

Selected Pathogens of Public Health Importance, continued Antibiotics

April 27, 2004

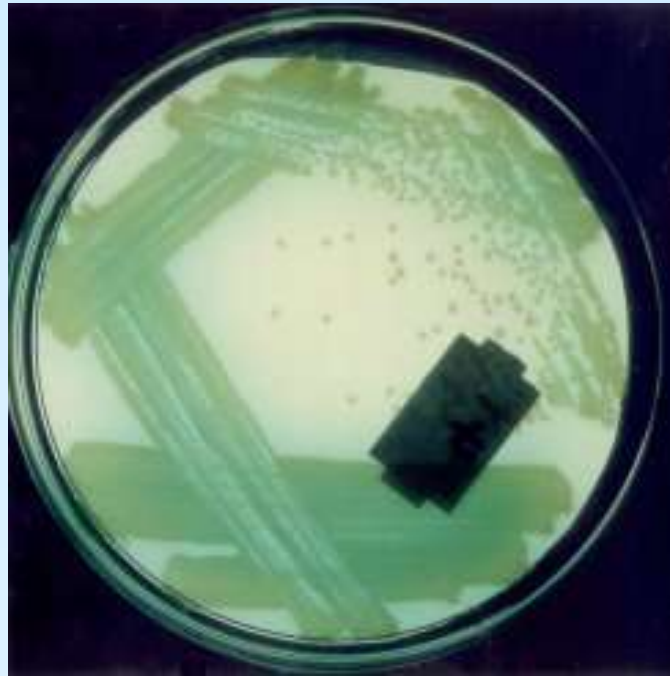
Pseudomonas aeruginosa

- Gram negative rod
- Motile
- Obligate aerobe – does not ferment
- Environmental organism – widespread in nature

Pseudomonas aeruginosa

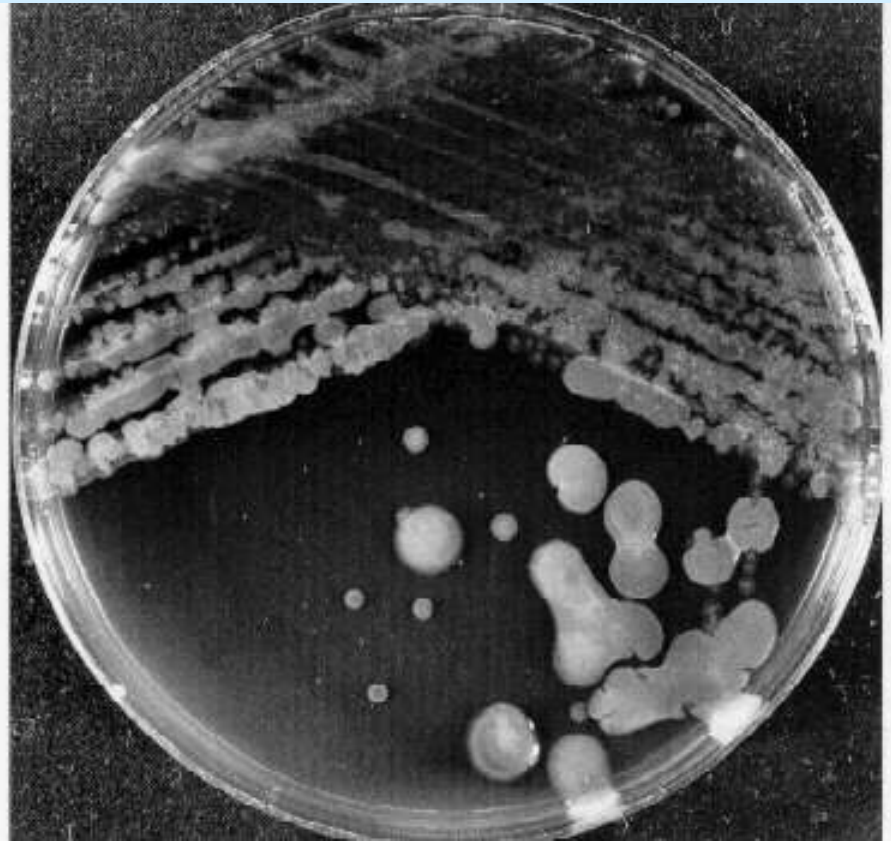
- Folliculitis
 - Associated with contact with hot water
- Bacteremia and septic shock
 - Hospitalized patients
- Cystic fibrosis patients
 - “Mucoid” phenotype

