BACTERIA

Kenneth Alonso, MD, FACP

Bacterial cell wall

- Mycoplasma is surrounded only by a cell membrane.
- All other bacteria have a cell wall composed of a single covalently linked macromolecule of alternating N-acetylmuramic acid and N-acetylglucosamine.
- Tetrapeptides attach to the muramic acid and cross-link the macromolecule.

Bacterial cell wall

- Glucosamine is converted into N-acetylmuramic acid and is activated by uridine triphosphate.
- A pentapeptide UDP-MurNAc is assembled and attached to bactoprenol in the cytoplasmic membrane.
- N-acetylglucosamine is added to make a disaccharide.
- Bactoprenol translocates the disaccharide peptide precursor to the outside of the cell.
- A transglycolase attaches it to the peptidoglycan chain.
- Peptide chains are cross-linked.
- Pyrophospho-bactoprenol is converted back to phospho-bactoprenol and is recycled.

Bacterial cell wall

- Between the outer cell membrane and the cell wall is the periplasmic space, the location of β-lactamases and other virulence factors.
- A proton pump in the membrane contains the same components as in the mitochondrial electron transport chain.
- Drives ATP production.

Bacterial cell wall characteristics

- Teichoic acid are fibers of glycerol or ribitol phosphate that extend from the outer layer of the cell wall of gram positive bacteria.
- They activate the same pathways as do lipopolysaccharide endotoxins.
- Spores have dipicolinic acid coat, are heat resistant.
- Metabolically inactive but contain DNA, ribosomes, other components essential to germination when nutrients provided.
- Bacteria lack mucin receptors, produce mucin degrading enzymes.

Bacterial cell wall

- Gram positive bacteria have a thick wall and no outer cell bilayer membrane.
- They are also associated with lipoteichoic (membrane) and teichoic (periplasmic space) acids.
- Mycobacteria have high concentrations of lipids, mycolic acids, in their cell walls.

Bacterial cell wall

- Gram negative bacteria have a thin peptidoglycan wall covered by an outer lipid containing membrane.
- The cell wall is not associated with teichoic or lipoteichoic acids.
- The outer lipid membrane contains a lipopolysaccharide.
- The lipid is anchored in the membrane
- The polysaccharide extrudes.
- Lipid A is a phospholipid, attached to a core polysaccharide of 5 sugars linked to lipid A, and O antigen, an outer polysaccharide.
- Induces fever and hypotension

Bacterial cell wall

- Anaerobic organisms lack catalase and super oxide dismutase that protect them from reactive oxygen species.
- They have a mechanism that permits transfer of reducing equivalents to nitrates instead of molecular Oxygen.

Bacterial cell wall characteristics

- Capsules limit the ability of neutrophils to engulf the bacteria.
- Capsules are invariably polysaccharide
- B. anthracis has a D-glutamate polypeptide capsule
- Pili mediate attachment of bacteria to the surface of human cells.
- They are glycoprotein filaments that extend from the surface of the bacterium.
- Afimbral adhesins are cell surface proteins made in bacteria that do not have pili

Bacterial cell characteristics

- Flagellae are protein filaments anchored in the membrane.
- H-antigen is flagellin.
- The glycolax is a slime layer secreted by certain bacteria that enables them to attach firmly to the surface of human cells.
- The genome consists of a single chromosome of circular DNA. No nuclear membrane; no histones, no introns.
- No mitochondria, Golgi apparatus, endoplasmic reticulum.

Bacterial cell characteristics

- Plasmids are extra chromosomal pieces of circular DNA.
- They may code for exotoxins and enzymes of antibiotic resistance.
- Transposons are small pieces of DNA that move between the chromosomal DNA and the plasmids.
- May be transferred between bacteria (and species).

Bacterial cell genetics

- DNA may be transferred between cells by:
- Conjugation
- F plasmid makes sex pilus
- Chromosome transfer
- F plasmid integrated into genome and may still transfer, a high frequency recombination
- Virulence genes clustered in pathogenicity islands.
- Usually inserted within or close to a tRNA gene.

Bacterial cell genetics

- Transduction
- Phage injects DNA, leads to incorporation into genome
- May lyse cell if stressed and release again as phage
- Transformation (transfection).

Bacterial cell growth characteristics

- Organisms communicate with each other.
- Controls gene expression and growth of bacterial mass. (Quorum sensing)
- Gram negative auto-inducer is an acetylated histone lactone.
- Gram positive auto-inducer is a peptide.
- Listeria monocytogenes and Shigella spp. Condense with actin, propel bacterium through host cell into adjacent sites.
- Protoplasts formed when cell wall lost (gram positive)
- Spheroplasts do not completely shed cell wall when lysed (gram negative).

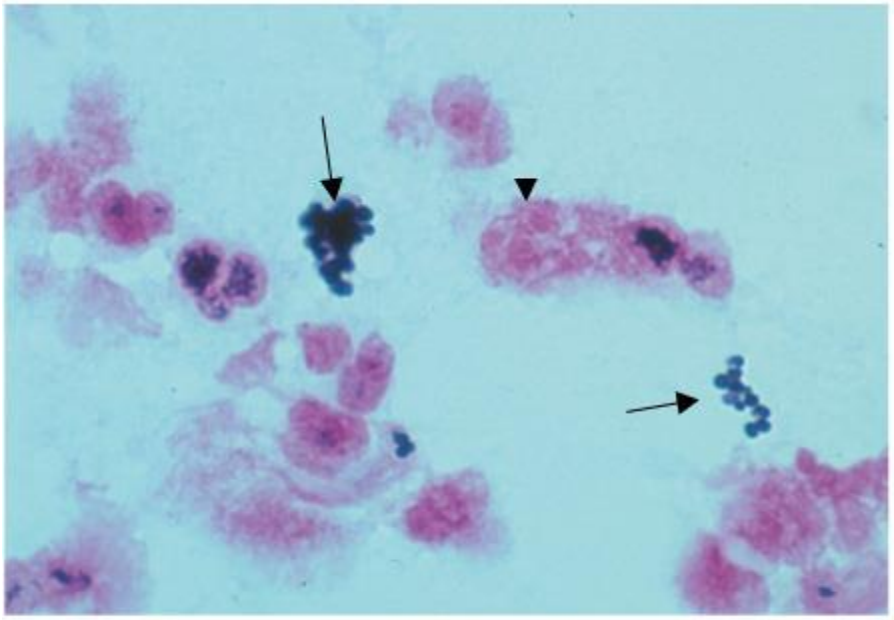
Bacterial metabolism

- Aerobic respiration converts glucose to carbon dioxide and water and forms ATP through substrate level and oxidative phosphorylation.
- Anerobic respiration also forms ATP through substrate level phosphorylation.
- However, sulfate or nitrite anions are used as terminal electron acceptors rather than Oxygen.
- In the absence of Oxygen and following substrate level phosphorylation, certain bacteria ferment pyruvic acid.
- Its end products act as electron receptors to recycle NADH to NAD.

Bacterial cell stain characteristics

- Gram positive bacteria stain purple with a crystal violet–Iodine complex as the cell wall retains the dye in the presence of a lipid solvent, acetone-alcohol.
- Gram negative bacteria stain pink with a safranin counterstain.
- Mycobacteria resist decolorization with acid alcohol after having been stained red with carbolfuchsin.
- Chlamydia, Rickettsia stain with Geimsa.
- Fungi best stained with Periodic Acid–Schiff (carbohydrate capsule) or Methenamine Silver.

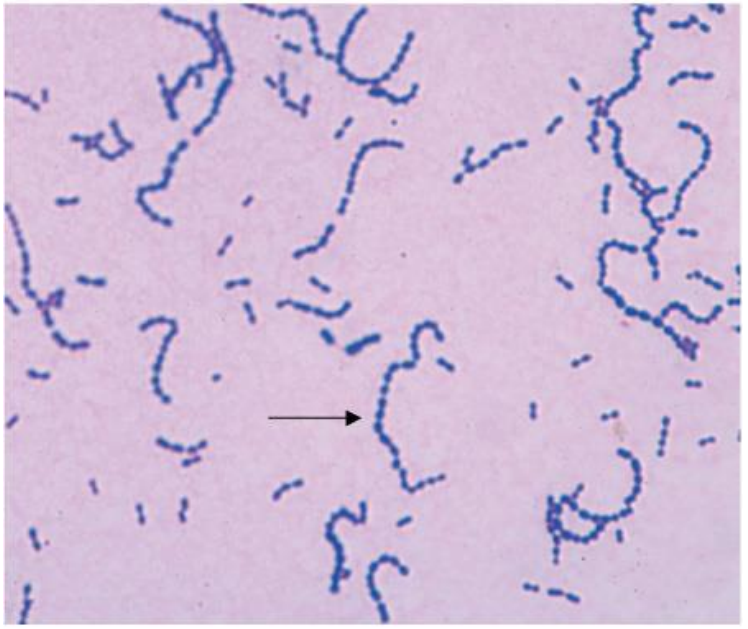
Gram positive cocci



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

In clusters. Staphylococcus.

Color plate 1 Accessed 07/01/2010



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

In chains. Streptococcus.

Color plate 2 Accessed 07/01/2010

Microbial growth media

Name of Agar	Organisms Isolated	Function
Blood	Virtually all	Detect hemolysis
Bordet-Gengou	Bordatella pertussis	Increased concentration of blood allows growth; peptone free
Charcoal yeast	Legionella pneumophila	Enriched with Iron and cysteine
Chocolate	Neisseria species	Heating the blood inactivates growth inhibitors
Chocolate plus X and V factors	Hemophilus influenzae	X and V factors required for growth
Egg Yolk	Clostridium perfringens	Lecithinase produces insoluble precipitate
Eosin Methylene Blue	Gram negative rods	Selects against gram positives and non-lactose fermenters

Microbial growth media

Name of Agar	Organisms Isolated	Function
Lowenstein-Jensen	Mycobacterium tuberculosis	Selects against gram positives and contains lipids for growth
MacConkey	Gram negative rods	Selects against gram positives and non-lactose fermenters
Middlebrook 7H10	Mycobacterium tuberculosis	Selects against gram positives
Saboraud	Fungi	Selects against gram negatives
Tellurite	Corynebacterium diphtheriae	Reduction to Tellurium by organism
Thayer-Martin	Neisseria gonorrheae from non-sterile site	Chocolate agar with antibiotics to limit growth of normal flora

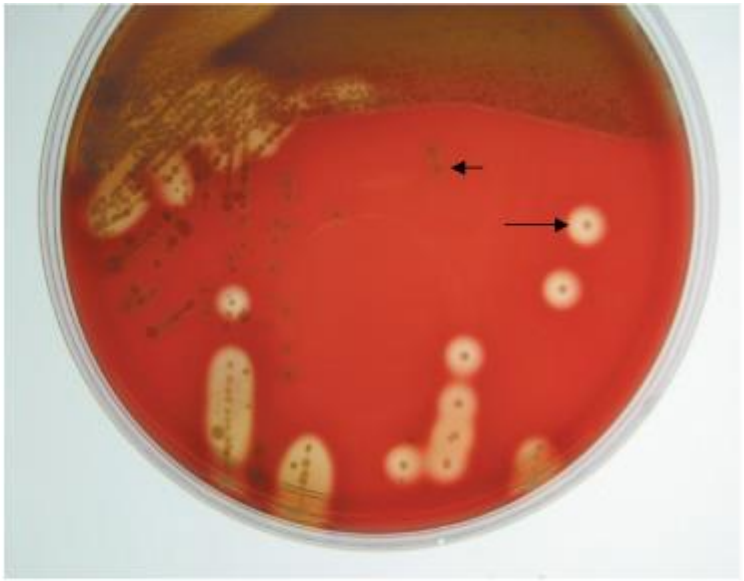
Hemolytic patterns

- α-Hemolysis:
- The membrane of the erythrocyte remains largely intact (incompletely lysed)
- The pathogen forms colonies on blood agar, producing a green envelope in which hemoglobin is reduced by bacterial produced hydrogen peroxide to biliverdin.
- β-Hemolysis:
- The erythrocyte is totally lysed and hemoglobin broken down
- The pathogen forms colonies on blood agar, producing a clear envelope of hemolysis.

Hemolytic patterns

- γ-Hemolysis:
- No hemolysis occurs.

Hemolytic patterns

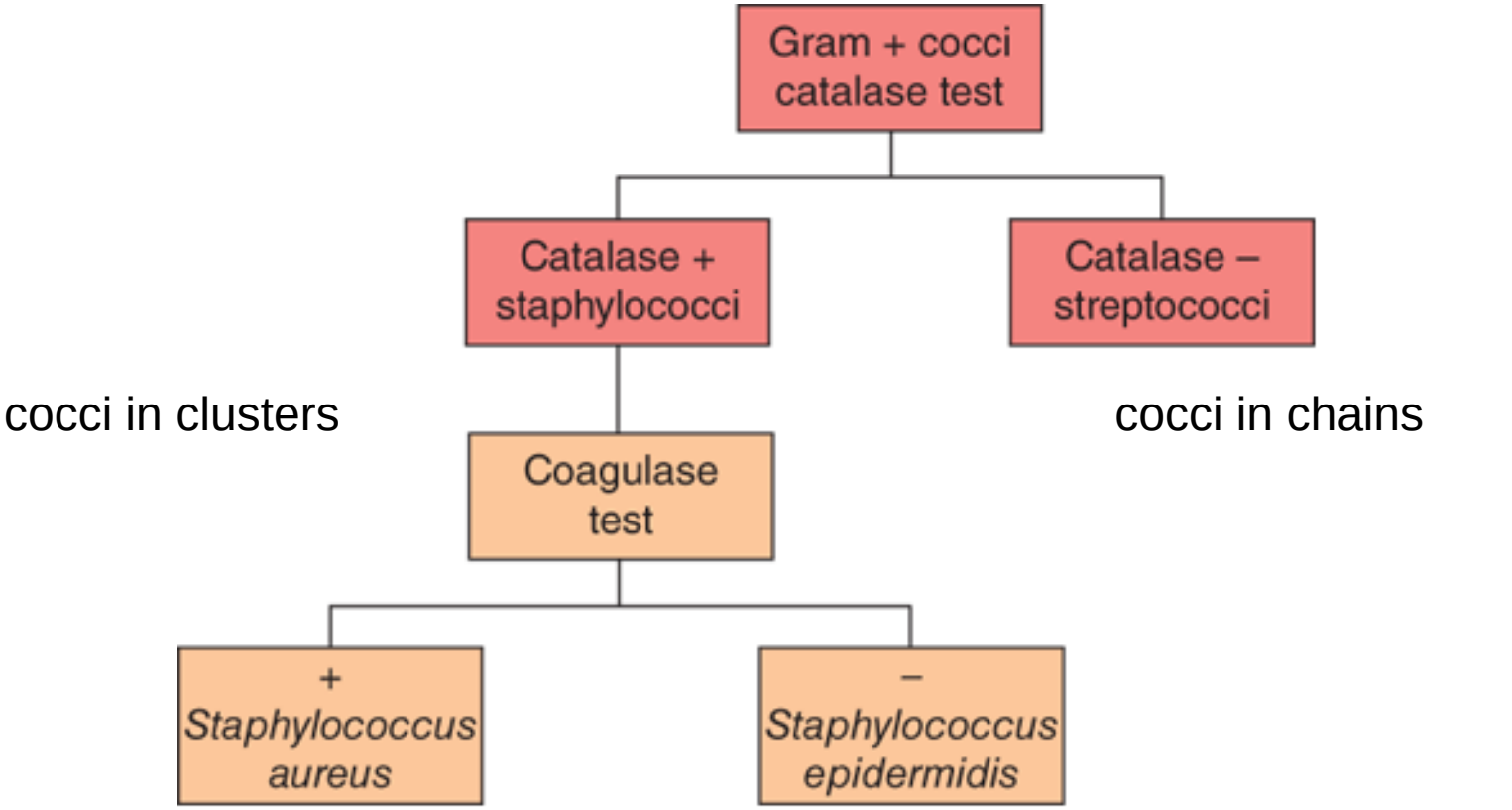


Short arrow points to an alpha-hemolytic colony, probably a viridans group streptococcus.
Long arrow points to a beta-hemolytic colony, probably Streptococcus pyogenes.
The specimen was a throat swab taken from a person with a sore throat.

Provider: Professor Shirley Lowe, University of California, San Francisco School of Medicine. With permission.

Color plate 16. Accessed 08/01/2010

GRAM POSITIVE ORGANISMS



Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

Algorithm for differentiating the Gram-positive cocci.

Gram positive organisms

- If gram positive bacilli
- Clostiridium
- Corynebacterium
- Listeria
- Bacillus

Streptococci

- If partial (α) hemolysis AND optochin positive
- Streptococcus viridians
- If partial (α) hemolysis AND optochin negative
- Streptococcus pneumoniae
- If complete (β) hemolysis AND bacitractin sensitive
- Streptococcus pyogenes (Group A)
- If complete (β) hemolysis AND bacitractin negative
- Streptococcus alagalactiae (Group B)

Streptococci

- If no hemolysis (γ)
- Enterococcus fecalis
- Streptococcus bovis (Group D)

Table 15–3

Streptococci of Medical Importance

Species	Lancefield Group	Typical Hemolysis	Diagnostic Features[1]
S. pyogenes	A	β	Bacitracin-sensitive
S. agalactiae	B	β	Bacitracin-resistant; hippurate hydrolyzed
E. faecalis	D	α or β or none	Growth in 6.5% NaCl[2]
S. bovis[3]	D	α or none	No growth in 6.5% NaCl
S. pneumoniae	NA[4]	α	Bile-soluble; inhibited by optochin
Viridans group[5]	NA	α	Not bile-soluble; not inhibited by optochin

[1] All streptococci are catalase-negative.

[2] Both *E. faecalis* and *S. bovis* grow on bile-esculin agar, whereas other streptococci do not. They hydrolyze the esculin, and this results in a characteristic black discoloration of the agar.

Streptococcus

- Gram positive cocci in chains
- Catalase negative
- Non-motile.
- Glycolax producer.
- C carbohydrate determines group
- Located in cell wall
- Amino sugar distinguishes antigenicity

Streptococcus

- M protein determines type
- Protrudes from cell wall
- Inactivates C3b (anti-phagocytic)
- Rheumatogenic (cross-reacts with normal tissues)
- Nephritogenic (M49)
- Antigen–antibody complexes on glomerular basement membrane
- Activate C5

Streptococcus pyogenes

- Group A streptococcus
- Gram positive cocci in chains
- Catalse negative
- Non-motile.
- β-hemolysis
- Bacitracin inhibits
- M protein is capsular substance and principal virulence factor.
- Inhibits phagocytosis and activation of alternate complement pathway.

Streptococcus pyogenes

- Predominant in epidermis binding.
- M12 strain is associated with acute glomerulonephritis.
- M and F protein expression is regulated by O_2 and CO_2 tension.
- Lipoteichoic acid is the adhesion molecule for the organism, enabling it to adhere to fibronectin.
- The F protein binds to fibronectin, establishing infection in the nasopharynx.
- G protein binds to Fc portion of antibodies, preventing complement activation.

