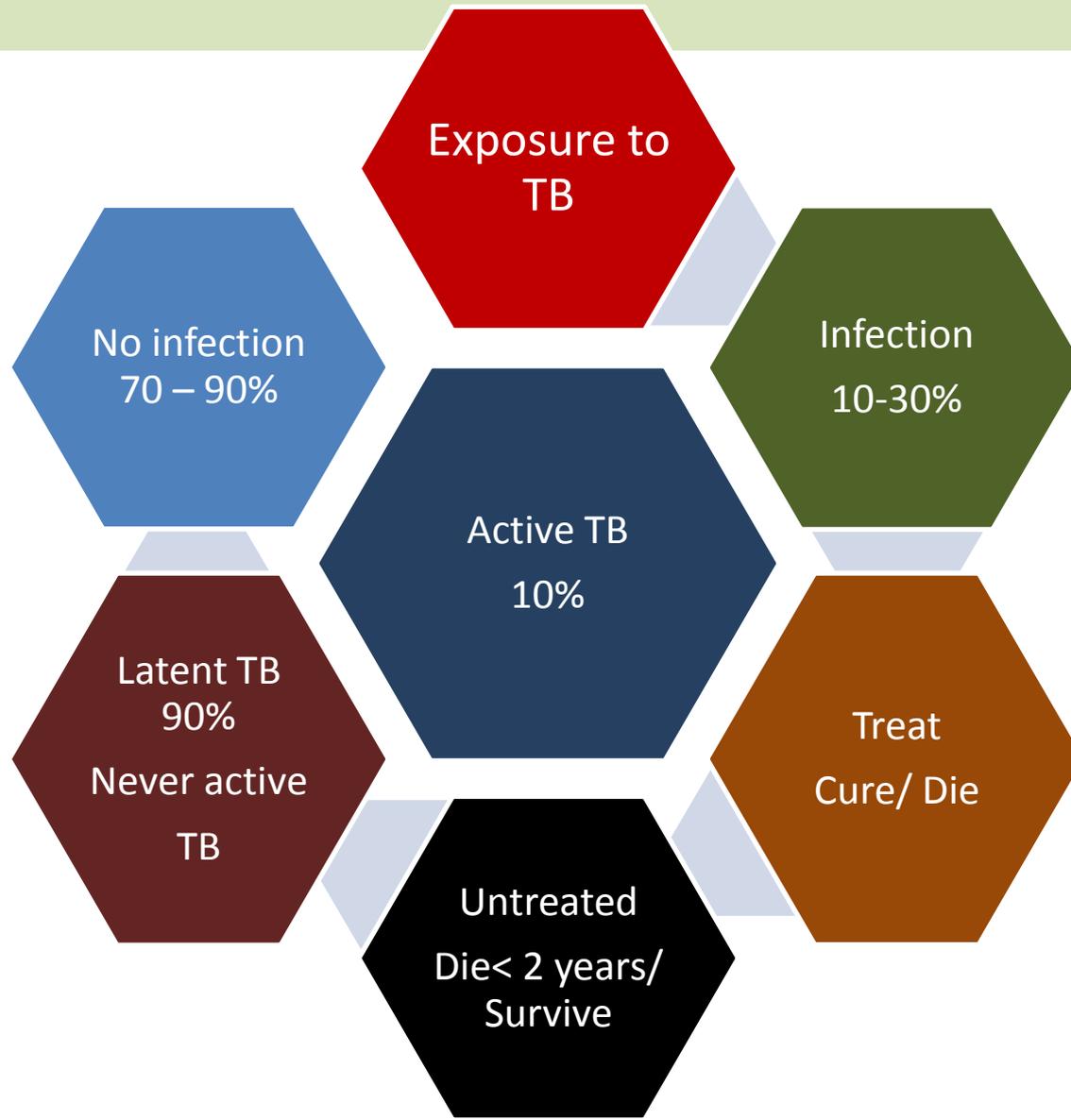
Antibodies are not protective

Cellular IR blocks disease extent < 4-6 weeks;  
granulomas – macrophages →  
Giant epithelioid cells