Pseudomonas aeruginosa



Fluorescent green color due to production of fluorescein

Mucoid *Pseudomonas aeruginosa* Colonies



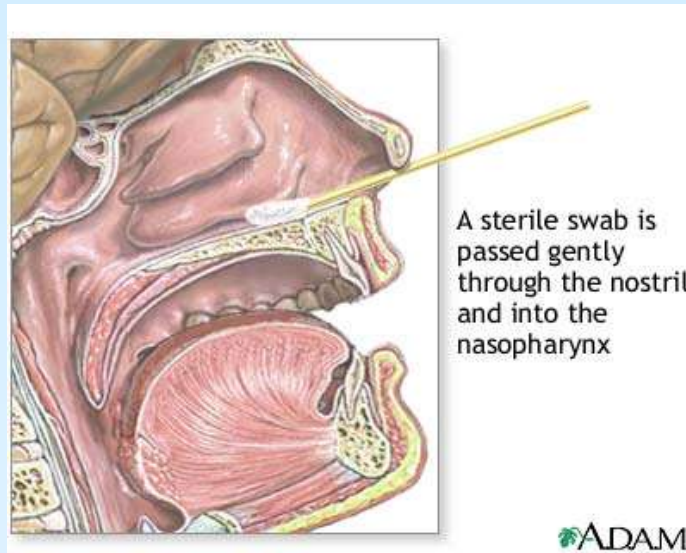
Pseudomonas aeruginosa



Bordetella pertussis

- Causative agent of whooping cough
- Small Gram negative coccobacilli
- Sensitive to toxic substances found in ordinary lab media
- Produces disease only in humans
 - *B. bronchiseptica* causes kennel cough in dogs

Specimen Collection for *B. pertussis* culture



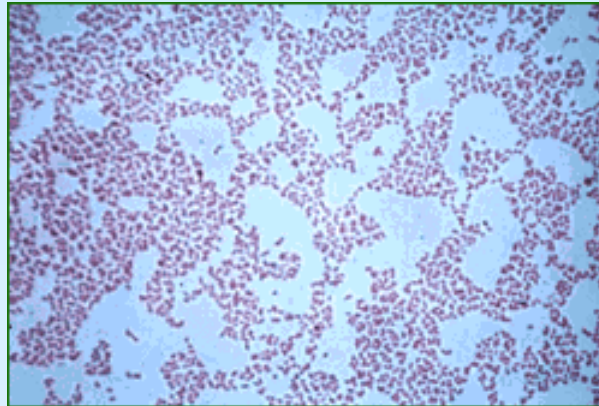
Direct Detection

- Culture
- Direct Fluorescent Antibody testing
- Nucleic acid production (PCR)

B. pertussis growth on Charcoal Blood Agar



B. pertussis Gram Stain



Cultural Confirmation of *B. pertussis*

- Slide agglutination test
- DFA

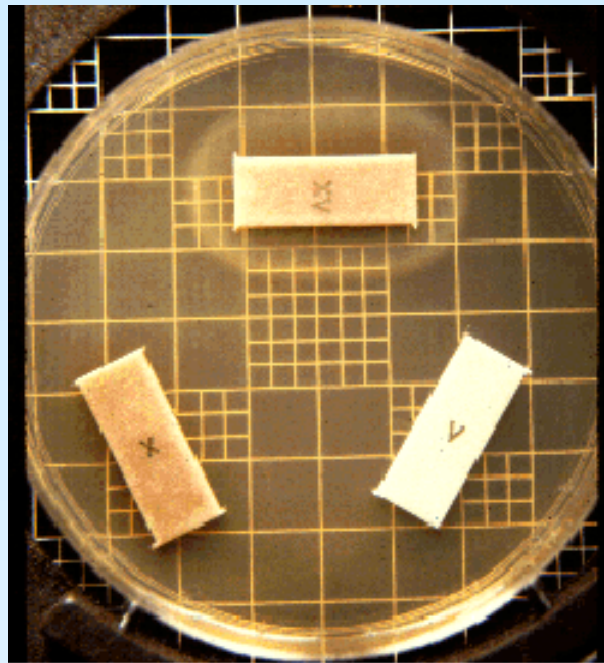
Haemophilus influenzae

- Bacterial meningitis
- Acute epiglottitis
 - Now both preventable by vaccination
 - <100 cases/year in USA
- Worldwide
 - 3 million cases/year
 - 400,000 – 700,000 deaths/year

Haemophilus influenzae

- Particular growth requirements
 - X factor = heme
 - V factor = NAD

X and V Factors

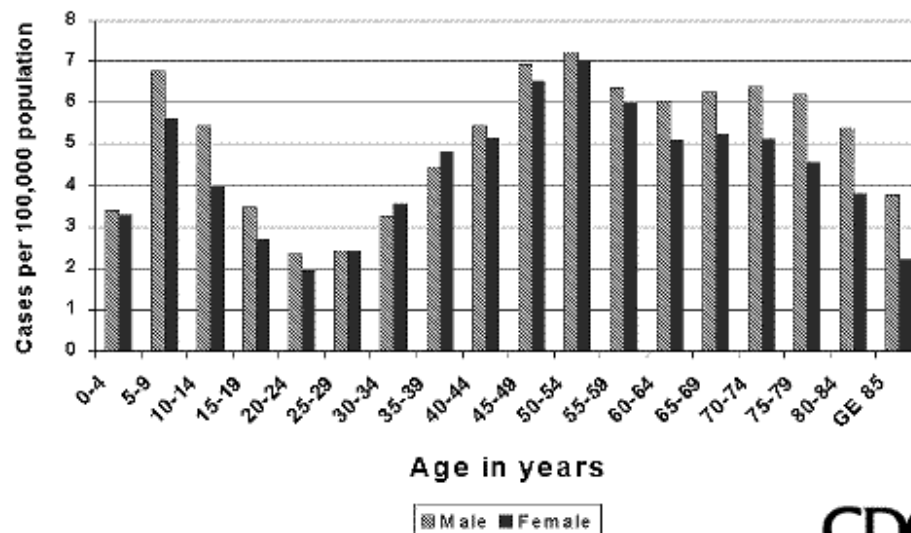


Haemophilus influenzae /nutritional factors
X=hemin V= NAD

Lyme Disease

- *Borrelia burgdorferi* is causative agent
- Leading cause of vector-borne infectious illness in the U.S.
- About 23,000 cases reported in 2002, though the disease is greatly under reported.

