put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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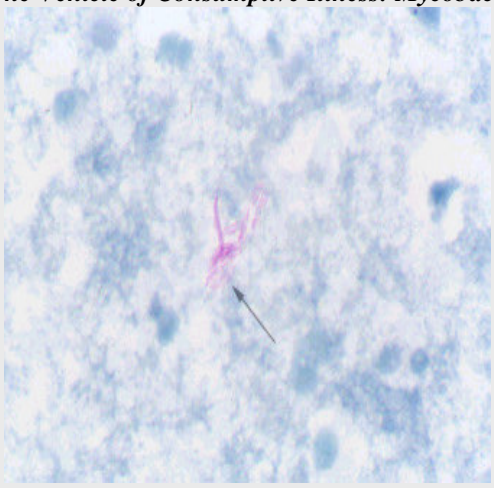
Mechanism of Tuberculosis

Shamelessly torn from "The secret lives of the pathogenic mycobacteria, by Cosma et.al, Annual Review of Microbiology. 2003.Vol.57 pg. 641

The Vehicle of Consumptive Illness: Mycobacterium Tuberculosis, "Captain among these Men of Death" (John Bunyon 1660)



- **Rod-shaped (bacillus)**
- **Gram-Positive** but not surrounded by peptidoglycan envelope, not even a cell wall
- **Obligate Aerobes** love the apex of lung, where the pO2 is highest
- **Facultative Intracellular Pathogens** living in macrophages
- **Slow-growing** with a generation time of 12 to 18 hours
- **Hydrophobic** with a high lipid content in the cell wall. Because the cells are hydrophobic and tend to clump together, they are impermeable to the usual stains
- **"Acid-fast bacilli"** because of their lipid-rich cell walls, which are relatively impermeable to various basic dyes unless the dyes are combined with phenol. Once stained, the cells resist decolorization with acidified organic solvents and are therefore called "acid-fast"
- Originally before multicellular life, the mycobacteria developed as intracellular pathogens who lived in amoeba parasitically, training for future battles with our macrophages.
- Became a human pathogen roughly 6000 BC, when we domesticated cattle. M.bovis jumped across species to the first humans who fraternised with cows. LET THAT BE A LESSON.

DROPLET TRANSMISSION:
Only require about 5 bacteria to penetrate…

Fail-safe host entry system: any number of receptors used

M. Tuberculosis

USING THE MACROPHAGE'S OWN RECEPTORS
to gain entry:
complement receptors
fibronectin receptors
mannose receptors
all of which induce phagocytosis

endocytosis

Intracellular survival

← MACROPHAGE →

phagosome

M. Tuberculosis

Alkalinisation of the phagosome (less caustic environment),
Reactive oxygen species scavengers released, reducing oxidative damage to the M.Tb

Prevents fusion of phagosome and lysosome

LYSOSOME
Full of nasty chemicals: acidic hydrolases etc…

Eventually the phagosome breaks… Mycobacteria spew forth and replicate inside the macrophage, eventually rupturing it and spreading into surrounding tissues

INDUCTION OF MACROPHAGE-SUPPRESSING CYTOKINES:
TGF-beta
Interleukin-10
Reduce macrophage activity, counteract production of lytic molecules and proteases

Because these are intracellular parasites, humoural immunity is useless..
BUT the macrophages can still secrete IL-12, to activate T-H1 cells

1 week post infection:
despite impaired monocyte function, some mycobacterial components do get presented by APCs at the hilar lymph nodes, which then ENLARGE
→ **HILAR LYMPHADENOPATHY**

T-helper 1 lymphocytes
Are crucial to the defensive mechanisms: they activate the dumbfounded macrophages with interferon-gamma; a cascade of responses results in
GRANULOMA FORMATION

GRANULOMAE
Macrophages transform into "epitheliod" cells, palisading around the central area of M.Tb infection. This are becomes avascular and necrotic, hence
CASEATING NECROSIS

T-cell Cytokines
Are all responsible for the constitutional symptoms of TB, including
ANOREXIA
WEIGHT LOSS
PYREXIA
NIGHT SWEATS

A large area of confluent granulomae places stresses on the healthy lung, and the inflammatory response causes a chronic dry cough. CONTINUOUS COUGHING CAN CAUSE BRONCIOLAR RUPTURE AND HENCE
HAEMOPTYSIS