Delayed hypersensitivity →  
Cytotoxic T cells →  
Degeneration of centre

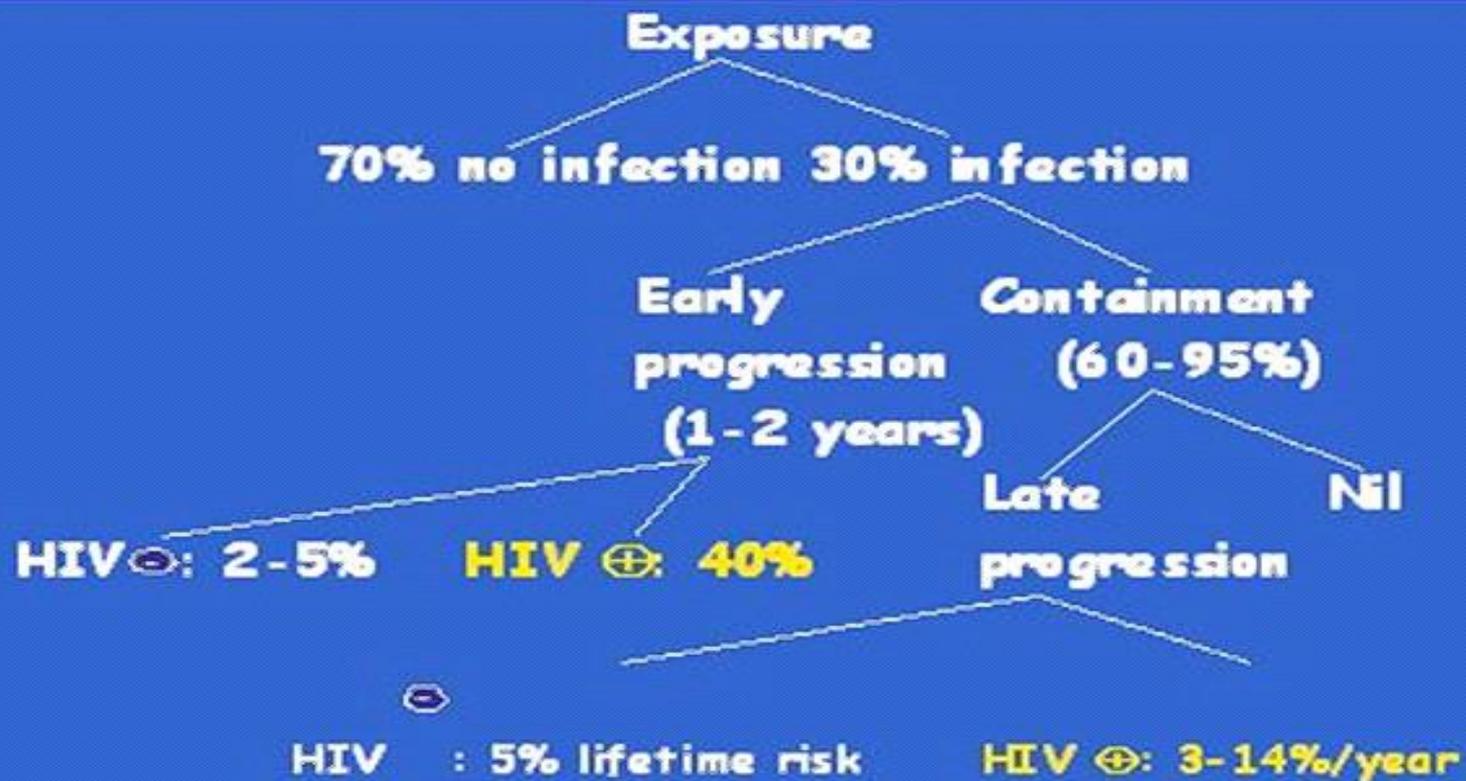
CD4(Th) cells dominate granulomas;  
CD8(Tc) cells sparser, more on the periphery –  
immunosurveillance function

# Natural Progression of TB



# South African gold miners cohort study – proportion with TB over time

## NATURAL HISTORY OF TB



## Hypoalbuminemia, MEDSCAPE

Updated: Aug 16, 2016

Author: Ruben Peralta, MD, FACS et al

### Background

Albumin, the body's predominant serum-binding protein, has several important functions.

Albumin comprises 75-80% of normal plasma colloid oncotic pressure and 50% of protein content. When plasma proteins, especially albumin, no longer sustain sufficient colloid osmotic pressure to counterbalance hydrostatic pressure, edema develops.

**Albumin transports** various substances, including bilirubin, fatty acids, metals, ions, hormones, and **exogenous drugs**. One consequence of hypoalbuminemia is that drugs that are usually protein bound are **free in the plasma**, allowing for higher drug levels, more rapid hepatic metabolism, or both.

Alterations in albumin level **affect platelet function**.