Average annual incidence of reported cases of Lyme disease, by age group and sex, United States, 1992-1998*

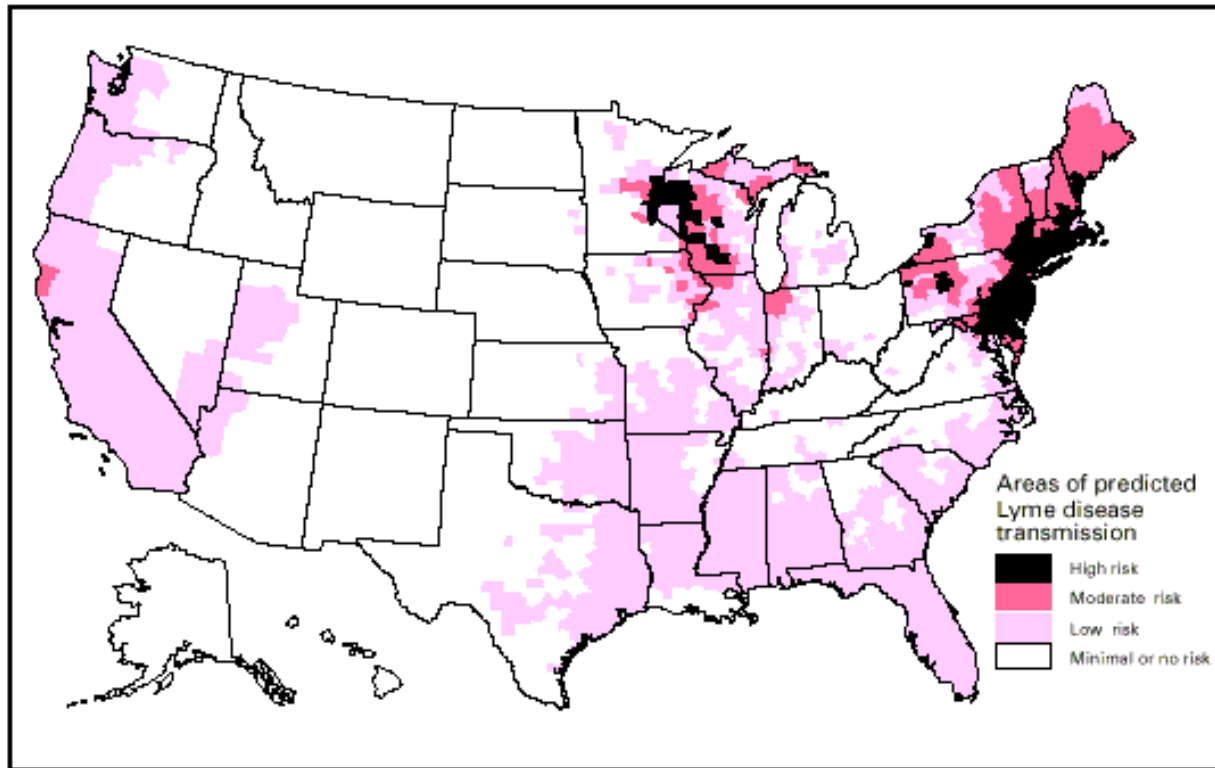


*n=74,732; PA excluded due to missing data



Lyme Disease Risk

National Lyme disease risk map with four categories of risk



Note: This map demonstrates an approximate distribution of predicted Lyme disease risk in the United States. The true relative risk in any given county compared with other counties might differ from that shown here and might change from year to year. Risk categories are defined in the accompanying text. Information on risk distribution within states and counties is best obtained from state and local public health authorities.

Lyme Disease

- Vector is tick
 - *Ixodes dammini* (now *I. Scapularis*)
 - *Ixodes pacificus*



Transmission Cycle

- Immature ticks become infected by feeding on small rodents
 - white-footed mouse
 - other mammals
- In later stages, these ticks then transmit *B. burgdorferi* to humans and other mammals during the feeding process
- *B. burgdorferi* is maintained in the blood systems and tissues of small rodents

Lyme Disease (2)

- Within days to weeks following a tick bite, 80% of patients will have a red, slowly expanding rash (called erythema migrans)
- Accompanied by
 - general tiredness
 - Fever
 - Headache
 - stiff neck
 - muscle aches
 - joint pain

Bull's Eye Rash



Lyme Disease (3)