Streptococcus pyogenes

- Complement C5 peptidase
- Many strains have hyaluronate capsule (anti-phagocytic)
- Produce hyaluronidase (spreading factor)
- Produce streptokinase (fibrinolysin)
- May dissolve fibrin exudate (fibrin-free pus) and produce disseminated intravascular coagulopathy
- Produce DNAase leads to liquefaction of cell nuclei
- Produce IgG degrading protease
- Permits colonization of upper respiratory mucosa

Streptococcus pyogenes

- Erythrogenic toxins A and C
- Causes rash of scarlet fever
- Resembles TSST superantigen
- Antigenic
- Streptolysin O and streptolysin S
- Oxygen-labile cytotoxins
- Affects erythrocytes, macrophages, and granulocytes
- Causes β-hemolysis
- Immunogenic

Streptococcus pyogenes

- Pyrogenic exotoxin (SPEA)
- Superantigen resembling TSST
- Exotoxin (SPEB)
- Protease
- Necrotizing fasciitis (flesh-eating)

Group B streptococcus

- S. agalactiae
- β-hemolytic
- Colonize genital tract
- Resistant to bacitracin
- Hydrolyze hippurate
- CAMP test positive
- Heat stable protein
- Enhances hemolysis of Staph. aureus sphingomyelinase damaged red cells
- Polysaccharide capsule is anti-phagocytic

Group D streptococcus

- Gram positive cocci in chains
- Catalase positive
- γ-hemolysis (but may see α- or β-hemolysis)
- Enterococcal:
- Enterococcus fecalis
- Enterocossus fecium
- Salt tolerant
- Bile esculin growth
- May be vancomycin resistant

Group D streptococcus

- Non-enterococcal:
- S. bovis
- Gram positive cocci in chains
- Catalase positive
- γ-hemolysis (but may see α- or β-hemolysis)
- Inhibited by salt
- Penicillin sensitive

Source: W. Levinson, P. Chin-Hong, E.A. Joyce, J. Nussbaum, B. Schwartz: Review of Medical Microbiology & Immunology: A Guide to Clinical Infectious Diseases, Sixteenth Edition: Copyright © McGraw Hill. All rights reserved.

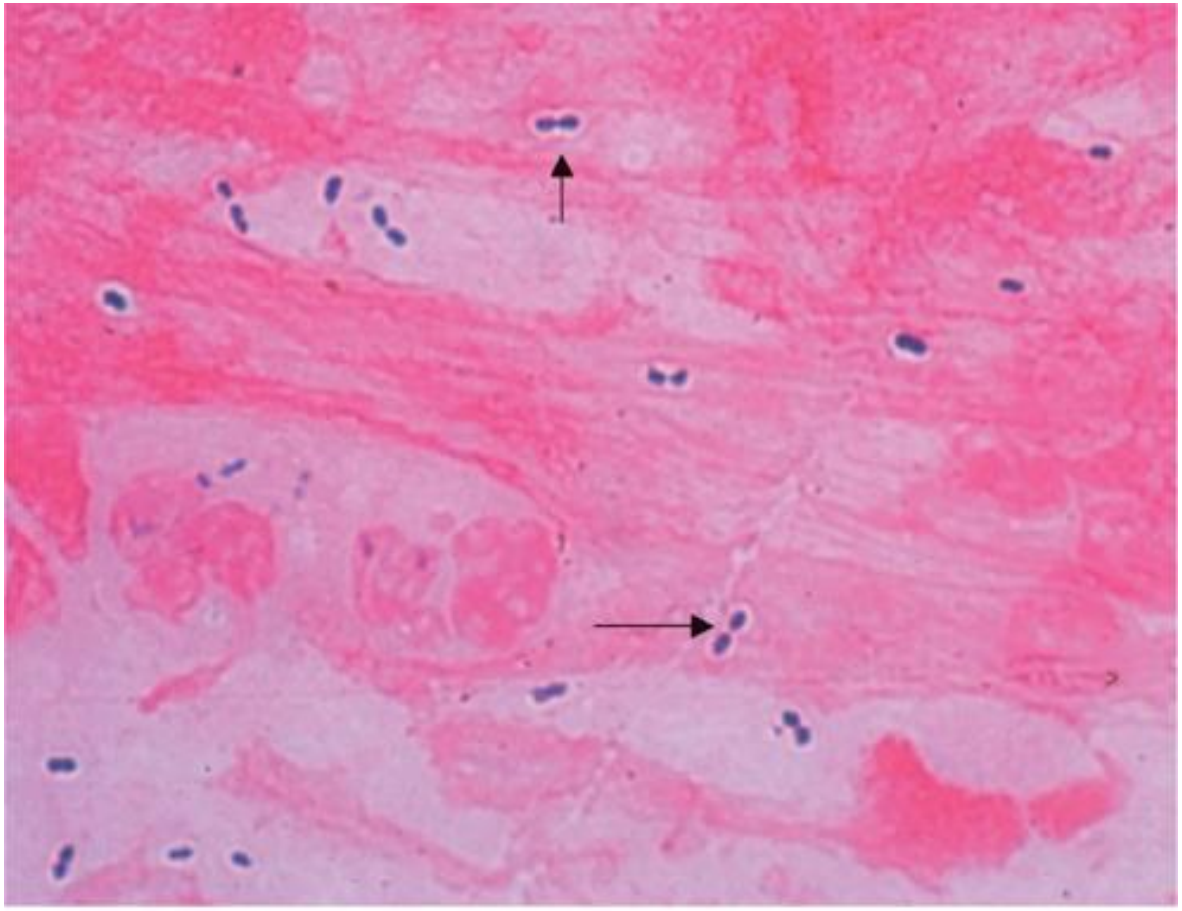
Pharyngitis. Note erythema of soft palate, uvula, and posterior pharynx and swelling of the uvula. The most common bacterial cause of pharyngitis is Streptococcus pyogenes. Note: The curved white lines on the uvula and the palate are artifacts of photography. (Reproduced with permission from Centers for Disease Control and Prevention. CDC #6323.)

Cellulitis. Note erythema and swelling of the dorsum of the foot. Streptococcus pyogenes is the most common cause of cellulitis. (Reproduced with permission from Usatine RP, Smith MA, Mayeaux EJ Jr, et al. The Color Atlas of Family Medicine. New York, NY: McGraw-Hill Education; 2009. Photo contributor: Richard P. Usatine, MD.)

Erysipelas. Note well-demarcated border of the inflamed area. Streptococcus pyogenes is the most common cause of erysipelas. (Reproduced with permission from Longo DL, Fauci AS, Kasper DL, et al. Harrison's Principles of Internal Medicine, 18th ed. New York, NY: McGraw-Hill Education; 2012.)

Other streptococci

- Streptococcus viridians
- α-hemolytic
- Optochin does not inhibit
- Bile insoluble
- S. mutans
- Synthesizes dextrans found in dental plaques
- Peptostreptococci
- Grow under anaerobic or microaerophilic conditions



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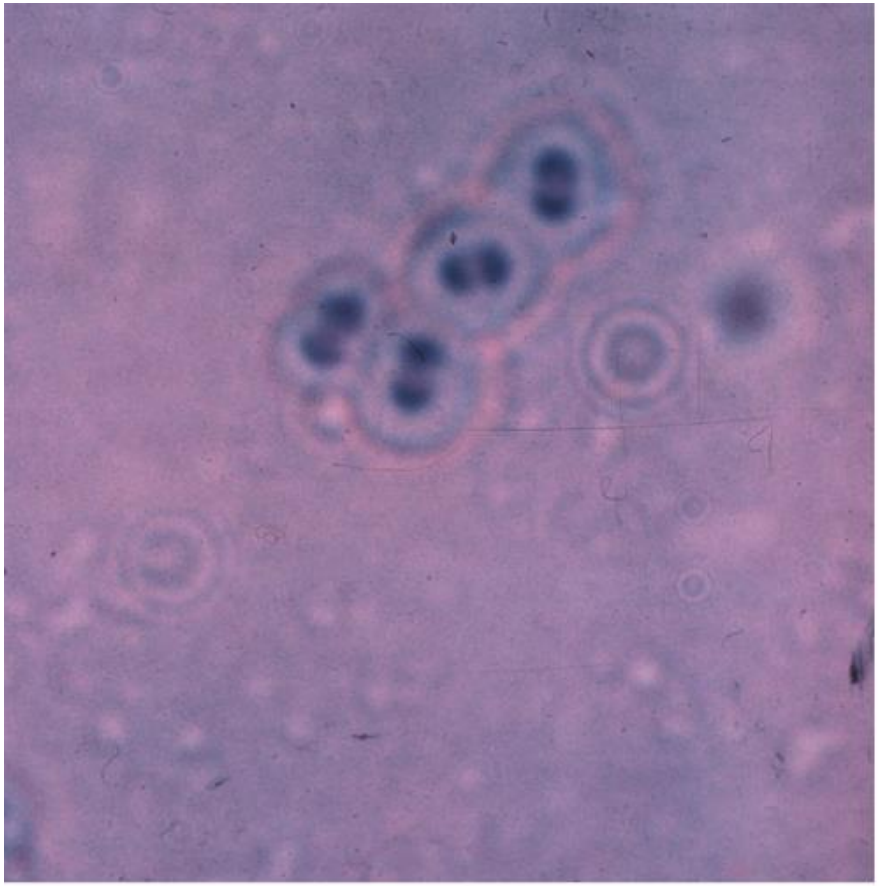
Streptococcus pneumoniae—Gram stain. Arrows point to typical gram-positive diplococci. Note that the clear area around the organism is the capsule. (Used with permission from Professor Shirley Lowe, University of California, San Francisco School of Medicine.)



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S. pneumoniae quellung reaction: a small amount of growth is mixed with saline, antisera against the capsule polysaccharide, and methylene blue stain. After incubation at room temperature for 1 hour, the reaction is observed under the microscope. The organisms are outlined in light blue. A positive reaction shows clumping because of cross-linking of the antibodies and pneumococci. The halo effect around the pneumococci is apparent capsular swelling. A negative control would show no clumping or capsular swelling. (Courtesy of H. Reyes.)

Streptococcus pneumoniae

- Gram positive diplococci (or lancet shaped, in pairs).
- Catalse negative
- Non-motile.
- α-hemolysis.
- Optochin inhibits.
- Bile soluble.
- Quellung reaction (capsule swells when anti-capsular antibody added).
- Polysaccharide capsule is surface virulence factor (resists phagocytosis).

Streptococcus pneumoniae

- Produces IgA protease
- Enables colonization of upper respiratory mucosa
- Pneumolysin O is a hemolysin; also inhibits leukocyte burst
- Lipoteichoic acid and peptidoglycan activate the alternative complement pathway, leading to recruitment of neutrophils.

Table 15–1

Staphylococci of Medical Importance

Species	Coagulase Production	Typical Hemolysis	Important Features[1]	Typical Disease
S. aureus	+	β	Protein A on surface	Abscess, food poisoning, toxic shock syndrome
S. epidermidis	–	None	Sensitive to novobiocin	Infection of prosthetic heart valves and hips; common member of skin flora
S. saprophyticus	–	None	Resistant to novobiocin	Urinary tract

[1] All staphylococci are catalase-positive.

Staphylococcus aureus

- Gram positive cocci in clusters
- Yellow colonies
- Staphyloxanthin inactivates superoxides and other reactive oxygen species within neutrophils
- Catalase negative
- Coagulase positive
- Salt tolerant
- Ferments mannitol
- Lyses red cells
- Weakly immunogenic polysaccharide capsule

Staphylococcus aureus

- 30% of patients, nasal colonization
- 30% of patients, skin colonization
- 5% of women, vaginal colonization
- 90% have plasmids that encode β-lactamases
- mecA gene encodes pencillin binding protein (PBP2) in the cell membrane that performs as a transpeptidase but does not bind penicillin
- Methicillin resistant
- Plasmid transposon contains genes that substitute D-lactate for D-alanine in the peptidoglycan
- Vancomycin resistant

Staphylococcus aureus

- Pathogenetic factors:
- Teichoic acids mediate adhesion to mucosal cells
- Surface receptors for fibrinogen (clumping factor), fibronectin, vitronectin permit binding to epithelial cells.
- Coagulase causes intravascular fibrin thrombi.
- Walls off infection site

Staphylococcus aureus

- α-toxin (leukocidin) is a pore forming hemolysin that depolarizes cell and destroys granulocytes and histiocytes
- Leads to marked skin necrosis as well as hemolysis
- P-V leukocidin is also a pore forming hemolysin
- Transmitted by phage
- β-toxin is a sphingomyelinase (hemolysin)
- γ-toxin lyses erythrocytes.
- Iron recovered used in synthesis of cytochrome enzymes

Staphylococcus aureus

- Catalase prevents toxic action of neutrophil derived hydrogen peroxide.
- Protein A binds to Fc region of IgG, preventing complement activation.
- Surface virulence factor.
- Staphylokinase dissolves fibrin.
- Hyaluronidase, lipase allow for extension into tissues.

Staphylococcus aureus

- Exotoxins:
- Enterotoxin is a superantigen that acts locally in the gastrointestinal tract and produces food poisoning.
- Il-1, Il-2 released from macrophages and CD4+ cells
- Vomiting as a result of serotonin release from enterochromaffin cells
- Resistant to heat, stomach acid, jejunal enzymes
- TSST toxin binds to MHC II protein and T-cell receptor, inducing Il-1, IL-2, and TNFproducing toxic shock syndrome. (Ritter disease is scalded-skin syndrome).
- Up to 25% of isolates

Staphylococcus aureus

- Exfoliative A and B toxins
- Serine proteases
- Cleave desmoglein in desmosomes
- Produce epidermal vesicles leading to necrotizing epidermolysis as well as exfoliative dermatitis over the entire body (scalded skin syndrome).

Impetigo (Staphylococcus aureus)

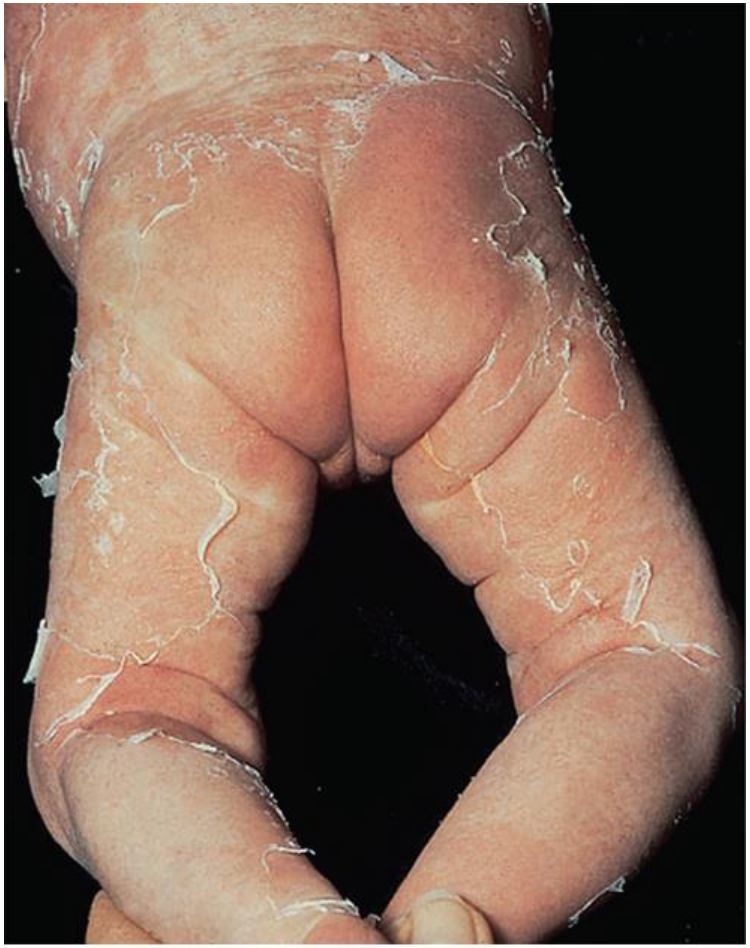
Fig. 177-2 Accessed 08/01/2010

Folliculitis. Note the multiple, small pustules on the chin and neck. Staphylococcus aureus is the most common cause of folliculitis. (Reproduced with permission from Wolff K, Goldsmith LA, Katz SI, et al. Fitzpatrick's Dermatology in General Medicine, 7th ed. New York, NY: McGraw-Hill Education; 2008.)

Carbuncle. A carbuncle is a multiheaded abscess often located on the back of the neck. Note drop of yellowish pus near the center of the lesion. Carbuncles are caused by Staphylococcus aureus. (Reproduced with permission from Wolff K, Johnson R. Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology, 6th ed. New York, NY: McGraw-Hill Education; 2009.)

Staphylococcus aureus

- Exotoxins:
- Penton-valentine leukocydin, cytotoxin on phage, causes leukocyte destruction and tissue necrosis.
- mecA gene confers methicillin resistance as it encodes the transpeptidase PBP2 with low affinity for β-lactoams



Source: W. Levinson, P. Chin-Hong, E.A. Joyce, J. Nussbaum, B. Schwartz: Review of Medical Microbiology & Immunology: A Guide to Clinical Infectious Diseases, Sixteenth Edition: Copyright © McGraw Hill. All rights reserved.

Scalded skin syndrome. Note widespread areas of “rolled up” desquamated skin in infant. Caused by an exotoxin produced by Staphylococcus aureus. (Reproduced with permission from Wolff K, Johnson R. Fitzpatrick’s Color Atlas & Synopsis of Clinical Dermatology, 6th ed. New York, NY: McGraw-Hill Education; 2009.)

Staphylococci NOT aureus

- Gram positive cocci in clusters
- White colonies
- Catalase negative
- Coagulase negative
- Staphylococcus epidermidis.
- Some strains may produce glycolax
- Staphylococcus saprophyticus.
- Novobiocin resistant

Bacillus anthracis

Arrow points to one large "box car-like" gram-positive rod within a long chain.

Provider: CDC.

Color plate 12 Accessed 08/01/2010

Bacillus anthracis

- Endospore forming gram positive bacillus
- Square end, blue black bacillus, pink capsule when stained with polychrome methylene blue.
- Non-motile
- Nonhemolytic gray to white, tenacious colonies with a rough texture and a ground-glass appearance.
- Comma-shaped outgrowths (Medusa head, “curled hair”) may project from the colony.

Bacillus anthracis

- Polyglutamyl capsule hinders phagocytosis and is the principal surface virulence factor.
- Genes encoding capsule and toxin formation are carried on plasmids pXO1 and pXO2
- Anthrax toxin consists of three proteins:
- Protective antigen (PA), edema factor (EF), and lethal factor (LF)

Anthrax toxin

- Exotoxin B is a protective antigen (PA).
- PA binds to a cell surface protein where a host protease partially degrades the subunit.
- The remaining fragment self-associates to form a heptamer.
- EF and LF are two Exotoxin A moieties
- Three Exotoxin A subunits bind to the heptamer
- This complex is endocytozed into the host cell.
- A conformational change induced by low pH leads to release of exotoxin A subunits through the endosomal membrane.

