Mechanism of Tuberculosis

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
- Faculative 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

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

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

**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 area 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**

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**