- If untreated, weeks to months later some patients may develop
 - Arthritis, including intermittent episodes of swelling and pain in the large joints
 - Neurologic abnormalities
 - aseptic meningitis
 - facial palsy
 - motor and sensory nerve inflammation (radiculoneuritis)
 - encephalitis
 - rarely, cardiac problems, such as atrioventricular block, myopericarditis or cardiomegaly

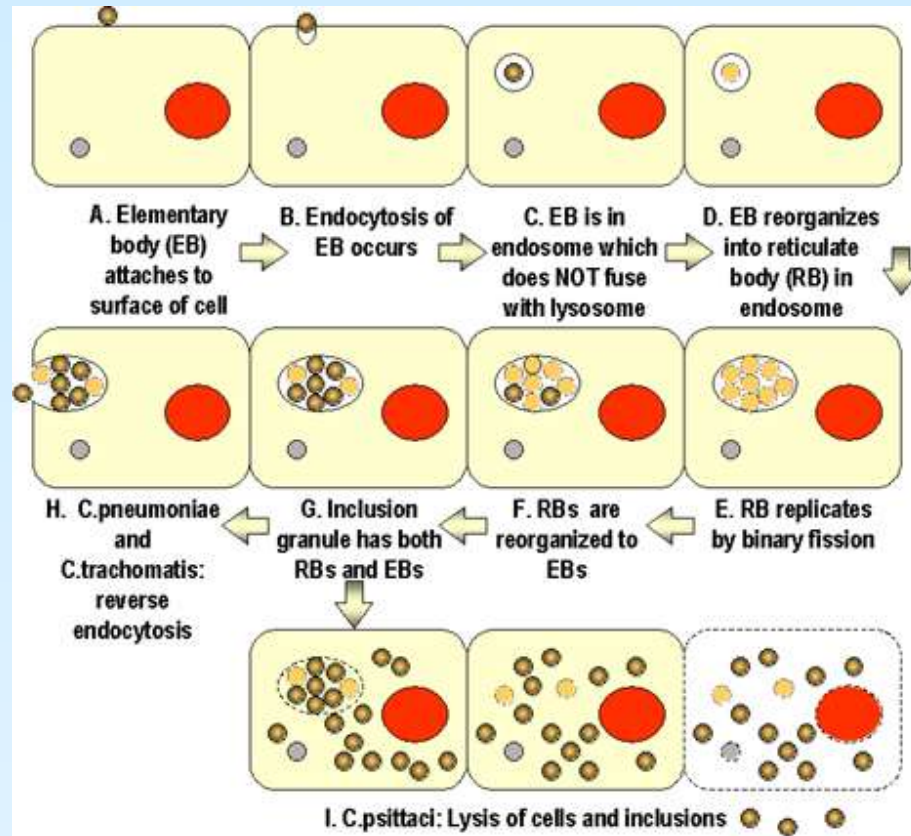
Borrelia burgdorferi



Chlamydia trachomatis

- Chlamydia are intracellular parasites
- Unique life cycle
 - Elementary body (EB)
 - Metabolically inert
 - Enters host cell
 - Becomes reticulate body
 - Reticulate body (RB)
 - Undergoes repeated binary fission
 - Daughter elementary bodies are released from cell

Chlamydia Life Cycle



Chlamydia in California Women, 2002

- 450/100,000 females
- Percent positive by clinic:
 - Family planning 4.3
 - STD clinic 10.3
 - Adult corrections 8.6
 - Juvenile detention 14.3
 - Other 6.7

Positive Tests from Family Planning Clinics

- Age 15-19 7.0%
- Age 20-24 5.5%
- Age 25-29 2.5%
- Age >30 2.0%

Laboratory Testing

- Culture based tests are difficult
 - Require cell culture capabilities
 - Can grow in many different cell cultures
 - Test sensitivity depends on quality of submitted specimen
- Prevalence of this infection requires screening techniques