Anthrax toxin

- PF binds to either EF or LF with high affinity
- Exotoxin A subunits produce microvascular damage as edema factor (EF) binds to Ca^{2+} and calmodulin to form an adenylate cyclase
- Exotoxin A subunits inhibit cell division as lethal factor (LF) is a protease that cleaves MAPK kinase.

Cutaneous anthrax

- 95% of cases
- Skin is usual site of entry.
- Initial lesion is erythematous and may be mistaken for an insect bite.
- Local wound edema within 12-36 hours.
- Necrosis begins 2-5 days after inoculation of spores as toxin accumulates.
- Eschar forms in 7-10 days.
- Bacteremia rare.

Inhalation anthrax

- 5% of cases
- Uptake of spores by pulmonary macrophages.
- Spores vegetate in lymph node (produce capsule and toxin), then disseminate, leading to hemorrhagic mediastinitis.
- 6 week incubation period
- 1-5 days of non-specific malasie, fever and non-productive cough.
- May improve prior to progression.

Inhalation anthrax

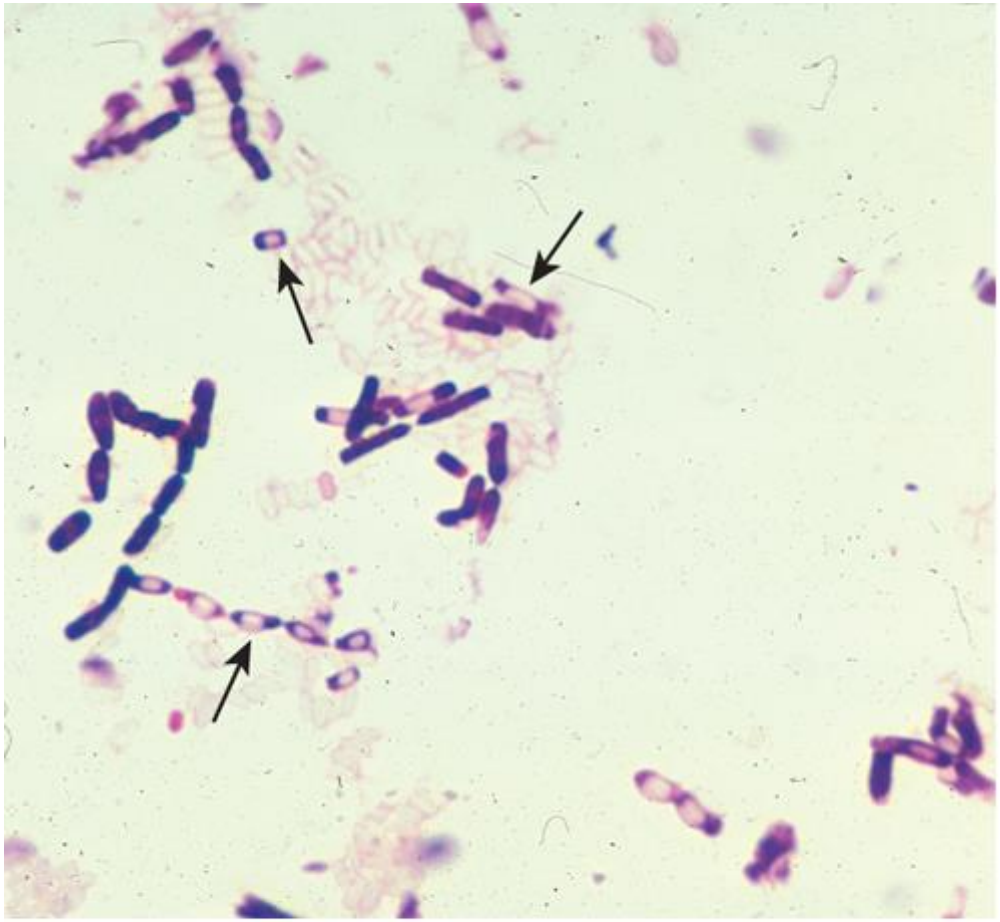
- Progressive respiratory distress and cyanosis (with massive edema of the neck, chest and mediastinum).
- Meningitis may follow bacteremia.
- 95% death rate if therapy with fluoroquinolones is not started within 48 hours of symptoms.

Anthrax syndromes

- A rare gastrointestinal form of anthrax results from eating undercooked meat contaminated with the organism.
- Nausea, abdominal pain, bloody diarrhea follow.
- Mortality rate, 50%.

Bacillus cereus

- Endospore forming gram positive bacilli
- Motile
- β-hemolysis
- Enterotoxin increases cyclic AMP within enterocytes.
- Food poisoning within 1 hour of ingestion.
- A second enterotoxin is a superantigen.
- A protective antigen permits entry of the two factors into the cell.



Clostridium Gram-stain. Individual Gram-positive bacilli are present. Many are in chains. Some of the bacilli have spores, which are the unstained or clear ovoid shapes (arrows).

Clostridium perfringens

- Anaerobic gram positive rod
- Motile
- Double zone of β-hemolysis.
- Produces collagenase, hyaluronidase, DNAase
- Produces α-toxin, a lecithinase (phospholipase C)
- Also promotes platelet aggregation
- Produces ε-toxin
- Edema and hemorrhage
- Produces θ-toxin, a cholesterol cytolysin
- Damage neutrophil pores

Clostridium perfringens

- Clostridium perfringens does not form endospores.
- Enterotoxin (CPE) is a portion of cell coat
- Induces secretory diarrhea within hours
- May be involved in necrotizing enterocolitis

Gas gangrene bacilli. C. perfringens typically does not form spores when grown on laboratory media.

Clostridium tetani

- Anerobic gram positive rod
- Terminal spore
- Motile
- Double zone of β-hemolysis.
- The vegetative cells produce the plasmid-encoded toxin tetanospasmin
- Cleaved by a bacterial protease into two peptides linked by a disulfide bond.

Clostridium tetani

- The larger peptide initially binds to receptors on the presynaptic membranes of motor neurons.
- It then migrates by the retrograde axonal transport system to the cell bodies of these neurons to the spinal cord and brainstem.
- The toxin diffuses to terminals of inhibitory cells, including both glycinergic interneurons and γ-aminobutyric acid (GABA)–secreting neurons from the brainstem.

Clostridium tetani

- The smaller peptide degrades synaptobrevin, a protein required for docking of neurotransmitter vesicles on the presynaptic membrane.
- Release of the inhibitory glycine and GABA is blocked, and the motor neurons are not inhibited.
- Hyperreflexia, muscle spasms, and spastic paralysis result.

Clostridium botulinum

- Anerobic gram positive rod
- Forms endospore
- Neurotoxin coded for by prophage.
- Heat labile.
- Botulinum toxins have three domains.
- Two facilitate binding to and entry of toxin into the nerve cell.
- The third domain is the toxin that is cleaved into a heavy chain and a light chain that are linked by a disulfide bond.
- Binds gangliosides on motor neurons

Clostridium botulinum

- Proteolysis of the L-chain by synaptobrevin or by syntaxin mediates fusion of neurotransmitter containing vesicles within the neuron membrane.
- Prevents exocytosis of vesicles containing acetylcholine, blocking motor end plates (myoneural junction).
- Zinc metalloproteinase hydrolyses synaptobrevin.

Classic botulism

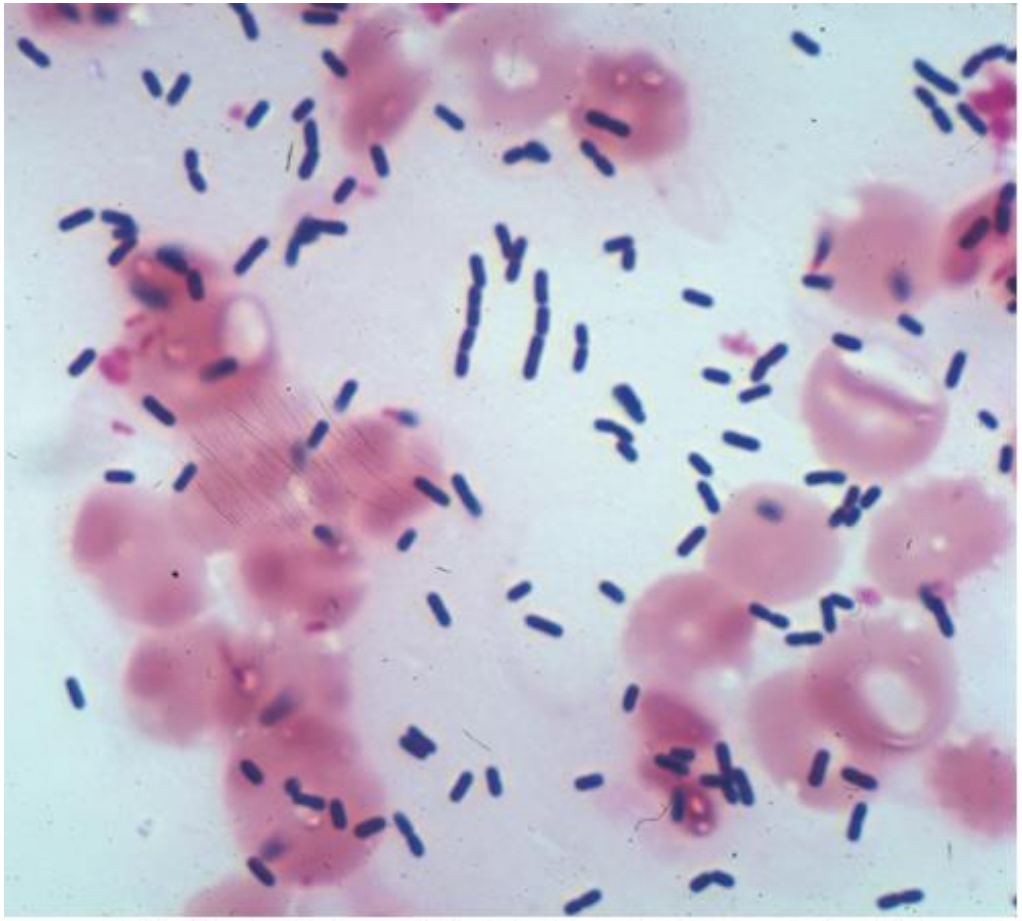
- Symptoms begin 18–24 hours after ingestion of the toxic food
- Visual disturbances (incoordination of eye muscles, double vision)
- Inability to swallow and speech difficulty
- Signs of bulbar paralysis are progressive
- Death occurs from respiratory paralysis or cardiac arrest.
- Gastrointestinal symptoms are not prominent.
- No fever.
- The patient remains fully conscious
- Recovering patients do not develop antibody

Infant botulism

- As common as or more common than the classic form of paralytic botulism associated with the ingestion of toxin-contaminated food.
- Usually from honey
- Poor feeding, weakness, and signs of paralysis (floppy baby).
- Infant botulism may be one of the causes of sudden infant death syndrome.
- C. botulinum and botulinum toxin are found in feces but not in serum.

Clostridium dificile

- Anerobic gram positive rod
- Forms endospore
- Produces enterotoxins.
- Toxin A binds to the brush border membranes of the gut at receptor sites.
- Toxin B is a potent cytotoxin.
- The toxins have glycosyltransferase activity and act by modifying signaling molecules that control various cellular functions.
- This results in apoptosis, capillary leakage, cytokine stimulation, and other consequences that lead to colitis.



Gram-stain of the Gram-positive bacillus L. monocytogenes in a blood culture. Original magnification ×1000. Red blood cells are present in the background. Listeria organisms isolated from clinical specimens frequently show variation in length and often in shape as well. Typically, they are 0.4–0.5 µm in diameter and 0.5–2 µm long. (Courtesy of H. Tran.)

Listeria monocytogenes

- In adults, associated with food poisoning
- Granulomatosis infantiseptica
- Disseminated in utero infection that presents with sepsis, pustules, and Listeria containing granulomas
- Late onset form
- Meningitis between birth and third week
- Type 4b usual cause
- High mortality rates
- Risk is to immunocompromised

Listeria monocytogenes

- Non-spore forming gram positive bacillus
- Motile (tumble) at room temperature but not at 37C
- β-hemolysis
- Facultative anaerobe
- Catalase positive
- Esculin hydrolysis positive
- Adhesin proteins (Amp, Fbp A, flagellin) bind to cell wassls
- Leucine rich surface proteins (internalins) bind to E-cadherin on host epithelial cells and are internalized.

Listeria monocytogenes

- Listeriolysin O and phospholipases release bacteria through pore formation in the phagolysosome.
- ACTA (bacterial surface protein) binds to host cell cytoskeleton, induces actin polymerization, propels bacteria into adjacent cells via membrane protrusions (filopods).
- May pass from cell to cell without being exposed to antibody
- Also produce siderophores to extract iron from transferrin

Listeria monocytogenes

- Survive in macrophages activated through classical pathway (C3)
- Killed by macrophages activated by IFN-γ.
- Monocytosis without T-cell activation.

Other gram positive rods

- Erysipelothrix rhusiopathae
- May appear singly, in short chains, randomly, or in long nonbranching filament
- α-hemolysis
- Not motile
- Catalase, oxidase, and indole negative
- Produces H2S on TSI agar
- Erysipeloid cellulitis (inoculation)

Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

Corynebacterium diphtheriae from Pai medium stained with methylene blue. Typically, they are 0.5–1 × 3–4 μm. Some of the bacteria have clubbed ends (original magnification ×1000).

Corynebacterium

- Irregular gram positive rod (V or L configuration).
- Metachromatic on methylene blue stain.
- Gray-black on Tellurite medium (reduced intracellulary)
- Catalase positive
- Non-motile
- Ferment maltose, not glucose
- Phage carries virulent gene (exotoxin).
- Toxigenicity is under the control of the phage gene
- Invasiveness is under the control of bacterial genes.

Corynebacterium diphtheriae

- Exotoxin has two components:
- The Fragment B receptor domain binds to host cell membrane proteins CD-9 and heparin-binding epidermal growth factor (HB-EGF) triggers the entry of the toxin into the cell through receptor-mediated endocytosis
- Acidification of the Fragment B translocation domain within a developing endosome leads to creation of a protein channel that facilitates movement of Fragment A into the host cell cytoplasm
- Fragment A irreversibly blocks protein synthesis by catalyzing the covalent transfer of ADP-ribose to elongation factor 2 in the presence of NAD

Diphtheria

- Spread via respiratory droplets or by contact with infected skin carriers.
- Onset 2-6 days following exposure.
- Fever
- “Brassy “ cough.
- Initial lesions in tonsils and oropharynx (organisms multiply in epithelial cells) with spread through upper respiratory tract.

Diphtheria

- Necrosis within the lesion due to exotoxin release.
- Gray-black pseudo-membrane adheres tightly to mucosa.
- Marked edema in underlying soft tissues.
- Prominent, painful cervical adenopathy. “Bull neck.”
- Myocarditis occurs in 20% of patients with diphtheria.
- Major cause of death in diphtheria.
- Onset 1 week or more after infection.
- Exotoxin leads to myocardial fiber necrosis.

Diphtheria

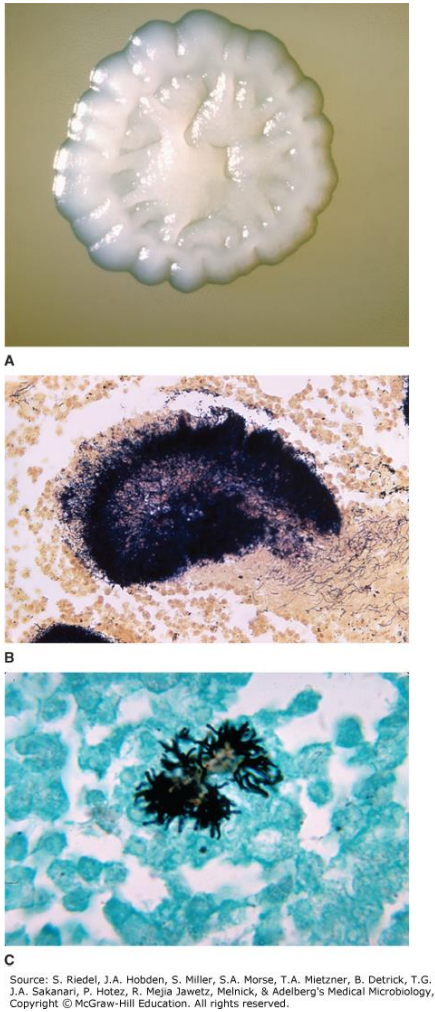
- Neurologic symptoms occur 1 or more months after infection.
- May see facial and ocular paralysis as well as paralysis of larynx.
- Improve with eradication of infection.
- Nephritis occurs as a result of parenchymal cell destruction in the kidney.
- Improve with eradication of infection.
- Antitoxin administration critical.

Nocardia asteroides

- Aerobic
- Filamentous with hyphae-like branching
- Beaded
- May be white to orange to red colonies
- Partially acid-fast (short chain mycolic acids in cell wall)
- Non-motile
- Catalase and urease positive
- Inhalation as mode of infection

Nocardia asteroides

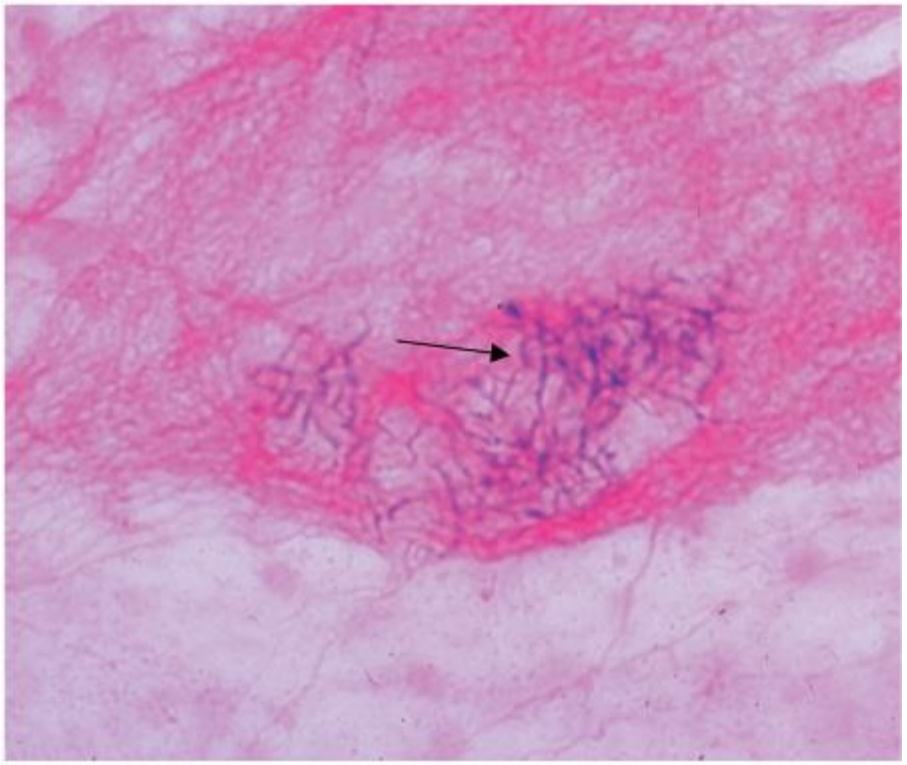
- N. asteroides associated with lung, CNS infections
- Usual pathologic process is abscess formation (neutrophilic inflammation).
- May see pulmonary consolidation
- Granuloma formation uncommon
- Hematogenous spread from the lung often involves the central nervous system, where abscesses develop in the brain
- N. brasiliensis associated with skin infections



Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

Actinomyces species. A: Colony of Actinomyces species after 72 hours growth on brain–heart infusion agar, which usually yields colonies about 2 mm in diameter; they are often termed “molar tooth” colonies. (Courtesy of CDC Public Health Image Library, L Georg.) B: Granule of Actinomyces species in tissue with Brown and Breen stain. Original magnification ×400. Filaments of the branching bacilli are visible at the periphery of the granule. Such granules are commonly called “sulfur granules” because of their unstained gross yellow color. (Courtesy of CDC Public Health Image Library.) C:Actinomyces naeslundii in a brain abscess stained with methylamine silver stain. Branching bacilli are visible. Original magnification ×1000. (Courtesy of CDC Public Health Image Library, L Georg.)

