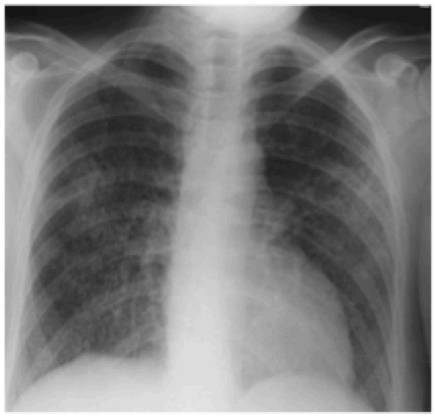
Adult with fever,cough and weight loss



Miliary shadowing

Observations: Multiple Miliary nodules in both lungs
Interpretation: Miliary TB

TB treatment history

- Before TB antibiotics,many patients were sent to sanatoriums and followed a regimen of bed rest, open air, and sunshine
  - TO try and avoid secondary infections

TB Vaccine

- An avirulent bacillus was produced. Result was inability to cause tuberculosis disease in research animals from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, *Mycobacterium bovis*
- BCG vaccine first used in humans in 1921

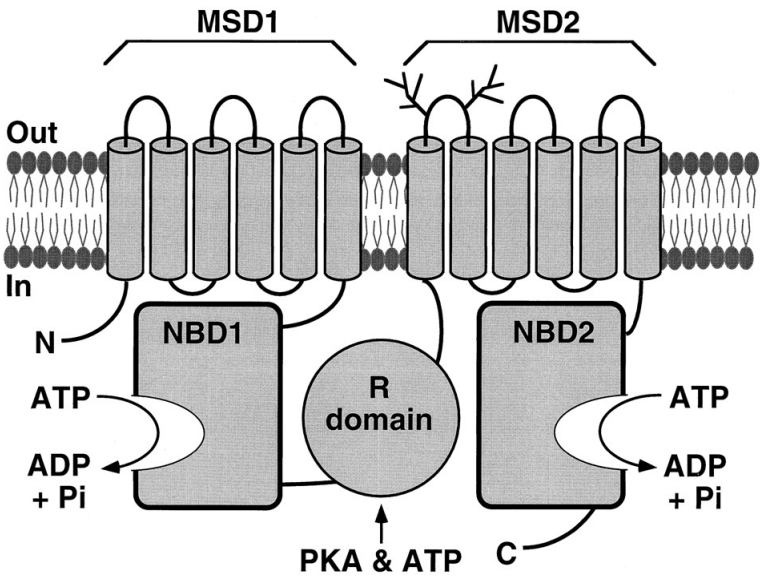
TB treatment

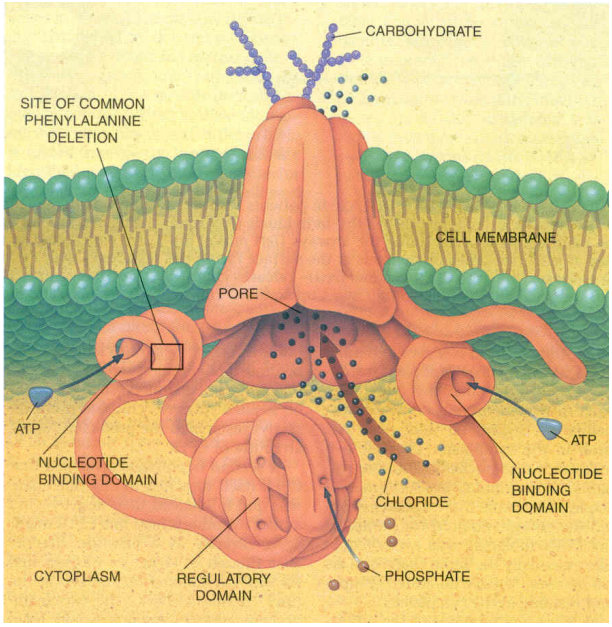
- First TB antibiotics were discovered in 1940s and 1950s
- Streptomycin (SM) discovered in 1943
- Isoniazid (INH) and p-aminosalicylic acid (PAS) discovered between 1943 and 1952
- First TB death rates began to drop dramatically

Present day TB antibiotics

- First line antibiotics:
  - Isoniazid (INH) – inhibits synthesis of mycolic acid, required for mycobacterial cell wall
  - Rifampicin (RIF) – suppresses initiation of RNA synthesis by inhibiting bacterial RNA polymerase
  - Pyrazinamide (PZA) – binds to the ribosomal protein S1 (RpsA) and inhibits translation
  - Ethambutol (EMB) – inhibits arabinosyl transferases involved in cell wall biosynthesis & inhibits metabolism
- Taken orally and absorbed in GI tract- into blood

CFTR model

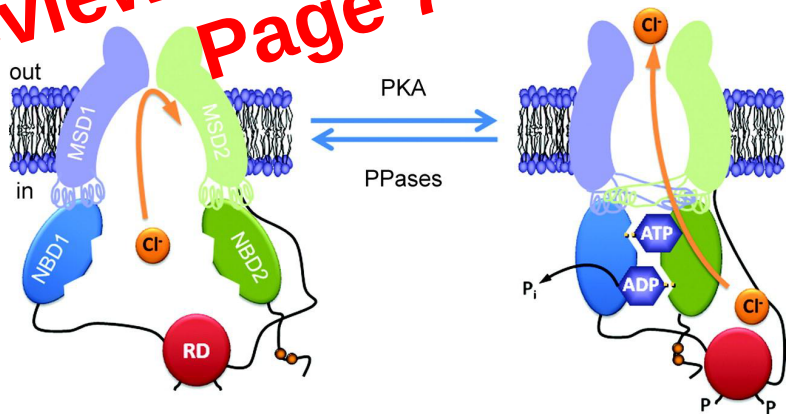




- Consists of: 2 Membrane Spanning Domains (MSD), 2 Nucleotide Binding Domains (NBD) and a Regulatory (R) domain

Model of ATP-dependant gating of CFTR

- In absence of R domain phosphorylation – channel is closed
- Cyclic AMP stimulates PKA to phosphorylate serine on R domain
- CFTR binds ATP at NBDs and conformational change occurs – channel opens



CFTR mutations

- Approx 1900 mutations in CFTR gene have been identified – highest density in two nucleotide binding regions
- Some in transmembrane regions
- Majority (~40%) are missense mutations
- Mutations cause varying degrees of CF
- Some have no effect