Commonly Used Laboratory Tests

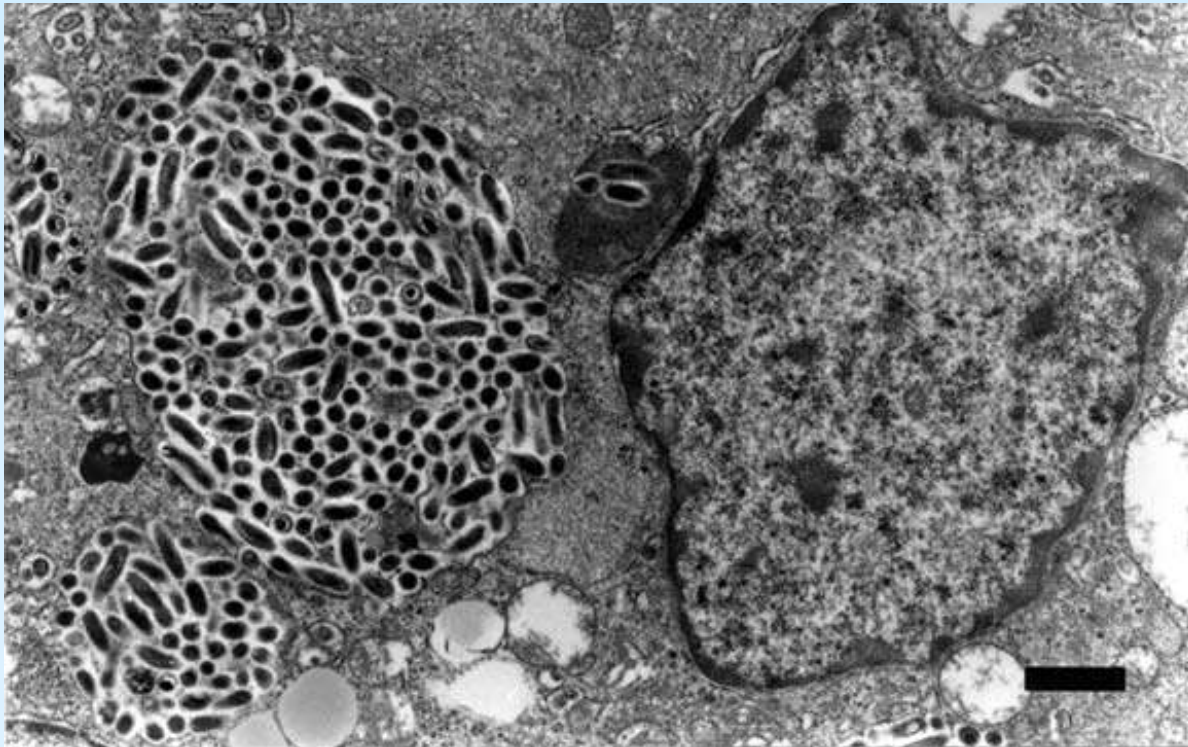
- Microscopy
 - Giemsa stain or DFA test
- Molecular tests - Amplification tests
 - PCR
 - Ligase chain reaction
 - Transcription mediated amplification
 - Molecular tests are not admissible as evidence in US courts
- Antigen tests – ELISA
 - Neither sensitive nor specific
 - Not suitable for use alone in screening

Q fever

- Causative agent is *Coxiella burnetii*
 - Obligate intracellular parasite
 - Depends on host cell for ATP
- Has been identified in
 - Arthropods
 - Fish
 - Birds
 - Rodents
 - Marsupials
 - Livestock
- Infects >40 species of ticks on 5 continents



Coxiella rickettsii



Q Fever (2)

- Cattle, sheep and goats are reservoirs for human infection
 - Organism is found in high concentrations in
 - Urine
 - Feces
 - Placental tissue
 - Amniotic fluid
- Route of transmission to human is often by aerosol following parturition of an infected animal
- Infectious particles can spread by wind
- Raw milk can be a source of infection

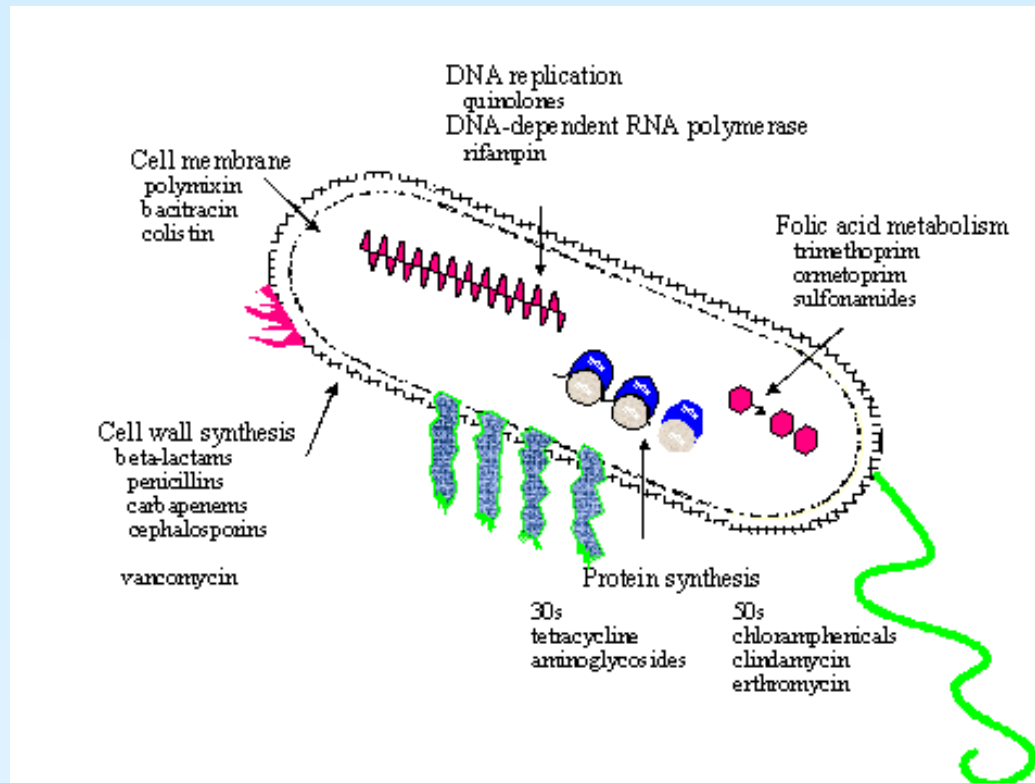
Q Fever (3)