Actinomycetes israelli



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

Arrow points to area of branching filaments of gram-positive rods.

Provider: Professor Shirley Lowe, University of California, San Francisco School of Medicine. With permission.

Color plate 12 Accessed 08/01/2010

Actinomycetes israelli

- 73% of all Actinomycetes infections
- Exudates contain yellow, red, brown, white or black granules sulfur granules.
- Branching filaments
- Murein walls
- Non-spore forming
- Catalase negative
- Urease positive
- Fimbriae permit attachment to cell walls

Actinomycosis

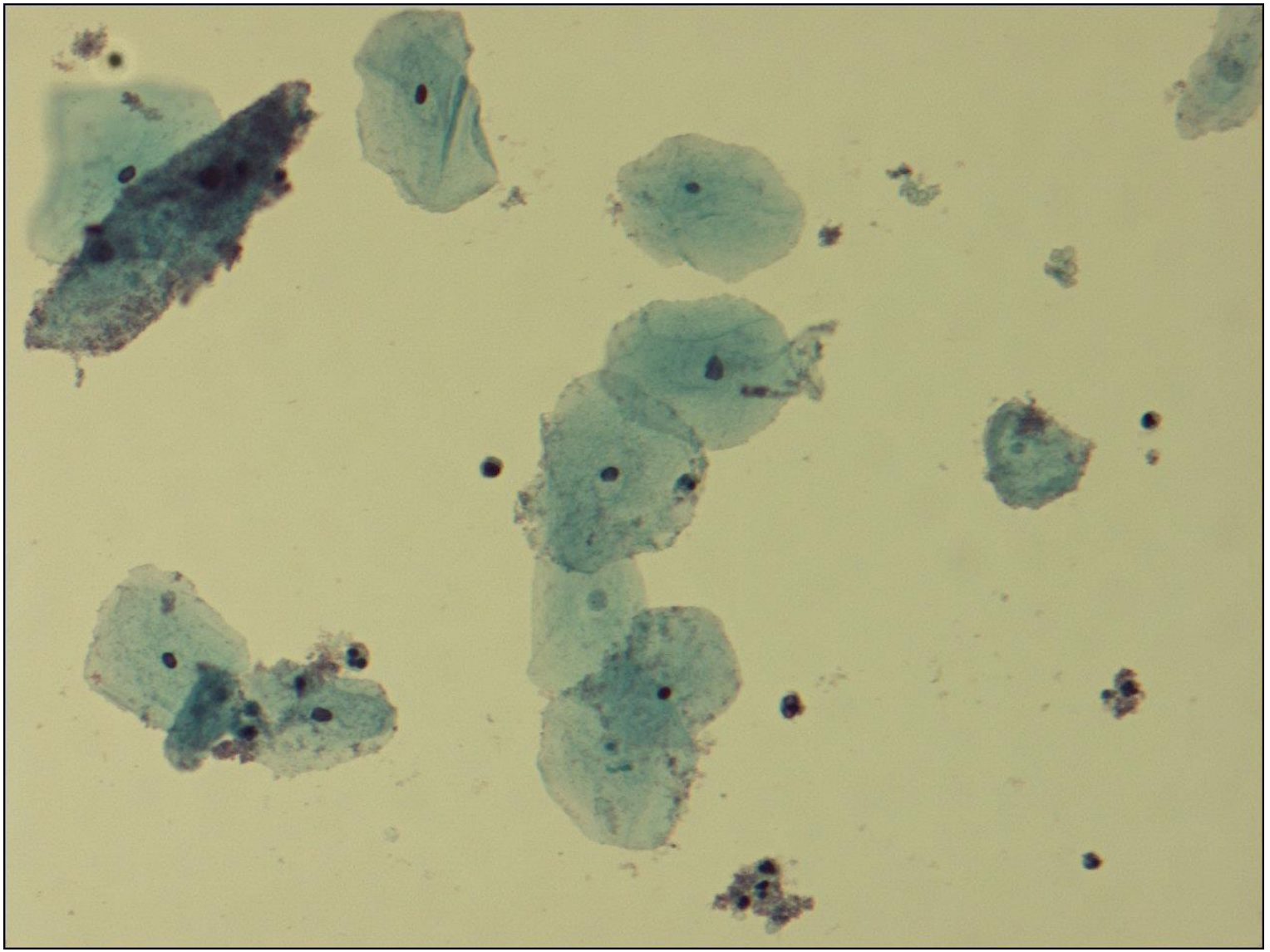
- Cutaneous infection may be primary or result from the spread of organisms from a primary pulmonary infection or from a dental infection
- Once in the tissue, the bacteria cause an abscess, producing a hard, red to reddish-purple lump, often on the jaw ("lumpy jaw.“)
- Eventually, the abscess breaks through the skin surface to produce a draining sinus tract.
- May cause endometritis in women with IUD

Actinomycosis

- Usually confluent bronchopneumonia.
- May be acute.
- Organisms are inhaled, multiply in lungs, and cause primary pneumonitis.
- Resist destruction by non-activated macrophages.
- Cough, dyspnea, fever as presenting signs.
- Production of cavities and extension to pleura are common.
- Pneumonia with cavitation and dissemination in an immunocompromised patient should prompt consideration of Nocardia as cause.

Tropheryma whipplei

- Actinomycete
- Whipple’s disease
- PAS positive organisms in macrophages
- Fever, abdominal pain, diarrhea, weight loss, and migratory polyarthralgia
- Middle-aged men.
- The primary site of involvement is the small intestine and mesenteric lymph nodes



Clue cells coated with Gardnerella.

https://upload.wikimedia.org/wikipedia/commons/f/fb/G.vaginalis.jpg

Gardnerella vaginalis

- Variable staining cocco-bacilli
- Thin Gram-positive cell wall
- Facultative anaerobes
- Non-spore forming
- Gray colonies on chocolate agar
- Produces a pore-forming toxin, vaginolysin
- Produces protease and sialidase enzymes

Bacterial vaginosis

- Thin, homogeneous discharge that adheres to the vaginal walls
- Elevated pH > 4.5 (anterior vaginal fornix)
- Addition of KOH to discharge elicits characteristic fishy odor
- Presence of clue cells on microscopic examination of wet mount (epithelial cells studded with large numbers of bacteria, Gardnerella vaginalis, which obscure the cells border)
- If woman has three episodes of bacterial vaginosis with same sexual partner, the partner should be treated as well with metronidazole.
- Condom use.

Anerobic cocci

- Gram positive
- Peptostreptoccus
- Gram negative
- Veilonella

GRAM NEGATIVE ORGANISMS

Gram negative organisms

- If cocci AND slow oxidase positive,
- Hemophilus influenzae (X and V factor dependent)
- Bordatella pertussis
- Brucella melitensis
- Pasturella multocida
- If cocci AND oxidase positive AND ferment maltose,
- Neisseria meningitidis
- If cocci AND oxidase positive AND do not ferment maltose,
- Neisseria gonorrheae
- Moraxella catarrhalis

Gram negative organisms

- If gram negative rods AND do ferment lactose AND do ferment indole,
- Escherichia coli
- If gram negative rods AND do ferment lactose AND do not ferment indole,
- Klebsiella pneumoniae
- If gram negative rods AND slowly ferment lactose,
- Citrobacter
- Serratia

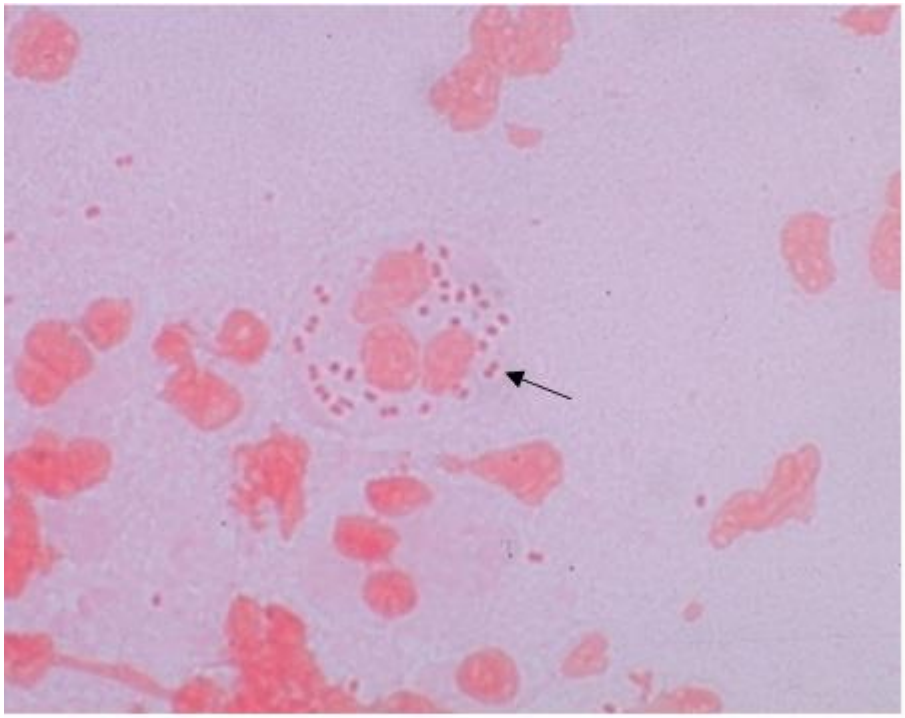
Gram negative organisms

- If gram negative rods AND do not ferment lactose AND are oxidase negative,
- Salmonella
- Shigella
- Proteus
- If gram negative rods AND do not ferment lactose AND are oxidase positive,
- Pseudomonas
- Acinetobacter

Moraxella

- Gram negative diplococcus (may also show rods)
- Oxidase positive
- Catalase positive
- Non-motile

Neisseria gonorrheae



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

Arrow points to typical "kidney-bean" shaped gram-negative diplococci within a neutrophil.

Provider: Professor Shirley Lowe, University of California, San Francisco School of Medicine. With permission.

Color plate 4
Accessed 08/01/2010

Neisseria gonorrheae

- Gram negative diplococci
- Oxidase positive
- Catalase positive
- Non-motile
- Acid production with glucose
- Chocolate or Thayer-Martin agar (requires Factors X and V)
- Proliferates in phagocytic vacuoles
- Produces IgA protease
- Ferric binding protein

Neisseria gonorrheae

- Attach by pili to CD46 (expressed by all nucleated cells and is a complement regulatory protein)
- Por protein may inhibit phagosome-lysosome fusion
- With RMP forms pores on the membrane surface
- Binds C3b and C4b complement
- OPA proteins in outer membrane increase binding to epithelial cell adhesion molecules
- Lipooligosaccharide wall (no capsule)
- Structurally resembles membrane glycophosphingoolipids
- Sialylation protects from destruction by complement system
- Leads to ciliary loss in fallopian tubes

Gonorrhea

- Dysuria, discharge.
- Women may be asymptomatic
- DNA Probe analysis for N. gonorrhoeae
- Ceftriaxone or cefixime single dose
- Concomitant treatment for chlamydia
- Should treat all sexual contacts.

Neisseria meningitidis

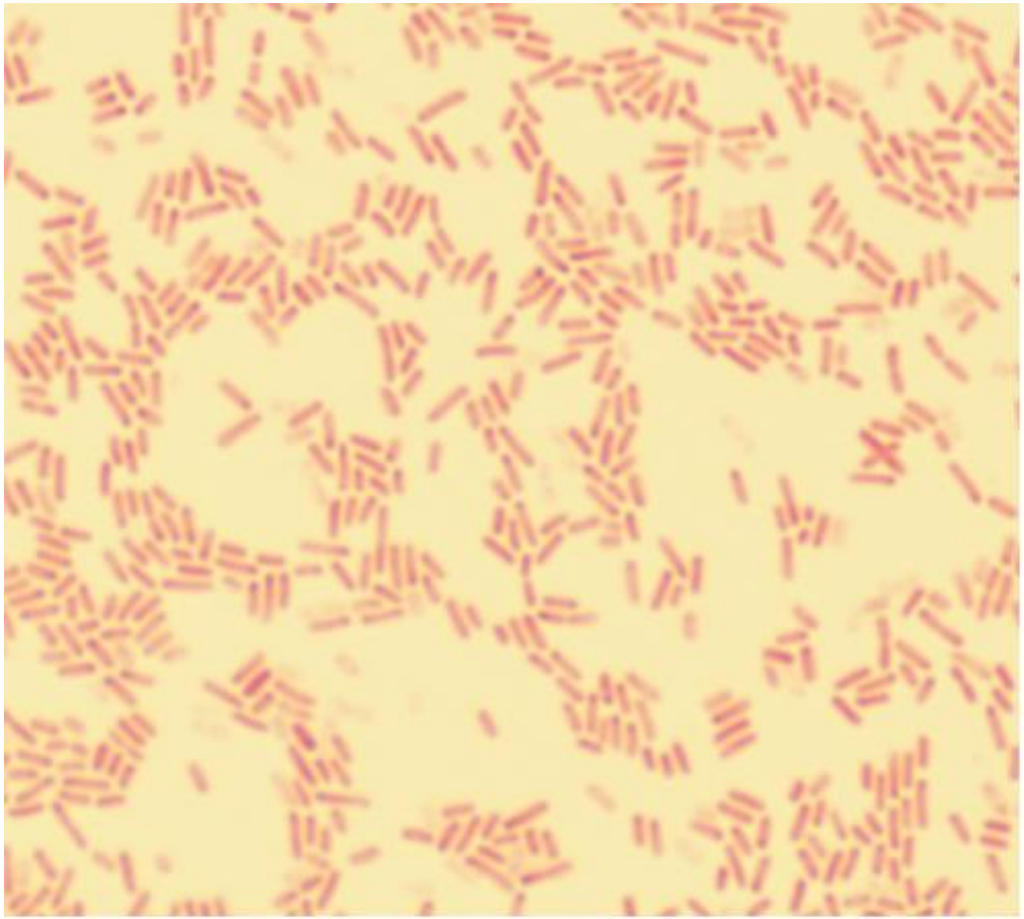
- Gram negative diplococci
- 70% homologous DNA with N. gonorrheae
- Oxidase positive
- Catalase positive
- Acid production with glucose and maltose
- Does not require Factors X and V for growth
- Non-motile
- Polysaccharide capsules
- No plasmids
- Produces IgA protease

Neisseria meningitidis

- Attach by pili to CD46 (expressed by all nucleated cells and is a complement regulatory protein)
- OPA proteins in outer membrane increase binding to epithelial cells
- Polysaccharide capsule as virulence factor
- Lipopolysaccharide wall shed in blebs as organism proliferates. Lipid A disaccharide activates toll like receptor (TLR4) and acts as endotoxin.
- Por A and B proteins

Other Neisseria

- N. catarrhalis produces DNAase
- Does not acidify carbohydrates



Gram-stain of P. aeruginosa, which are about 0.6 × 2 µm. Original magnification ×1000. (Courtesy of H Reyes.)

Pseudomonas aeruginosa

- Aerobic gram negative rod
- Oxidase positive
- Motile
- Non-lactose (or glucose) fermenter
- Produces pyocyanin pigment (blue green) and may fluoresce with UV light if also producing pyoverdin pigment
- Pyocyanin responsible for superoxide production and stimulation of IL-8 (neutrophil attracan)
- Pyoverdin is a siderophore (reactive Oxygen species)
- β-hemolysis
- May grow at 42C

Pseudomonas aeruginosa

- Capsule (glycolax), connective tissue hydrolases are virulence factors.
- Alginate (mucoid exopolysaccharide) protects from phagocytosis
- Pili and adherence proteins bind to epithelial cells and lung mucin.
- Phospholipase C is heat labile, hemolyzes and also degrades lung surfactant
- A heat-stable glycolipid is also produced and is a hemolysin.