# Severe Burns

The immune-  
with hypo-  
naemia plays a role  
results.

COLOGY LETTERS

SPANDIDOS PUBLICATIONS

TERS 7: 373-377, 2014

indicate that **chronic inflammation** may be associated with impaired immune function, such as an impaired T-cell response. Various inflammatory proteins, including sIL-2R, VEGF and IL-17. The key mechanisms leading to cancer cachexia, in which nutritional impairment is a major clinical issue, appear to be primarily immune reactions caused by chronic inflammation.

# Discussion: Reliability of laboratory TB tests

- Comparative Study of GeneXpert with ZN Stain and Culture in Samples of Suspected Pulmonary Tuberculosis Monika Agrawal et al. May 2016, J Clin and Diagn Res
- There are number of tests available for the diagnosis of tuberculosis but conventional microscopy has low sensitivity and culture although gold standard, takes longer time for positivity.
- On the other side, Nucleic acid amplification techniques due to its rapidity and sensitivity not only help in early diagnosis and management of tuberculosis especially in patients with high clinical suspicion like immunocompromised patients, history of contact with active tuberculosis patient etc., but also curtail the transmission of the disease.
- **Materials and Methods:** We retrospectively reviewed the respiratory samples of suspected pulmonary tuberculosis (including Bronchoalveolar lavage and sputum) of 170 patients from Jan 2015 to Nov 2015 for ZN stain, culture and GeneXpert (Xpert<sup>®</sup> MTB/Rif assay).
- The sensitivity, specificity, PPV and NPV of GeneXpert and ZN microscopy were calculated using Liquid culture of Mycobacterium tuberculosis as gold standard.
- **Results:** 170 samples. 14 samples were positive by all three methods (8.2 %). The overall sensitivity, specificity, PPV and NPV of GeneXpert were 86.8%, 93.1%, 78.5% and 96% respectively and for BAL sample, 81.4%, 93.4%, 73.3% and 95.7% respectively. The overall sensitivity and specificity of AFB smear microscopy were 22.2%, and 78.5% respectively and for BAL sample 22.2% and 100% respectively. For AFB negative samples sensitivity and specificity were 79.1% and 93.1% respectively.
- **Conclusion:** GeneXpert = higher sensitivity 86,8% > AFB smear microscopy 79.1% in respiratory samples.
- GeneXpert can be a useful tool for early diagnosis of patients with high clinical suspicion of pulmonary tuberculosis = < 2 hours for diagnosis.
- Positive GeneXpert, but culture negative results should be read cautiously and be well correlated with clinical and treatment history of the patient.
- Gene Xpert simultaneously detects Rifampicin resistance - especially beneficial - MDR and HIV associated tuberculosis – further studies.

# Test Reliability

- Khalil & Butt. J Coll Physicians Surg Pak, 2015
- Diagnostic yield of Gene-expert with BPL higher if patient was smear negative or sputum scarce TB.

# Discussion: Role of the Lungs

- Clearance of bacteria from the lungs in ARDS could also play a role. The development of biofilms in the airways where the PTB can grow without being dislodged or detected could play a role as well.

# PIM2 vs PTB

- PIM - integral -composition -mycobacterial envelope = found in various phosphatidyl-myo-inositol mannosides (PIM).
- PIM2 - many biological functions:
  - a. PIM2 fostered active macrophages mediated by TLR2, led to activation of mitogen-activated protein kinases (MAPK), AP-1, and nuclear factor- $\kappa$ B (NF- $\kappa$ B)
- PIM2 recruited NKT cells into granulomas and has pulmonary granuloma-forming properties
- PIM induces adherence of *M. tuberculosis* bacilli to cells that are nonphagocytic
- inflammatory responses similar to mycobacteria bacilli could be initiated or affected by PIM2, the mycobacterial envelope antigen.
  
- *Hoppe HC et al. Identification of phosphatidylinositol mannoside as a mycobacterial adhesin mediating both direct and opsonic binding to nonphagocytic mammalian cells. Infect Immun. 1997;65(9):3896–905*

# Discussion: Infections Contribute to Mortality in Severe Burns

MRAB

RSA

RTB

Herpes S

# Conclusion

- **Observation:** Improved Outcome Empirical TB Treatment
- **Common Pattern:** Inhalation Burn w/wo HIV - difficult to get off the ventilator; > likely absence lab confirmation

# Thank You





The South African Burn Society  
**17th Congress 2017**

Vineyard Hotel • Cape Town  
3rd - 5th August 2017