- High fever
- Headache
- Flu-like symptoms
- About half of patients develop pneumonia

Antimicrobials

- Spectrum of activity
 - Broad
 - Effective against Gram positive and Gram negative organisms
 - Narrow
 - Effective against a single taxonomic group
- Modes of action
 - Bacteriocidal
 - Bacteriostatic

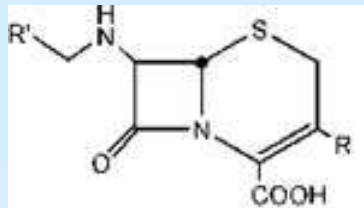
Action of Antimicrobials



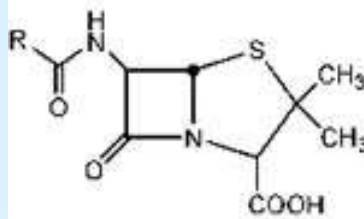
Inhibition of Cell Wall Synthesis

- Penicillins and Cephalosporins
 - Contain β -lactam ring
 - Attach to enzymes that crosslink peptidoglycans
 - PBP's = penicillin binding proteins
 - Fungi not affected
- Vancomycin
 - Attaches to peptide link during cell wall synthesis

Inhibition of Cell Wall synthesis

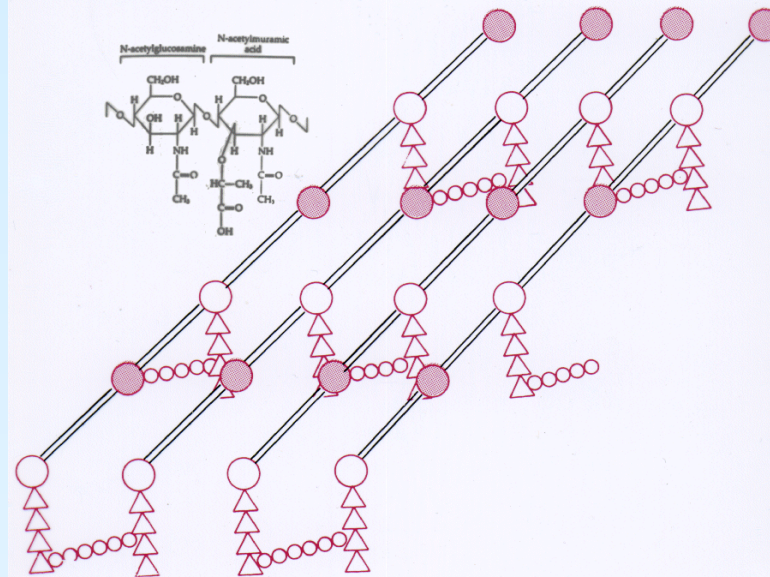


Cephalosporin

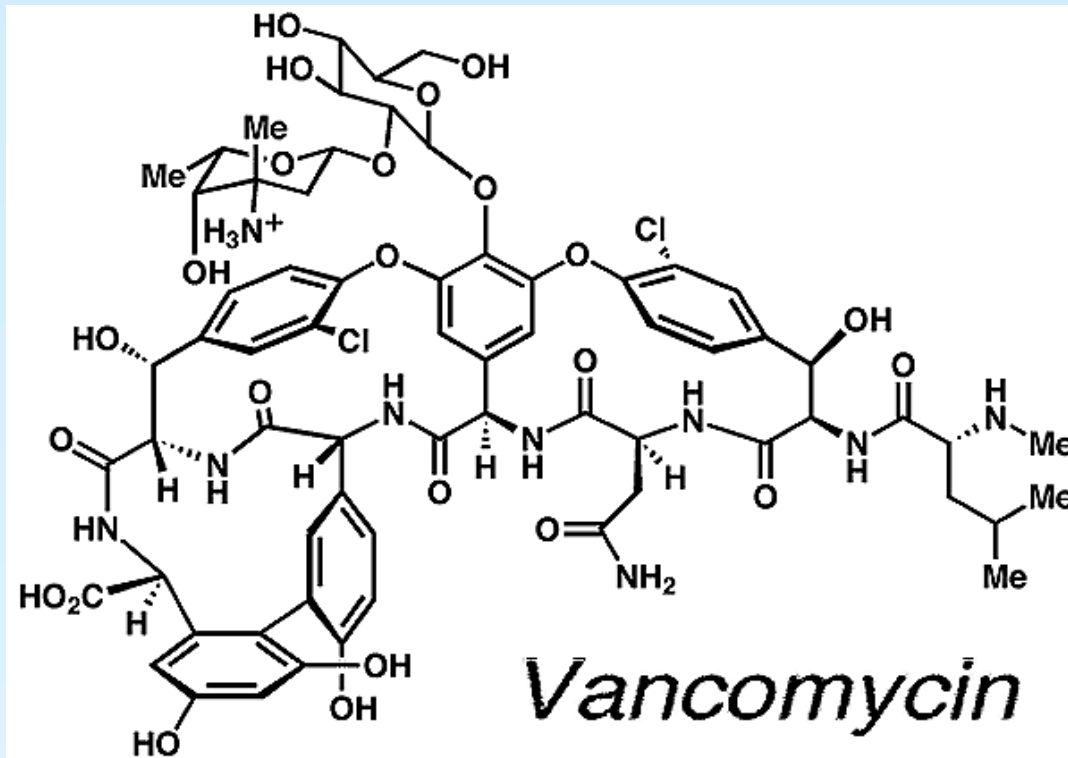