Pseudomonas aeruginosa

- Elastase degrades immunoglobulins and extracellular matrix proteins (important in tissue distruction, particularly of the cornea)
- Exotoxin A covalently transfers ADP-ribose to elongation factor 2, inhibiting protein synthesis

Pseudomonas aeruginosa

- Type III secretion system also virulence factor (hollow syringe-like structure that projects from bacterial surface to bind host cells to facilitate injection of bacterial toxins)
- Exoenzyme S has ADP-ribosyl transferase activity
- Exoenzyme T has GTPase activity
- Exoenzyme U is a phospholipase
- Exoenzyme Y is an adenyl cyclase

Pseudomonas aeruginosa

- Ecthyma gangrenosum in immunocompromised
- External otitis (“swimmer’s ear”)
- Folliculitis from chlorinated swimming pools
- Necrotizing pneumonitis in ventilator patients (organism grows well in water)
- Wound infections
- Pneumonia in cystic fibrosis patients
- Immunocompromised hosts

Burkholderia

- Small
- B. pseudomallei is motile; B. mallei is not motile
- Creamy colonies that become rough and orange over 48 hours
- Oxidase-positive
- Grows at 42C
- Oxidizes lactose and glucose
- Indole negative
- Resistant to colistin
- Safety pin appearance (bipolar staining) on Wright's stain

Burkholderia pseudomallei

- Melioidosis
- Southeast Asia and Northern Australia
- Fever and pneumonitis that leads to consolidation of upper lobes
- May become afebrile while cavitary disease develops in upper lobes
- Chronic disease is indolent, with metastatic abscesses to brain, liver, heart, and skin
- High mortality rate if untreated
- Biological warfare use

Burkholderia mallei

- Glanders
- Usually involves livestock
- Ulcerative necrosis of upper airway with later pneumonia
- If percutaneous exposure, suppurative skin lesion and regional adenopathy
- High mortality rate if untreated
- Biological warfare use

Burkholderia cepacia complex

- Contaminated water
- Can be passed from patient to patient
- Usually with cystic fibrosis
- May cause patient to be removed from lung transplant list
- Grows on colistin containing media
- Oxidase positive
- Lysine decarboxylase positive
- Produce acid from glucose

Opportunitistic organisms

- Stenotrophomonas maltophilia
- Resistant to heavy metals
- Tolerant to silver-lined catheters
- Seen in patients on long-term broad spectrum antibiotic therapy
- Acinetobacter
- Pathogenicity related to capacity to form biofilms
- Oxidase negative

Facultatively aerobic gram negative rods

- Motile species have H (flagellar) antigen
- Two forms, phase 1 and phase 2
- May see phase variation within bacterium
- All have O antigen (lipopolysaccharide)
- Heat-stable
- Caspular antigen is K antigen
- Heat-labile
- External to O antigens
- Cause attachment of bacteria to epithelial cells

Facultatively aerobic gram negative rods

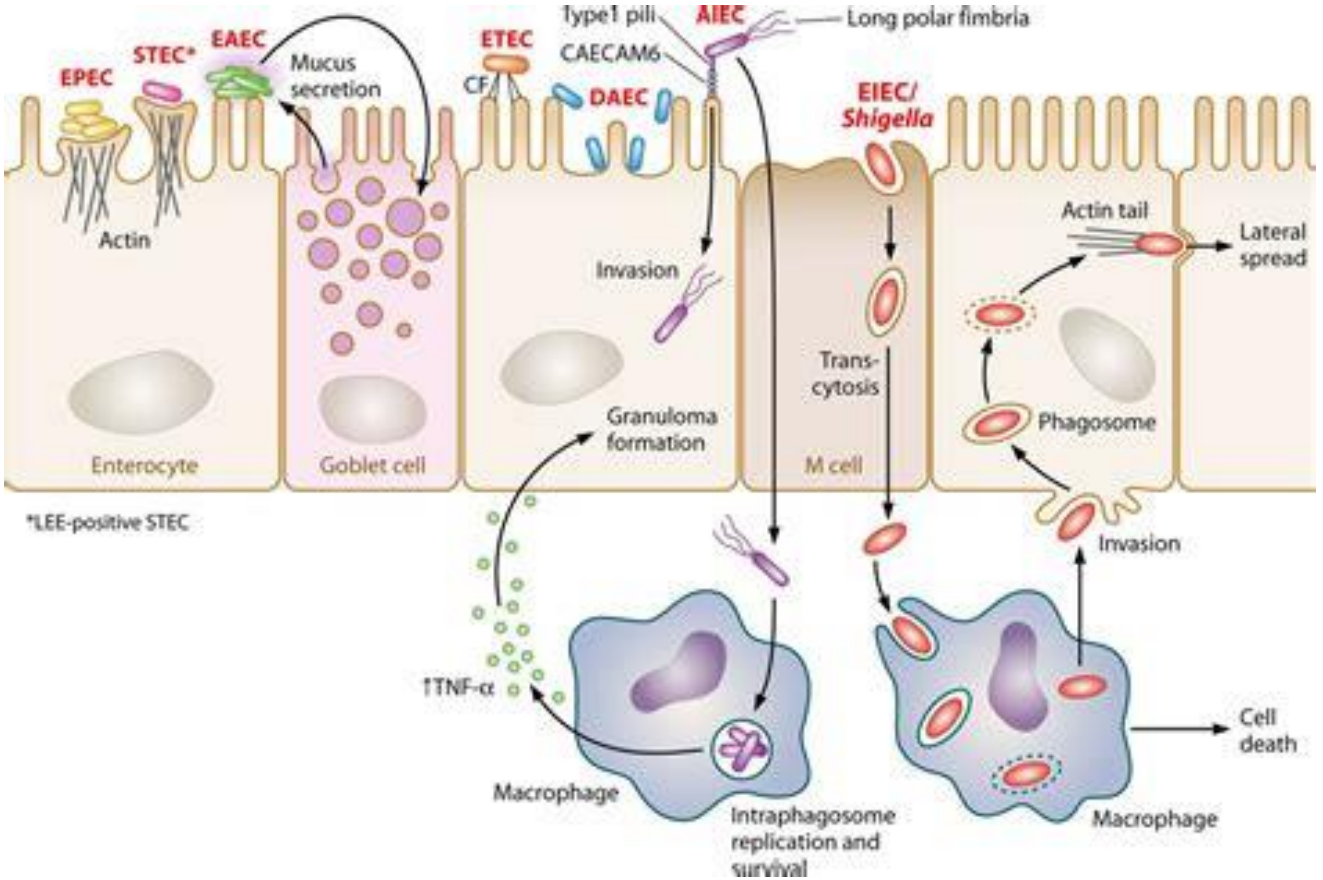
- E. coli with K1 antigen prominent in neonatal meninigitis
- Klebsiella type 2 polysaccharide capsule similar to that of Strep. Pneumoniae type 2 polysaccharide capsule
- E. coli 075:H100;H5 may induce antibody response to Hemophilus influuenzae type b

Escherichia coli

- Facultatively aerobic gram negative rod
- Oxidase negative
- Lactose fermenter
- Green sheen on EMB agar
- Pink on McConkey agar
- Positive test results for indole, lysine decarboxylase, and fermentation of mannitol
- Produces gas from glucose
- β-glucoronidase positive.

Escherichia coli

- Motile (H antigen). O antigen (lipopolysaccharide). Caspular antigen is K antigen
- Pili as virulence factor
- Heat labile toxin stimulates adenylate cyclase by ADP ribosylation; stable toxin stimulates guanylate cyclase. Leads to watery diarrhea.



https://duckduckgo.com/?t=ffab&q=shigella+toxin+mechanism&iax=images&ia=images&iai=https%3A%2F%2F163602-560839-raikfcquaxqncofqfm.stackpathdns.com%2Fwp-content%2Fuploads%2F2019%2F01%2FAdherence-patterns-of-enteric-E.-coli.jpg

Emteropathogenic strain

- The bundle forming pilus is encoded by a plasmid EPEC adherence factor (EAF) and the chromosomal locus of enterocyte effacement (LEE) pathogenicity island that promote the tight adherence and loss of microvilli characteristic of EPEC (attachment and effacement)
- Severe, watery diarrhea

Enterotoxigenic strain

- Pili known as colonization factor antigens [CFAs] are specific for humans and promote adherence of ETEC to epithelial cells of the small bowel.
- (1) Some strains of ETEC produce a heat-labile enterotoxin (LT) that is under the genetic control of a plasmid and is closely related to cholera toxin.
- The subunit B of LT attaches to the GM_1 ganglioside in the apical membrane of enterocytes and facilitates the entry of subunit A of LT into the cell, where the latter activates adenylyl cyclase
- CFTR deactivated

Enterotoxigenic strain

- (2) Some strains produce a heat-stable enterotoxin ST_a, under the genetic control of a heterogeneous group of plasmids.
- ST_a activates guanylyl cyclase in enteric epithelial cells and stimulates fluid secretion.
- Many ST_a-positive strains also produce LT.
- The strains with both toxins produce a more severe diarrhea.
- Plasmids also carry genes for CFAs.
- Important cause of diarrhea in children <5 years of age in developing countries
- “Traveler’s diarrhea”

Shigella toxin producing strain

- STEC has been associated with mild non-bloody diarrhea, hemorrhagic colitis, a severe form of diarrhea, and with hemolytic uremic syndrome
- Shiga-like toxin 1 is identical to the Shiga toxin of Shigella dysenteriae type 1
- Shiga-like toxin 2 also has many properties that are similar to the Shiga toxin
- The two toxins are antigenically and genetically distinct
- STEC O157:H7 does not use sorbitol nor does it have β-glucoronidase

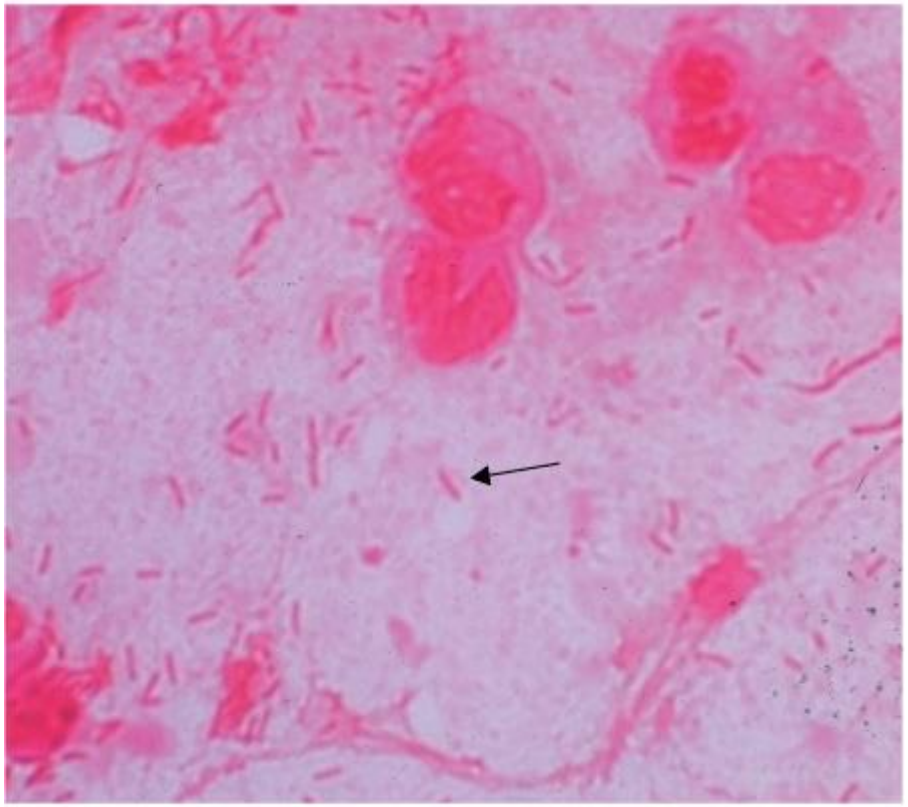
Other E. coli strains

- Enteroinvasive E. coli (EIEC) produce a disease very similar to shigellosis.
- Non-lactose fermenters
- Invade enterocytes
- Enteroaggregative E. coli (EAEC) causes acute and chronic diarrhea
- Some strains of EAEC produce ST-like toxin; others a plasmid-encoded enterotoxin that produces cellular damage; and still others, a hemolysin

Endotoxin activation

- TNF 1
- Adhesion of neutrophils to endothelium
- Enhances microbicidal activity of neutrophils
- Increased expression of MHC II and MHC II antigens
- Platelet activation and increased adhesiveness
- IL-1
- Fever
- Bradykinin, nitric oxide
- Vascular dilatation
- Alternative complement pathway
- Inflammation
- Activation of factor XII (Hageman)
- Increased clotting activity

Escherichia coli



Arrow points to a gram-negative rod.

Provider: Professor Shirley Lowe, University of California, San Francisco School of Medicine. With permission.

Color plate 8 Accessed 08/01/2010

Shigella

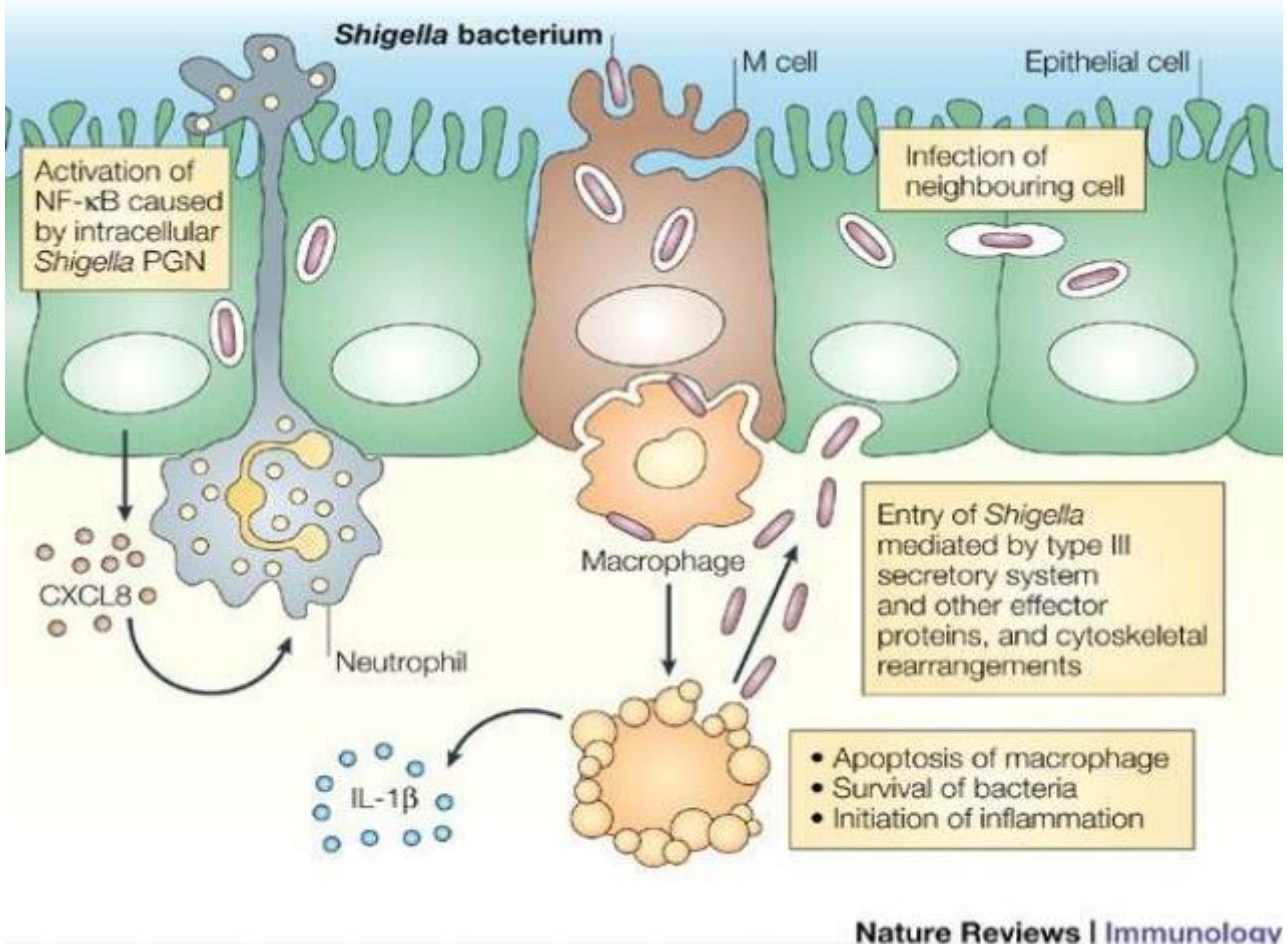
- Facultatively aerobic
- Oxidase negative
- Do not ferment lactose
- Ferment glucose, producing acid but not gas.
- Not motile
- They do not produce H_2S.
- Shigella dysenteriae does not ferment mannitol; all other strains do
- Shigella sonnei produces ornithine decarboxylase; all other strains do not
- All produce toxic lipopolysaccharide

Shigella

- Shigella toxin type 1 is a heat-labile exotoxin
- Antigenic
- Acting as an enterotoxin, it produces diarrhea
- Binds to NOD1 receptor
- After entering the cell, the toxin functions as an N-glycosidase, cleaving a specific adenine nucleobase from the 28S ribosome, halting protein synthesis
-

Shigella

- There is invasion of the mucosal epithelial cells (eg, M cells) by induced phagocytosis, escape from the phagocytic vacuole, multiplication and spread within the epithelial cell cytoplasm, and passage to adjacent cells (polymerize actin jet trails) without leaving cell.
- Microabscesses in the wall of the large intestine and terminal ileum lead to necrosis of the mucous membrane, superficial ulceration, bleeding, and formation of a “pseudomembrane”


Shigella bacterium
M cell
Epithelial cell
Activation of NF-κB caused by intracellular *Shigella* PGN
Infection of neighbouring cell
CXCL8
Neutrophil
Macrophage
Entry of *Shigella* mediated by type III secretory system and other effector proteins, and cytoskeletal rearrangements
IL-1β
• Apoptosis of macrophage
• Survival of bacteria
• Initiation of inflammation
Nature Reviews | Immunology

Salmonella

- Facultatively aerobic
- Motile
- Do not ferment lactose or sucrose
- Ferment glucose and mannose without producing gas
- Oxidase negative
- Produce H_2S
- Motile (H antigen).
- O antigen (lipopolysaccharide).
- Polysaccharide capsule is Vi antigen.

Salmonella

- Citrobacter is citrate positive and differ from the salmonellae in that they do not decarboxylate lysine
- Urease positive
- Non-Salmonella thyphimurium produces food poisoning.
- Polysaccharide capsule is virulence factor for Salmonella typhimurium
- Not important for other Salmonella.

Salmonella typhimurium

- Enters via Peyer's patches.
- Reproduces in blood and histiocytes in bowel wall.
- Pathogenicity island encodes an Iron uptake system that promotes virulence and systemic dissemination.
- Organism secreted into the bowel via the bile.
- Elicits B-cell response in MALT tissue leading to endotoxemia in response to antigen-antibody reaction.
- Massive necrosis of MALT tissue results.
- Gallbladder as organism reservoir.

Klebsiella-Enterobacter-Serratia

- Klebsiella
- Exhibit mucoid growth
- Large polysaccharide capsules (virulence factor)
- Non-motile
- Positive test results for lysine decarboxylase and citrate.
- Pathogenicity island encodes an Iron uptake system that ehances virulence and promotes sytemic dissemination

Klebsiella-Enterobacter-Serratia

- Enterobacter
- Positive test results for motility, citrate, and ornithine decarboxylase
- Produce gas from glucose.
- E. cloacae is urease positive
- No capsule
- Serratia
- 10% have red color
- Produces DNase, lipase, and gelatinase
- S. marcessens does not ferment lactose

Proteus-Morganella-Providencia

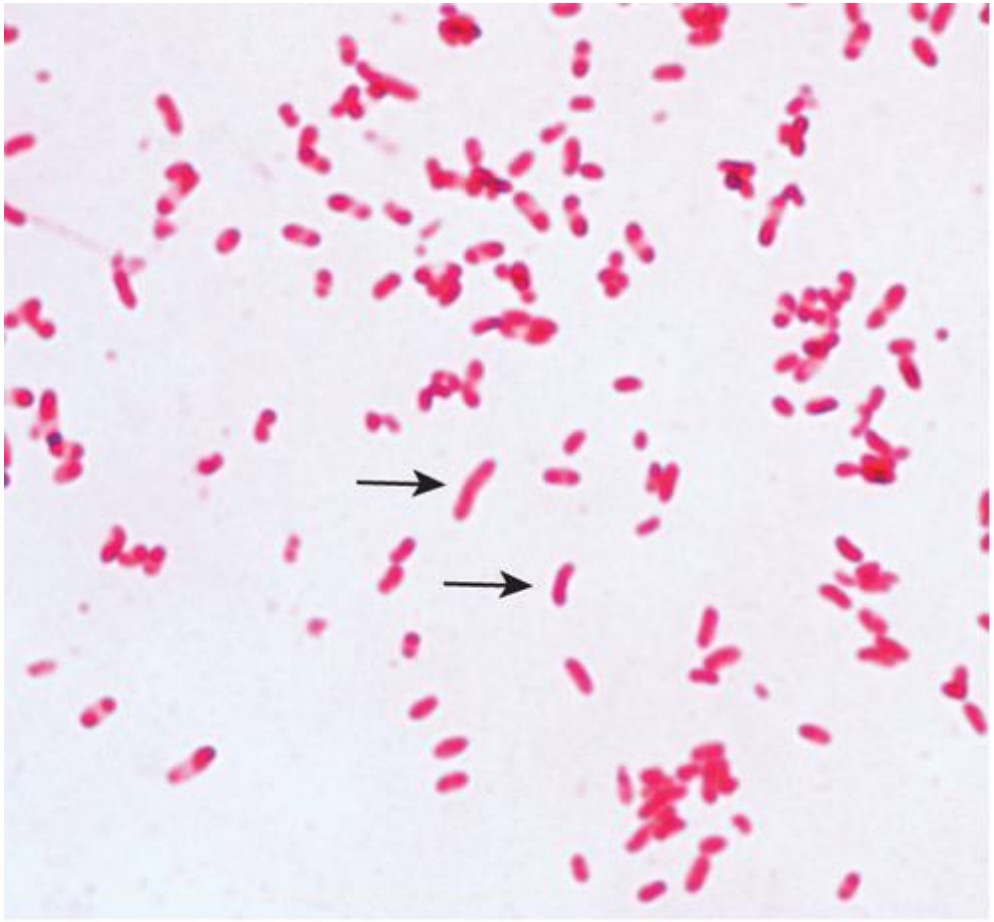
- Non-lactose fermenter
- Deaminate phenylalanine
- Motile (may swarm)
- Grow on potassium cyanide medium (KCN)
- Ferment xylose
- Oxidase negative
- Catalase positive
- May reduce Iron sulfide to Hydrogen sulfide
- Urease as virulence factor

Proteus-Morganella-Providencia

- Proteus and Morganella morganii are urease positive
- Providencia is urease negative
- P. Mirabilis is indole negative
- P. vulgaris, Morganella morganii, and Providencia rettgeri are indole positive

Vibrios

- Comma shaped
- Motile
- Catalase positive
- Oxidase positive
- Require 1% NaCl for growth
- Grow at pH 8.5-9.5
- Grow on thiosulfate-citrate-bile salts-sucrose agar (TCBS)
- V. cholera is orange (sucrose metabolism)
- V. parahemolyticus and V. vulnificus are green (do not metabolize sucrose)



Gram-stain of V. cholerae. Often they are comma shaped or slightly curved (arrows) and 1 × 2 to 4 µm. Original magnification ×1000.

Vibrio cholerae

- Motile (polar flagellum)
- Oxidase positive
- Ferments sucrose and mannose but not arabinose
- May grow without increased need for salt
- Non-invasive
- Heat labile flagellar (H) antigen
- Endotoxin is a part of the lipopolysaccharide complex integrated into the bacterium's outer membrane.
- O1 and O139 strains cause cholera

Vibrio cholerae

Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

Long arrow points to a curved gram-negative rod. Arrowhead points to a flagellum at one end of a curved gram-negative **rod.**

Provider: CDC.

Color plate 9
Accessed 08/01/2010

Cholera

- In the lumen of the bowel, the B component of enterotoxin (choleragen) allows it to adhere to a GM-1 monosialo-ganglioside molecule on the intestinal enterocytes.
- The A component of the cholera enterotoxin enters the cell, activates adenylate cyclase by ribosylation, and stimulates chronic production of cAMP
- Antigenically related to LT of E.Coli
- There is increased sodium-dependent chloride secretion, and absorption of sodium and chloride by the microvilli is inhibited
- Hypersecretion of water
- “Rice water” stools

Other vibrios

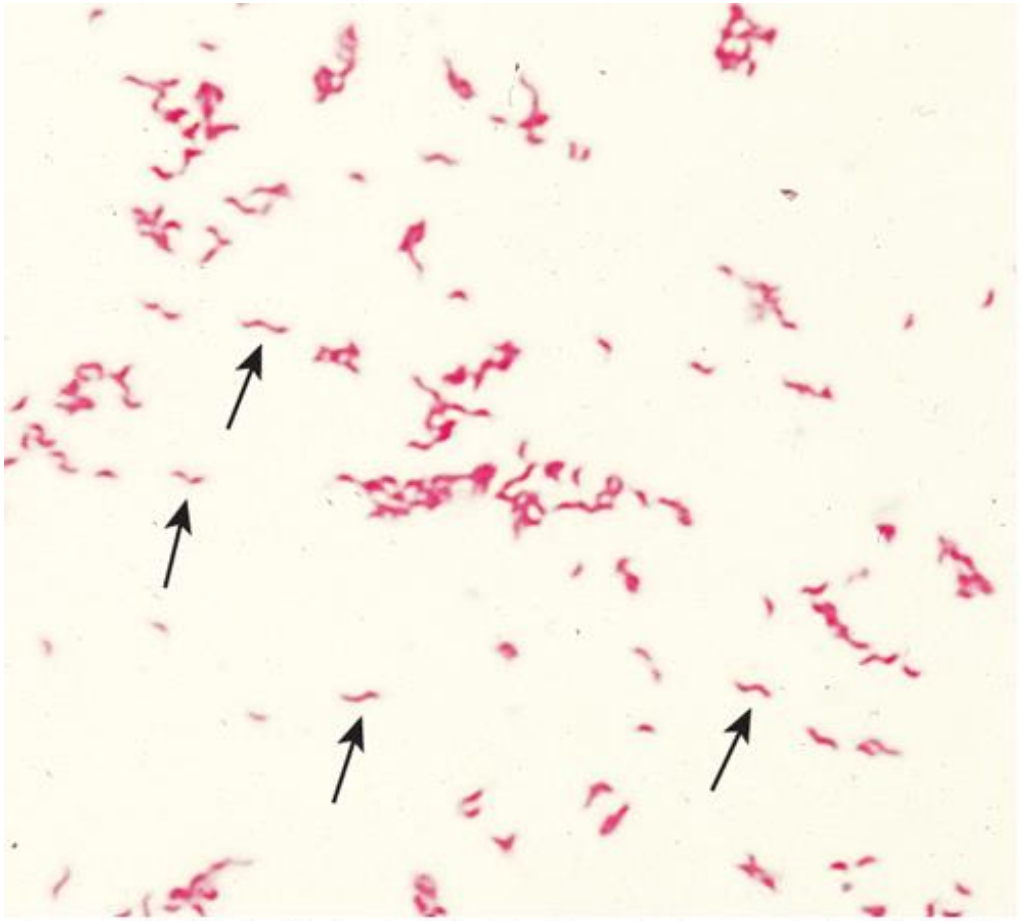
- Vibrio parahemolyticus
- Thermostable direct hemolysin (Kanagawa hemolysin)
- β-hemolysis on human blood agar, but not sheep blood.agar.
- No known enterotoxin
- Gastroenteritis following consumption of shellfish

Other vibrios

- Vibrio vilnificus
- Ferments lactose
- Anti-phagocytic polysaccharide capsule.
- May cause rapidly progressing wound infections
- Acquired by consumption of raw shellfish, particularly oysters.
- May progress to sepsis.
- 50% mortality rate if untreated

Aeromonas

- Oxidase positive
- β-hemolysis
- A. caviae causes gastroenteritis
- A. hydrophila associated with cellulitis
- Complication of use of medical leeches



Gram-stain of C. jejuni showing “comma”- or “gull wing”-shaped Gram-negative bacilli (arrows). Campylobacters stain faintly and can be difficult to visualize. Original magnification × 1000.

Campylobacter jejunii

- “Sea gull” wing shape
- Motile with single or multipolar flagella
- Oxidase positive,
- Catalase positive
- Requires 5-7% O_2, 10% CO_2 atmosphere at 42C for optimum growth
- Have liposaccharides with endotoxin activity
- Major cause of inflammatory diarrhea.
- Self-limiting
- Reiter’s disease may follow
- Associated with Guillan-Barré syndrome

Helicobacter pylori

- Microaerophilic gram negative organism (spiral rod)
- Slow growing
- Oxidase positive
- Catlase positive
- Urease positive
- Often acquired in early childhood
- High urease activity triggers local ammonia production. This neutralizes gastric acid.
- Flagellar-mediated activity allows movement of organism through gastric mucosa to gastric mucosa.

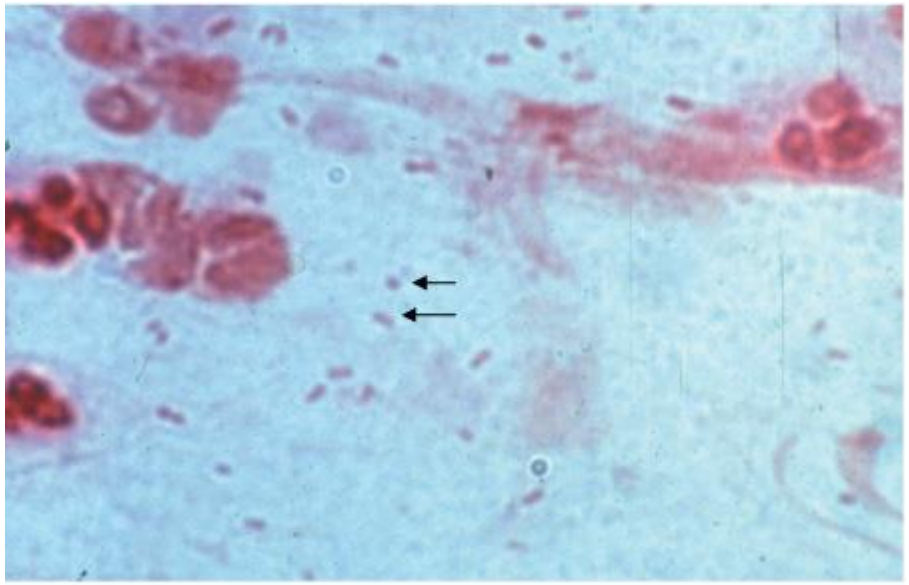
Helicobacter pylori

- BabA (blood-antigen-binding protein A) binds to fucosylated Lewis b receptor on gastric epithelial cells, and SabA binds to sialyl Lewis X receptors of the parietal cells of the stomach.
- CagA gene enters gastric cells by a Type IV secretion mechanism
- Interferes with cytoskeletal structure
- Induces IL-8 production (neutrophil chemotaxis)
- Local erosion (vac A gene activates IL-8 mediated inflammation).

Helicobacter pylori

- CagA gene associated with acute gastritis as well as adenocarcinoma.
- Stimulate mucosal associated lymphoid tissue.
- May lead to lymphoma.
- Therapy with proton pump inhibitor, clarithromycin, amoxicllin, and metronidazole for 7-14 days eliminates infection in 70% of patients.

Hemophilus influenzae



Source: Levinson W: *Review of Medical Microbiology and Immunology*, 10th Edition: http://www.accessmedicine.com

Arrows point to two small "cocco-bacillary" gram-negative rods.

Provider: Professor Shirley Lowe, University of California, San Francisco School of Medicine. With permission.

Color plate 10 Accessed 08/01/2010

Hemophilus influenzae

- Gram negative cocco-bacillus
- Catalase positive
- Ferments glucose
- Polysaccharide capsule (polyribitol ribose phosphate) as virulence factor
- Produces IgA protease
- Hemophilus influenzae requires hematin (X factor) and NAD (V factor) for growth as well as elevated CO_2 atmosphere.
- Grows on chocolate agar
- May satellite Staphylococcus on blood agar

Hemophilus influenzae

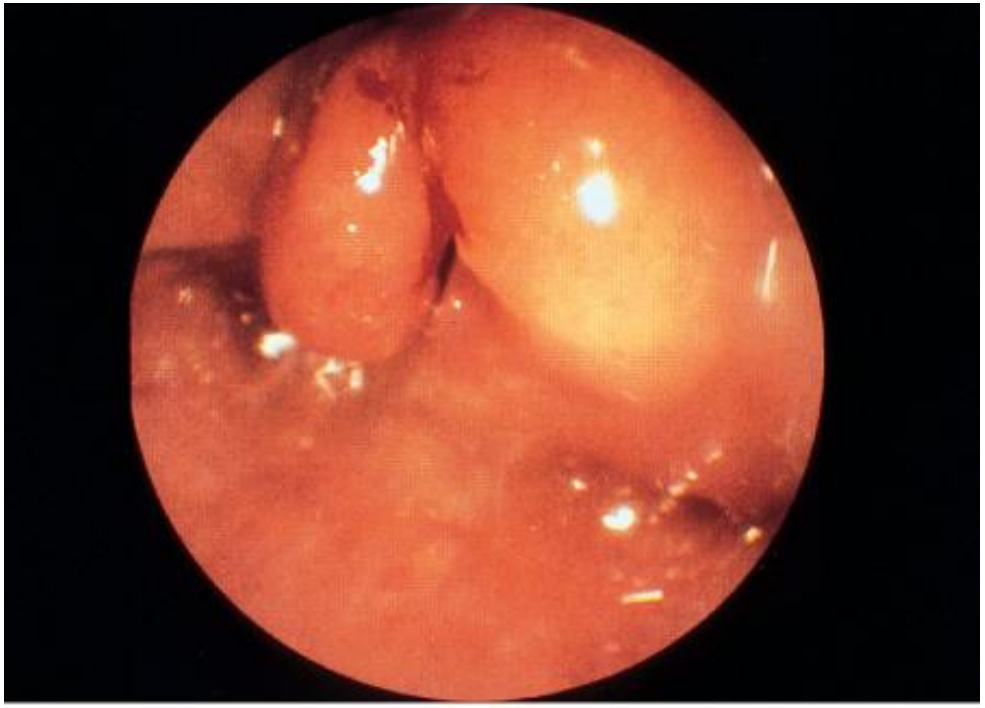
- Prior to vaccination, serotype b was the most common cause of meningitis in children
- Common infecting organism in adults with chronic bronchitis
- Occasionally causes acute obstructing laryngotracheitis
- Cherry-red, swollen epiglottis
- H. influenza biotype III causes purpuric fever
- H. aegyptius is closely related but causes acute conjunctivitis (“pink eye”)

Acute epiglottitis

Endoscopic view. Note the slit-like opening of the airway.

(Photo contributor: Department of Otolaryngology, Children's Hospital Medical Center, Cincinnati, OH.)

Fig. 14.55 Accessed 07/01/2010



Haemophilus ducreyi

- Requires X factor (hematin) and a 5% CO_2 atmosphere for growth.
- Polysaccharide capsule as virulence factor.
- Produces IgA protease.
- Causes chancroid

Chancroid

- Genital papule or pustule
- Painful ulcer develops
- May have “kissing” ulcerations.
- Painful, unilateral lymphadenopathy
- Responds to azithromycin or ceftriaxone
- Should treat sexual partner as well.
- Condom use.

Chancroid

Painful ulcer with marked surrounding erythema and edema.

(Courtesy of Prof. Alfred Eichmann, MD.)

Fig. 30-27 Accessed 07/01/2010

Bordatella

- Gram negative coccobacillus
- Strict aerobe
- Catalase positive
- Bordatella pertussisis oxidase positive
- Bordatella parapertussis is oxidase negative
- Nitrate, citrate, urea negative
- Does not require hematin or NAD (factors X or V)
- Bordet-Gengou media (potato-blood-glycerol agar)
- Bordatella parapertussis produces brown pigment

Bordatella

- The filamentous hemagglutinin adhesin binds to MAC-1 (CR3) integrins on macrophages as well as to carbohydrates on surface of respiratory epithelial cells.
- Bordatella virulence genes (bvg) locus regulates coordinated expression of virulence factors.
- bvgA is transcriptional activator
- bvgS responds to environmental signals
- . Adenylate cyclase toxin (ACT), dermonecrotic toxin (DNT), and hemolysin also are regulated by the bvg system

Bordatella

- ACT inhibits phagocytosis
- Tracheal cytotoxin kills respiratory cells directly
- Not regulated by bvg system
- Pertussis Exotoxin consists of five proteins:
- Catalytic peptide S1 shows homology with cholera toxin and Escherichia coli heat labile toxin.
- Subunit A, stimulates adenylate cyclase by ADP ribosylation of inhibitory $G_{\alpha 1}$ protein while subunit B binds the toxin to cell surface receptors.

Bordatella

- Mucus production increases.
- Cilia are paralyzed.
- As signal transduction is blocked, chemokine receptors C3a/C5a are inhibited.
- Bordatella parapertussis has a silent copy of the exotoxin gene
- Following 2 week incubation, “catarrhal phase” begins.
- Chronic cough with characteristic “whoop”
- Erythromycin may be useful in catarrhal phase

Brucella

- Fever, night sweats, malaise, anorexia, arthralgias, fatigue, weight loss, and depression.
- Few objective findings.
- Sacroiliitis present in 30% of patients.
- Epidydimitis in up to 40% of men.
- Granulomata form in many organs
- Streptomycin plus doxycyline.

Brucella species

- Gram negative coccobacillus (short rods)
- Non-motile
- Slow growth (obligate intracellular parasite)
- Endotoxin
- The onset of symptoms of brucellosis may be abrupt or insidious, developing over several days to weeks.
- Infected milk is usual source
- Granulomatous abscess in lymph nodes and in many organs

Francisella tularensis

- Gram negative coccobacillus
- Does not ferment lactose
- Cysteine enriched medium
- Type A occurs only in North America
- Ferments glycerol
- Contains citrulline ureidase
- Type B lacks these biochemical features
- Typhoidal form is not associated with lymphadenopathy nor with skin lesions
- Organism inhaled

Francisella tularensis

- Fever, chills, headache, and malaise, after an incubation period of 2 to 10 days.
- Associated with wild rabbits, ticks, and tabanid flies.
- Ulceroglandular disease accounts for 60 to 80 percent of cases.
- Fever and a single erythematous papuloulcerative lesion with a central eschar.
- Regional lymphadenopathy.
- Follows bite, usually

Francisella tularensis

- Typhoidal form is not associated with lymphadenopathy nor with skin lesions
- Organism inhaled
- Streptomycin curative.
- Because of poor CSF penetration, add chloramphenicol if meningitis.