Penicillin

- N-acetylmuramic acid
- N-acetylglucosamine
- △ Tetrapeptide amino acid
- Interbridge amino acid



Vancomycin

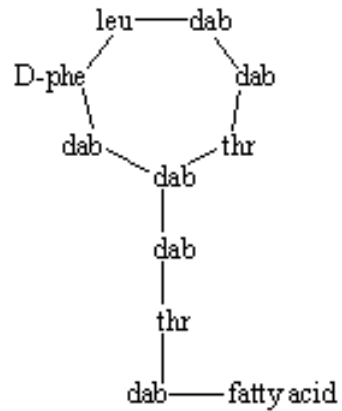


Disruption of Cell Membrane Function

- Bacterial cell membranes differ from animal cell membranes
- Polymyxin
 - Polypeptide
 - Acts as a detergent
 - Binds to phospholipids
 - Cytoplasm leaks
 - Membranes of Gram negative organisms are rich in phospholipids

Polymyxin

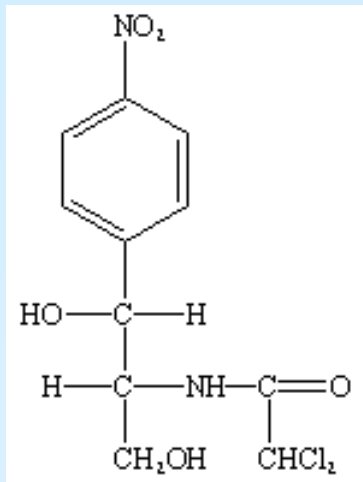
dab = l-diaminobutyric acid



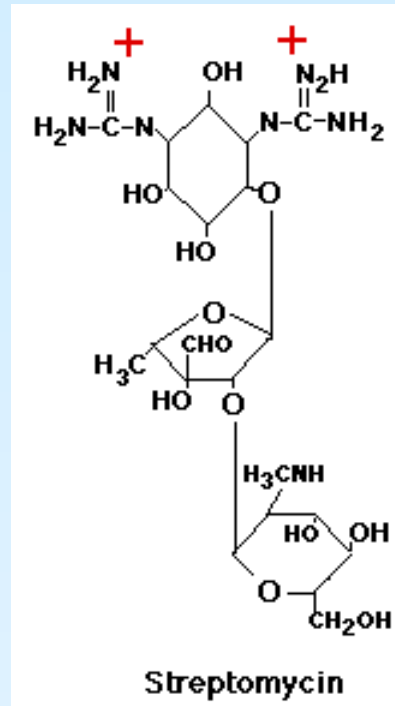
Inhibition of Protein Synthesis

- Bacterial (prokaryote) ribosomes = 70S
- Eukaryote ribosomes = 80S
- Streptomycin and tetracycline
 - Interfere with reading messenger RNA
- Chloramphenicol and erythromycin
 - Inhibit formation of polypeptide