Yersinia

- Facultatively aerobic gram negative rods
- Bipolar staining (“safety pin”)
- No acid from lactose
- May grow at low temperatures
- All varieties have lipopolysaccharide endotoxins
- V and W proteins as virulence factors
- Type III secretion system injects proteins that inhibit the regulation of actin polymerization (Yop E, H, T) as well as inhibiting lipopolysaccharide activated signaling pathways.
- Envelope antigen blocks phagocytosis
- Coagulase positive

Yersinia pestis

- May present with pneumonic or bubonic disease
- Has pathogenic island that encodes an Iron uptake system that enhances virulence and stimulates systemic dissemination.
- Non-lactose-fermenting colonies on MacConkey agar
- Grows better at 25°C than at 37°C.
- Catalase positive
- Indole, oxidase, and urease negative
- Nonmotile

Yersinia enterocolitica

- Multiplies in the cold
- Invades M cells.
- Adhesins bind host cell β-1 integrins.
- Enterocolitis
- Reiter's syndrome
- Pathogenicity island that encodes an Iron uptake system that enhances virulence and stimulates systemic dissemination.
- Urease positive and oxidase negative

Yersinia pseudotuberculosis

- Mesenteric adenitis with inflammation of terminal ileum
- Pathogenicity island that encodes an Iron uptake system that enhances virulence and stimulates systemic dissemination.
- Urease positive and oxidase negative

Pasturella multocida

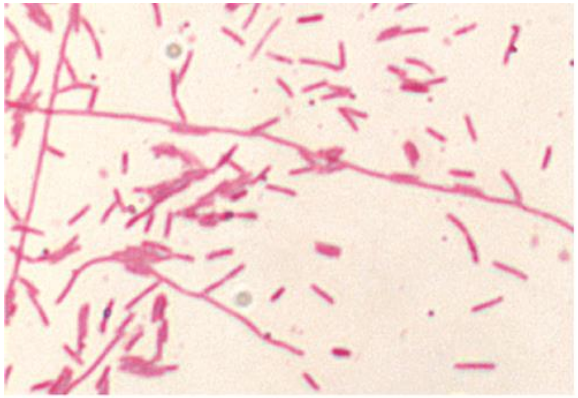
- Gram negative coccobacillus
- Bipolar staining (“safety pin”)
- Non-fermenter
- Iridescent
- Non-motile
- Soft tissue infections (animal bite usually)
- High degree of antibiotic resistance

Anerobic gram negative rods

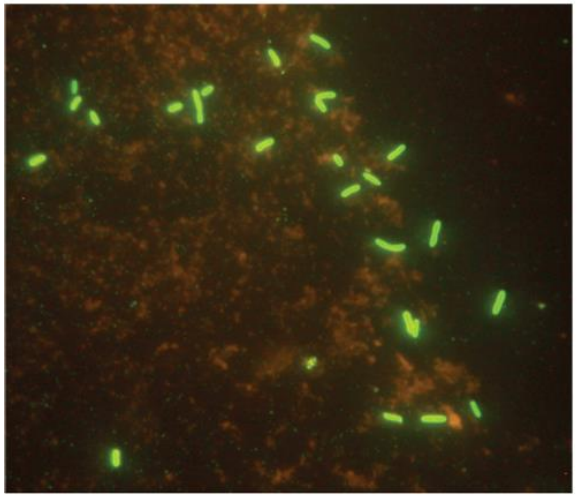
- Bacteroides fragilis
- Non-spore forming
- Bile resistant
- Capsule is anti-phagocytic.
- Rounded ends, vacuolated on Gram stain
- Weak endotoxin
- Found in bowel
- Prevotella melaninogenicus
- Produces black pigment.
- Rounded ends, vacuolated on Gram stain
- Usually in upper respiratory tract
- P. bivia and P. bisiens found in female genital tract

Anerobic gram negative rods

- Porphyromonas
- Found in gingiva
- Fusobacterium nucleatum
- Found in gingiva
- Tapered ends, filamentous forms
- Fusobacterium necrophorum
- Bizarre forms
- Not found in healthy gingiva
- Lemierre’s disease (acute jugular septic thrombophlebitis with metastatic abscesses)



A



B

Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

A: Gram-stain of a L. pneumophila; the legionellae stain faintly with basic fuchsin and poorly with safranin. Original magnification ×1000. (Courtesy CDC Public Health Image Library.) B: Direct fluorescent antibody stain of Legionella of mixed species using antibodies against legionellae genus antigens conjugated with fluorescein. Original magnification ×1000. (Courtesy R Nadarajah.)

Legionella pneumophilia

- Pleomorphic gram negative bacillus
- Buffered charcoal yeast extract with α-ketoglutarate, Iron and Cysteine for growth
- Highly motile
- Catalase positive
- Oxidase positive
- Produce gelatinase and β-lactamase
- Hydrolyze hippurate (other Legionellas do not)
- Silver or fluorescent staining to visualize in tissue.
- Serogroup1 most common

Legionella pneumophilia

- Mip protein promotes adherence and phagocytosis by alveolar macrophages.
- Phagosomes do not fuse with lysozomes
- Type IV secretion mechanism
- Ifn-γ activates macrophages.
- Inhalation may result in a severe, progressive illness
- Responds to macrolides and quinolones

Legionella pneumophilia

- Legionnaire's disease
- Fever, chills, malaise, nonproductive cough, hypoxia, diarrhea, and delirium.
- Leukocytosis, hyponatremia, hematuria (and even renal failure), or abnormal liver function
- Chest radiography reveals patchy, often multilobar consolidation
- "Pontiac fever" is self-limited
- Fever and chills, myalgia, malaise, and headache
- Dizziness, photophobia, neck stiffness, and confusion alos described
- Respiratory symptoms not as prominent

Bartonella bacilliformis

- Andes
- Transmitted by sandfly (Lutzomyia)
- Oroya fever
- Masses of bartonellae fill the cytoplasm of cells lining the blood vessels, and endothelial swelling may lead to vascular occlusion and thrombosis.
- Deformin protein promotes deformation of red cells and flagellum powers entry
- Rapid red cell destruction
- Hepatosplenomegaly and lymph node hemorrhage
- High mortality rate if untreated
- Ciprofloxacin

Bartonella bacilliformis

- Verruga peruana
- Vascular nodular skin lesions that develop post acute infection and resolve spontaneously within 1 year

Bartonella henselae

- Cat-scratch disease
- Low-grade fever and occasionally headache, malaise, and sore throat.
- The regional lymph nodes (axillary, epitrochlear, or cervical most commonly) are markedly enlarged and sometimes tender
- Intracellular
- Warthin-Starry stain to demonstrate
- Generally self-limited
- May also cause bacillary angiomatosis

Bartonella quintana

- Trench fever
- Sudden onset of fever accompanied by headache, malaise, restlessness, and shin pain.
- Symptoms coincide with release of organism in blood every 3–5 days with each episode lasting 5 days.
- May also cause bacillary angiomatosis

Bacillary angiomatosis

- Enlarging red (cranberry-like) papule, often with surrounding scale and erythema
- Characterized histopathologically as circumscribed lesions with lobular capillary proliferation and round, open vessels with cuboidal endothelial cells protruding into the vascular lumen.
- A prominent finding is epithelioid histiocytes surrounded by a loose fibromyxoid matrix.
- May cause Peliosis hepatis

Streptobacillus moniliformis

- Irregular chains of bacilli interspersed with fusiform enlargements and large round bodies.
- It grows best at 37°C in media containing serum protein, egg yolk, or starch,
- Rat bites
- Septic fever, blotchy and petechial rashes, and very painful polyarthritis

Spirochete

- Obligate pathogen.
- Reproduces by transverse fission.
- Helically coiled or corkscrew shaped.
- May be visualized with darkfield microscopy.
- Glycosaminoglycan coating
- Peptoglidocan outer membrane.
- Endoflagella within periplasmic space
- Inner membrane inside endoflagella
- Virulent species produce hyaluronidase (facilitate perivascular entry) and are coated with host-cell fibronectin (preventing phagocytosis).
- B-cell response leads to inflammatory damage of small vessels and obliterative endarteritis.
- T-cell response leads to granuloma formation.

Treponemal diseases

- Treponema pallidum causes syphilis
- T. pallidum subspp. endemicum causes endemic syphilis (bejel)
- T. pallidum subspp. pertenue causes yaws
- Treponema carateum causes pinta
- T. vincentii causes acute necrotizing ulcerative gingivitis (Vincent's infection)

Treponema pallidum

- Has hyaluronidase that breaks down the hyaluronic acid in the ground substance of tissue and enhances the invasiveness of the organism.
- The endoflagella are composed of three core proteins that are homologous to other bacterial flagellin proteins plus an unrelated sheath protein.
- Cardiolipin is an important component of the treponemal antigens.
- Basis for RPR and VDRL assays

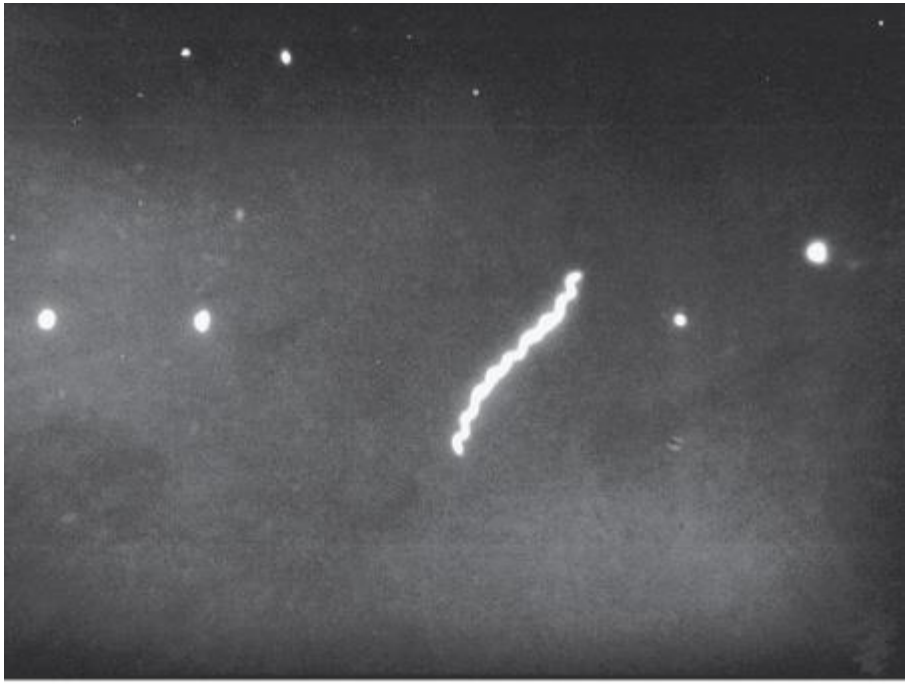
Primary syphilis

- Painless chancre develops at inoculation site.
- 3-4 wk incubation (10-90 day range).
- Begins as papule then erodes to painless ulcer with raised borders. (Hard chancre)
- Usually present on genitalia.
- Ulcer is highly contagious as is the site of replicating spirochetes.
- Painless regional lymphadenopathy develops weeks after chancre.
- Ulcer heals on its own by 2 mos.

Primary syphilis

- RPR or VDRL likely negative in primary syphilis
- Darkfield exam is positive.
- Responds to penicillin.

Treponema pallidum



Dark field microscopy. The coiled form of this spirochete is in the center of the field.

Provider: CDC/Dr. Schwartz.

Color plate 13
Accessed 08/01/2010

Primary syphilis

A 28-year-old male with penile lesion for 7 days. Painless ulcer on distal penile shaft with smaller erosion on the glans. The ulcer is quite firm on palpation.

Fig. 30-18 Accessed 07/01/2010

Secondary syphilis

- Early latent.
- Exposure less than one year and no clinical signs.
- RPR or VDRL positive; FTA confirmation.
- Secondary.
- Exposure less than a year and clinical signs of ulceration or rash.
- Begins as flu-like syndrome usually 4-10 wks after appearance of chancre.
- Several days later a copper-colored rash (macular, papular, or pustular) can cover entire skin surface including palms and soles.

Secondary syphilis

- Rash resolves after several months.
- Rash is highly infectious.
- May manifest with optic neuritis, arthropathy.
- Contagious lesions may recur after 3-5 years.
- 30% may resolve spontaneously.
- Thereafter the patient is not infectious and will have anti-Treponemal antibodies and will not reinfect later
- Responds to penicillin.
- If treated, may re-infect later.

Secondary syphilis

B

A

Papulosquamous truncal eruption (left); palmar eruption (right). May see mucosal lesions as well. Occur up to 3 months following primary infection.

Figs. 30-21B and 30-22A Accessed 07/16/2010

Tertiary syphilis

- Late Latent (30%)
- Exposure more than one year and no clinical signs.
- RPR or VDRL may be negative; FTA confirmation.
- Aneurysm of thoracic aorta.
- Blindness and dementia may also be presenting signs.
- The gumma is a scar-like granulomatous lesion that may be found on skin or in other organs.
- Endarteritis and a plasma cell infiltration are clues to its origin.
- 30% progress to tertiary syphillis

Tertiary syphilis

- Tertiary without neurologic signs.
- RPR or VDRL may be negative; FTA confirmation.
- Tertiary with neurologic signs.
- RPR or VDRL may be negative; FTA confirmation.
- Responds to penicillin.
- All sexual contacts require treatment.
- Though there is no clinical trial to demonstrate efficacy, tetracycline is used if the patient is allergic to penicillin.
- Worsening of symptoms with antibiotic therapy is the Jarisch-Herxheimer reaction.

Congenital syphilis

- Serious fetal disease.
- Transplacental passage at 10^{th}-15^{th} week
- Latent infection, multi-organ malformations, or fetal death.
- Most infants born without clinical disease.

Congenital syphilis

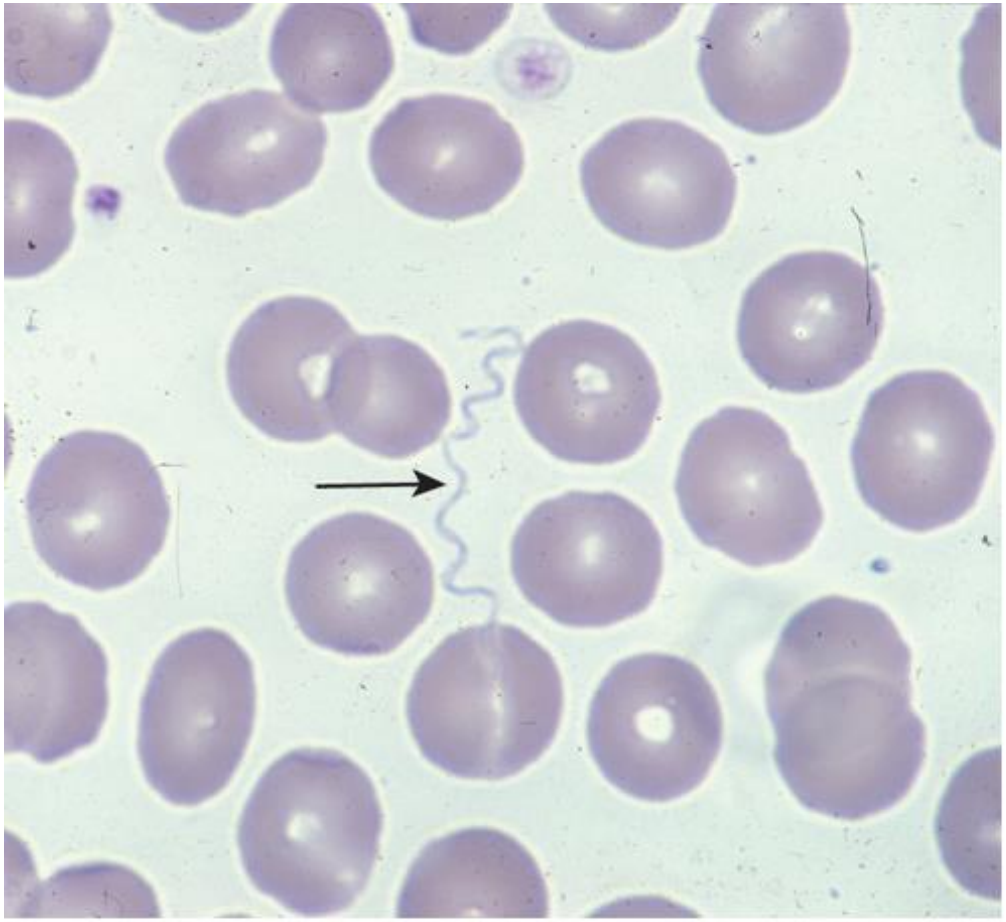
- Of those symptomatic:
- Rhinitis, desquamating maculopapular rash
- Blindness, deafness
- Liver, heart, lungs, CNS affected
- Hutchinson teeth (notched, peg shaped teeth)
- Osteochondritis, periostitis particularly of vomer (saddle nose) and lower legs (saber shin)
- Late manifestations include interstitial keratitis and CNVIII deafness

Testing

- T. pallidum–particle agglutination (TP-PA) test
- Gelatin coated particles sensitized with Treponemal antigens agglutinate in presence of anti-Treponemal antibody
- T. pallidum hemagglutination (TPHA) and the microhemagglutination T. pallidum (MHA-TP) use sheep erythrocytes, not gelatin, hemolyze in presence of antibody
- Fluorescent treponemal antibody absorbed (FTA-ABS) detects reactive antibodies to (dead, Reiter) spirochete

Testing

- The presence of IgM FTA in the blood of newborns is a good evidence of in utero infection.
- A negative FTA-ABS result on CSF tends to exclude neurosyphilis
- A positive FTA-ABS result on CSF can occur by transfer of antibodies from serum and is not helpful in the diagnosis of neurosyphilis.



Borrelia (arrow) in a peripheral blood smear of a patient with relapsing fever. Original magnification ×1000.

Borellia recurrentis

- In louse borne relapsing fever, the first episode of fever is unremitting for three to six days
- It is typically followed by a single milder episode.
- The fever may be as high as 43ºC and is usually above 39ºC.
- Headache, neck stiffness, arthralgia, myalgia, and nausea.
- The patient with relapsing fever may experience dizziness and unsteady gait.
- A nonproductive cough is common during louse borne relapsing fever.

Borellia recurrentis

- In tick borne relapsing fever, multiple febrile periods last from one to three days each.
- Borrelia hermsii in US West
- It is typically followed by a single milder episode.
- The fever may be as high as 43ºC and is usually above 39ºC.
- Headache, neck stiffness, arthralgia, myalgia, and nausea.
- The patient with relapsing fever may experience dizziness and unsteady gait.
- Localizing neurologic symptoms common
- Direct invasion of spirochetes

Borellia recurrentis

- The first fever episode ends by crisis (rigors, a further elevation in temperature, and increases in pulse and blood pressure) lasting approximately 15 to 30 minutes.
- The crisis phase is followed by profuse diaphoresis, falling temperature, and hypotension which usually persists for several hours.
- Mortality from untreated relapsing fever is most common during the crisis and its immediate aftermath.