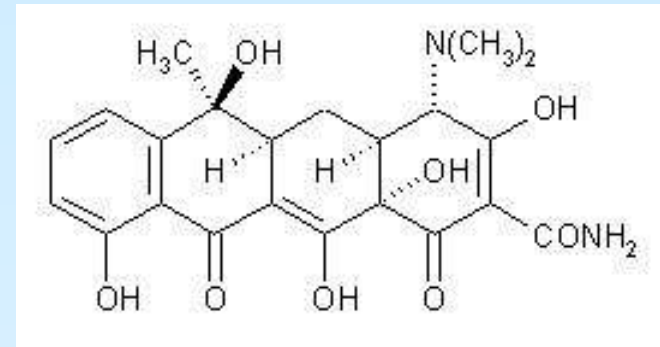
Protein Synthesis Inhibitors



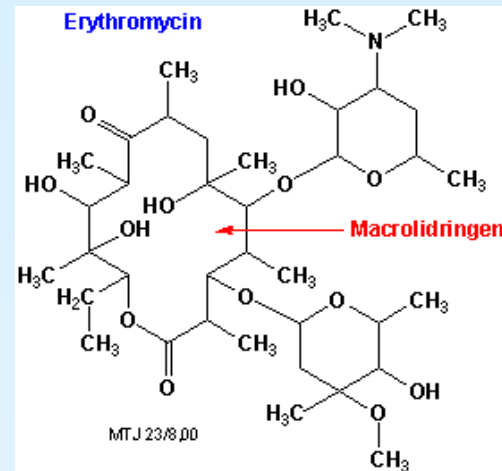
Chloramphenicol



Streptomycin



Tetracycline

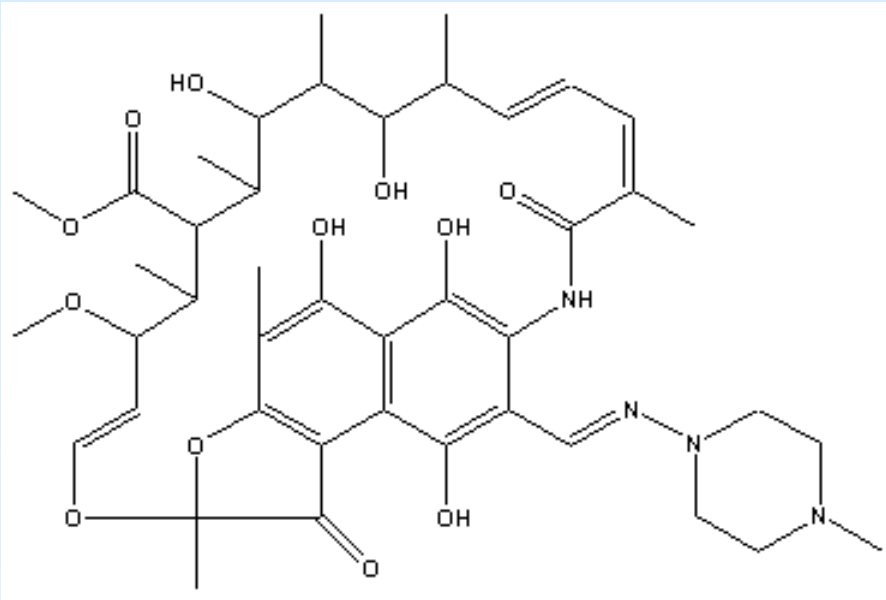


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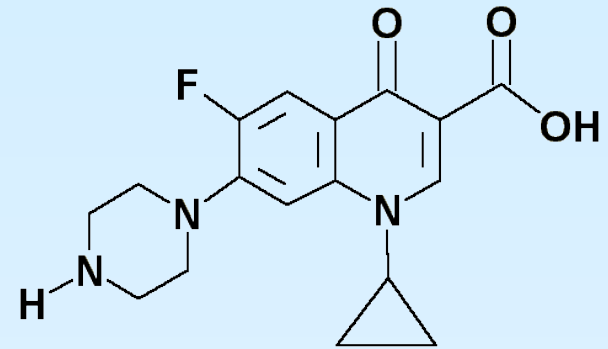
Inhibition of Nucleic Acid Synthesis

- Rifampin
 - Blocks RNS transcription
- Quinolones (eg., ciprofloxacin)
 - Block DNA gyrase (unwinds DNA to prepare for replication)

Inhibition of Nucleic Acid Synthesis



Rifampin

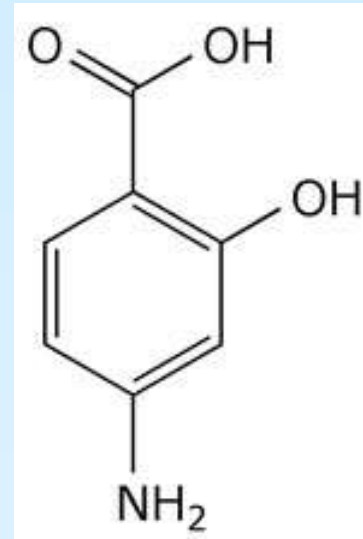
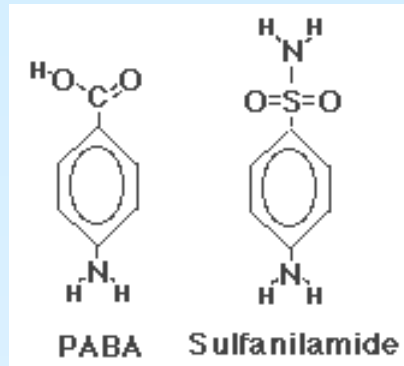


Ciprofloxacin

Action as Antimetabolites

- Competitively inhibit enzymes
- Erroneously incorporated into important molecules
- Sulfanilamide and p-amino benzoic acid (PABA)
- Bacteria require PABA to produce folic acid
- Animals do not make folic acid, so are not affected by the drugs

Antimetabolites



P-aminosalicylic acid (PAS)

Side Effects

- Toxicity
- Allergy
 - Penicillin bound to enzymes is now a foreign substance
- Disruption of normal flora

Antimicrobial Resistance

- Due to natural selection
- Alteration of targets
 - Antimicrobial can no longer bind to target
- Alteration of membrane permeability
 - Agent can no longer cross membrane
- Development of inactivating enzymes
 - B-lactamase

Antimicrobial Resistance (2)

- Alteration of an enzyme
 - Sulfonamide resistance – enzyme with a high affinity for PABA
- Alteration of a metabolic pathway to bypass a reaction
 - Sulfonamide resistance – organisms can use ready made folic acid and no longer need to make it from PABA

B-Lactamase