Borrelia recurrentis

- Delirium or apathy and occasionally stupor or coma can occur in both forms, but localizing neurologic symptoms are more common in tick borne relapsing fever.
- The majority of patients with louse borne relapsing fever have hepatomegaly.
- In both forms, the interval between fevers ranges from 4 to 14 days.

Borrelia recurrentis

- Epistaxis, petechiae, and ecchymoses are common during louse-borne relapsing fever but not tick-borne relapsing fever.
- The bleeding disorder is probably the consequence of thrombocytopenia, impaired hepatic production of clotting factors, and/or blockage of small vessels by aggregates of spirochetes, erythrocytes, and platelets.
- Splenomegaly common.

Borrelia recurrentis

- Myocarditis is common.
- CNVII and CNVIII neuritis common.
- Visual impairment from iridocyclitis may be permanent.
- Penicillin adequate treatment for louse borne relapsing fever.
- Doxycycline is both adequate treatment for tick borne relapsing fever as well as for prevention.
- Ceftriaxone if neurologic involvement.
- Jarisch-Herxheimer reaction may be seen.

Borellia spiralis (burgdorferi)

- Lyme disease
- Spirochete is large
- Moves both by rotation and twisting
- May be visualized on light microscopy with Wright stain.
- Bacterial proteins bind to TLR2 expressed in macrophages. CD4 mediated response.
- Plasmid with single promoter sequence and multiple coding sequences for V1sE antigenic surface protein permits antigen variation to escape immune recognition

Lyme disease

- Stage 1:
- Erythema migrans and flu-like symptoms.
- Appears 3-30 days after bite and persists if Ixodes tick not removed and antibiotic treatment begun.
- Painless target lesion at site of tick bite.
- One third of patients do not progress beyond the cutaneous manifestation.
- An acute rapid progression to encephalitis is seen in immunocompromised patients.
- Fatal if not treated.

Lyme disease

- May have many such recurrences that diminish in intensity
- Stage 2:
- Six months later may present with intermittent arthritis, cranial nerve palsies, atrioventricular (AV) nodal block, severe malaise and fatigue.

Lyme disease

- Stage 3:
- Prolonged arthritis; chronic encephalitis, myelitis; symptoms consistent with fibromyalgia.
- Rarely fatal.
- Borrelia miyamotoi also produces Lyme-like illness
- Fevers >40C

Lyme disease

- Chronic skin involvement (acrodermatitis chronica atrophicans).
- Doxycycline or amoxicillin single dose with 72 hours of removing tick can prevent disease.
- If target lesion has presented, 30 days of daily amoxicillin.

Leptospirosis

- Actively motile
- Hook shaped
- Grow best in egg medium
- Stain with silver
- Rely on oxidation of long-chain fatty acids for energy and ammonia for Nitrogen
- Spirochetes penetrate mucous membranes or cuts in skin.

Leptospirosis

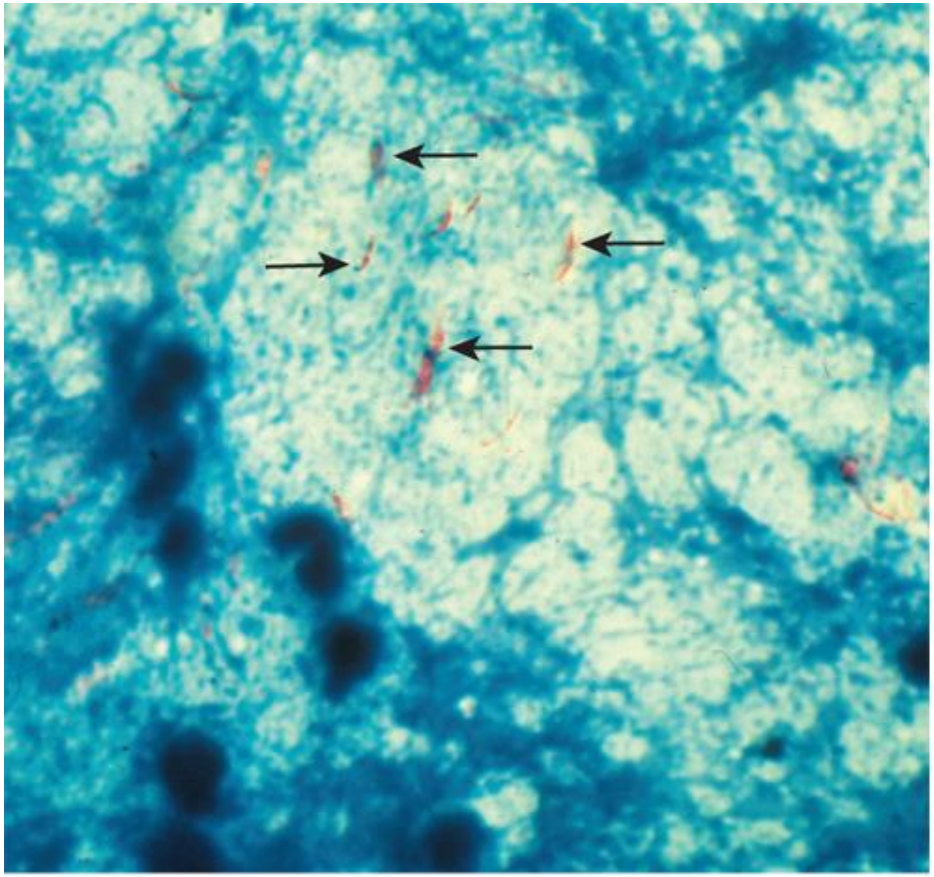
- Endemic Fever
- Incubation period: 3-10 days.
- Spirochetes in blood.
- Shaking chills, abrupt fever, muscle aches, headache.
- Splenomegaly and hepatomegaly common as spirochetes established. May lead to hemorrhage and organ dysfunction.
- Fever lasts 3-5 days; followed by weakness.

Leptospirosis

- Relapsing Fever .
- Afebrile period lasts 4-10 days as IgM titer rises.
- Spirochetes absent.
- Second attack starts with chills, fever, intense headache (“aseptic meningitis”) and malaise.
- 3-10 relapses occur.
- Severity diminishes with each relapse as antigen altered.
- Severe disease affects liver and kidneys.
- Produce hemorrhage and organ dysfunction

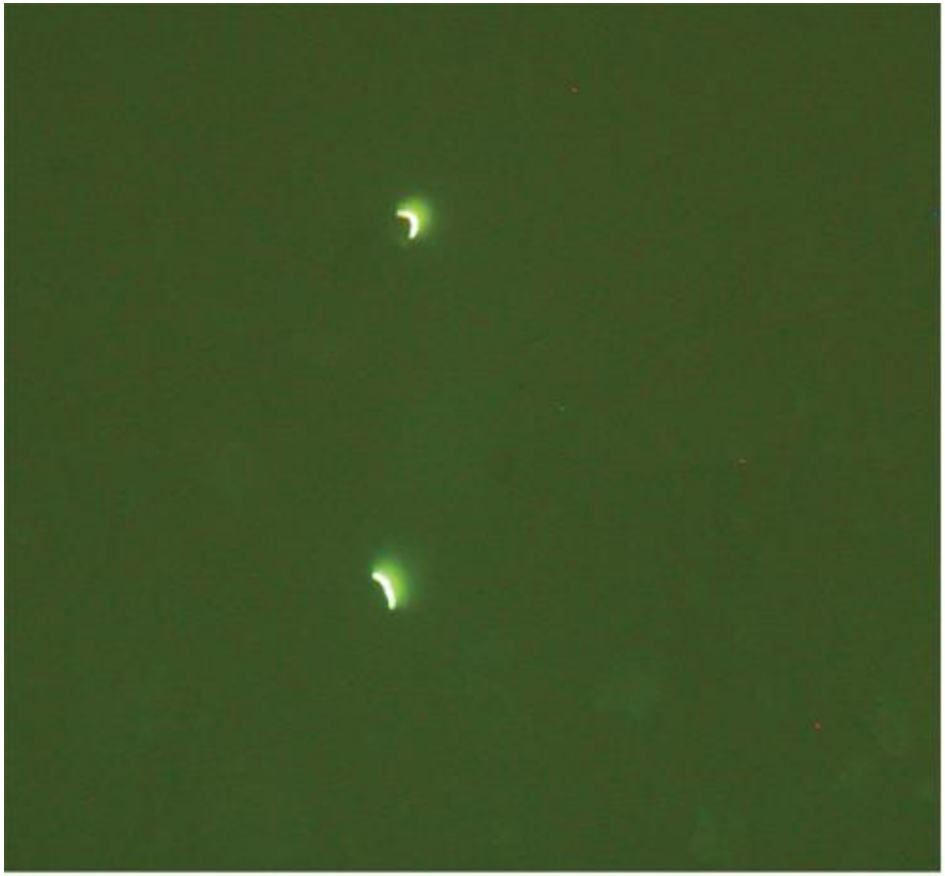
Leptospirosis

- Weil disease
- Hepatic symptoms with jaundice.
- No permanent damage.
- Congenital leptospirosis
- Flu-like symptoms and diffuse rash



A

A:M. tuberculosis (arrows) in a processed sputum specimen stained by Ziehl-Neelsen stain. The M. tuberculosis is red against a blue background. B: The fluorescent dye Auramine O was used to stain a sputum sample. It shows two fluorescent M. tuberculosis. Original magnification ×1000. (Courtesy of G Cunningham.)



B

A:M. tuberculosis (arrows) in a processed sputum specimen stained by Ziehl-Neelsen stain. The M. tuberculosis is red against a blue background. B: The fluorescent dye Auramine O was used to stain a sputum sample. It shows two fluorescent M. tuberculosis. Original magnification ×1000. (Courtesy of G Cunningham.)

Mycobacterium tuberculosis

- Acid fast (Ziehl-Neelsen stain)
- Fluoresce with auramine O or rhodamine dyes
- Grow on Middlebrook or Lowenstein-Jensen (egg) media
- A facultative intracellular parasite and obligate aerobe.
- Peptidoglycolipid cell walls (mycolic acid).
- Sulfatide waxy coat (D) resists enzyme and acid degradation in macrophage.
- Block priming of monocytes (little superoxide radical production).

Mycobacterium tuberculosis

- Cord factor (trehalose mycolate) permits organism to grow in rope-like cords and inhibits fusion of phagosome with lysosome (disrupts Ca^{2+} signaling).
- Slows granulocyte chemotaxis and disrupts respiratory chain.
- Muramyl dipeptide (from peptidoglycan) complexed with mycolic acids can cause granuloma formation
- Phospholipids induce caseous necrosis.

Mycobacterium tuberculosis

- Lipoprotein produces ligands for TLR2 and induces IL-12 by dendritic cells.
- IFN-γ activation stimulates formation of phagolysosomes in infected macrophages
- Also induces nitric oxide synthase in phagolysozome.
- T_{H1} cell predominant responder.
- NRAMP1 mutation affects endosome transmembrane protein and may limit loss of Fe^{2+} and other divalent cations from lysosome, promoting microbial growth

Mycobacterium tuberculosis

- Primary infection
- After several weeks the Mycobacteria stop multiplying and the pneumonic process resolves.
- Generally confined to apical region of lung. Dissemination to other organs stops.
- Disease resolution is associated with positive Mantoux skin test.
- Cellular mediated immune response has controlled disease
- If previously vaccinated, must examine levels of specific IFN-γ.

Mycobacterium tuberculosis

- Initial lesions characterized by necrosis and by being localized (principally, in the lung).
- Necrosis is due to the destructive inflammatory response (allergic response to tuberculoprotein).
- Localization is due to cellular mediated immune response preventing spread.
- If PPD positive, 5-10% will develop TB over lifetime

Mycobacterium tuberculosis

- Bacilli multiply initially only in necrotic area
- Caseation necrosis
- Spreads as the necrosis erodes bronchus or blood vessels.
- Cavitation may occur.
- Preferentially, upper lobes of lung affected.
- The primary lesions or granulomas are called tubercles and often calcify.
- Ghon complex consists of enlarged perihilar lymph nodes adjacent to a calcified granuloma.

Mycobacterium tuberculosis

- Tubercle bacilli may remain viable but dormant within tissues for years or even lifetime unless host resistance is lowered.
- Reactivation poorly understood.
- Secondary tuberculosis
- Usually cause by reactivation of an old infection.
- Higher incidence in those with HLADR2
- India, Russia, Indonesia
- Occurs in the presence of tuberculin hypersensitivity (positive TB test) and in spite of the acquired cellular immunity.

Mycobacterium tuberculosis

- Miliary (disseminated) form associated with generalized small nodules throughout lung fields
- Nodular skin lesion may be seen (erytherma induratum).

Mycobacterium tuberculosis

- INH+rifapentine+Pyridoxine given weekly for 3 months in non-cavitary patients
- INH+Rifampin+Pyridoxine given daily for 3 months
- Rifampin given daily for 4 months
- NO Rifampin+Pyrazinamide
- Ethambutol should be added if there is risk of INH resistance.
- Must follow patient for 1 year after treatment is stopped to check for relapses.

Mycobacterium tuberculosis

- Short course therapy for uncomplicated pulmonary TB only
- In latent infection, INH+Pyridoxine for 9 months
- If cavitation on an initial chest radiograph and with positive cultures following two months of therapy, a seven-month continuation phase (total of nine months of treatment).
- An extended three-month continuation phase is also recommended for any patient with at least one cavity on a follow-up radiograph.
- Surgery for drug resistant disease early in course

Other mycobacteria

- 95% of mycobacterial infections are M. tuberculosis, M. kansasii, M. avium complex, M. gordonae
- Growth rate separates rapid growers (<7days) from other mycobacteria
- M. chelonae
- M. smegmatis
- M. marinium
- Cutaneous granulomas in tropical fish enthusiasts or scuba divers from abrasions on coral.

Other mycobacteria

- Photochromogens
- Produce pigment when exposed to light
- M. kansasii
- Pulmonary disease
- Scotochromogens
- Produce pigment in the absence of light
- M. scrofulaceum
- Cervical adenitis
- Non-chromogens
- Do not produce chromogen
- M. avium complex

Mycobacterium intracellulare (MAI)

- 98% of MAI infections are in AIDS patients.
- Believed to enter immunocompromised patients through the gastrointestinal tract.
- MAI organisms in the intestine multiply in the gut associated lymphoid tissue for 4-5 months after which they enter the blood.
- MAI rarely form granulomas.
- Histiocytes have heavy organism load (characteristic on stain).
- Intestinal erosion causes the patient to suffer from chronic diarrhea.

Mycobacterium intracellulare (MAI)

- Pulmonary disease
- Most often seen in white males 45-65 years old with preexisting pulmonary disease (COPD, TB, emphysema).
- Clinical manifestations include chronic productive cough, dyspnea, fever, night sweats, malaise and fatigue.
- Lesions of MAI pulmonary disease are granulomas that may or may not show caseation.

Mycobacterium avium-intracellulare

- Subacute lymphadenitis (scrofula)
- MAI is the most common cause of subacute lymphadenitis in children under 5 years of age.
- The lymph nodes involved are most often in the neck and face.
- Usually several nodes on one side of the body are swollen but not painful.
- Surgical removal of infected lymph nodes is often sufficient treatment for children with subacute lymphadenitis.

Table 2

Treatment of *Mycobacterium avium* complex pulmonary disease

Indications	Regimen	Duration of therapy
Non-cavitary nodular bronchiectatic form	Azithromycin 500 mg tiw or clarithromycin 1,000 mg tiw and rifampin 600 mg tiw and ethambutol 25 mg/kg tiw	12 Months beyond sputum culture conversion to negative
Fibrocavitary form or cavitary nodular bronchiectatic form	Azithromycin 250–500 mg daily or clarithromycin 1000 mg daily and rifampin 450–600 mg daily and ethambutol 15 mg/kg daily and/or amikacin 15 mg/kg IV or IM tiw	12 Months beyond sputum culture conversion to negative
Macrolide-resistant	Rifampin 450–600 mg daily and ethambutol 15 mg/kg daily and/or moxifloxacin 400 mg daily and/or clofazimine 100 mg daily and/or inhaled amikacin and/or bedaquiline	12 Months beyond sputum culture conversion to negative

tiw: three times weekly; IV: intravenous injection; IM: intramuscular injection.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6304322/

Mycobacterium intracellulare (MAI)

- Fail to respond to usual mycobacterial therapy.
- Immunocompetent patients with pulmonary disease or disseminated disease are treated with daily azithromycin plus ethambutol and amikacin three times a week
- Immunocompromised patients are treated with clarithromycin and ethambutol daily
- In patients with CD4 <50 cells/fl, fluoroquinolone with or without amikacin.
- Lifetime therapy

Mycobacterium leprae

- An obligate intracellular parasite.
- Prefers lower temperatures for growth.
- Found in armadillo
- Contain o-diphenoloxidase
- Acid fast rods abundant in lepromatous, not tuberculoid, form.
- Few granulomas in tuberculoid form.
- Absent in lepromatous form (weak T_{H1} response).

Leprosy

- Hansen's disease is a chronic slowly progressing systemic disease involving skin, mucous membranes, testes, and peripheral nerves in limbs
- Extensive nerve damage and hypopigmented areas of skin as a result of cellular response to infecting organism.
- Nerve damage and anesthesia noted.
- Often suffer from clawing of the hands, foot drop or facial palsy.

Leprosy

- Lepromatous leprosy is most severe form
- Poor cellular immune response
- Mitsuda (lepromin) skin test is negative
- However, a strong non-protective antibody response is noted. Circulating antigen-antibody complexes deposited in tissues.
- Strong cellular mediated immune response in tuberculoid form.
- Mitsuda (lepromin) skin test is positive.
- Untreated cases are terminal in 16-18 years.

Leprosy

- Tuberculoid leprosy (Paucibacillary)
- Rifampin monthly plus dapsone daily for 6 months.
- Lepromatous leprosy (Multibacillary)
- Monthly rifampin plus dapsone and clofazimine daily for 12 months
- Single skin lesion (Paucibacillary)
- Single dose of rifampicin, ofloxacin, and minocycline

Group	Organism	Disease	Geographic Distribution	Vector	Mammalian Reservoir	Clinical Features
Typhus group	*Rickettsia prowazekii*	Epidemic typhus (louse-borne typhus), Brill-Zinsser disease	Worldwide: South America, Africa, Asia, North America	Louse	Humans	Fever, chills, myalgia, headache, rash (no eschar); severe illness if untreated
	Rickettsia typhi	Murine typhus, endemic typhus, flea-borne typhus	Worldwide (small foci)	Flea	Rodents	Fever, headache, myalgia, rash (no eschar); milder illness than epidemic typhus
Scrub typhus group	*Orientia tsutsugamushi*	Scrub typhus	Asia, South Pacific, northern Australia	Mite	Rodents	Fever, headache, rash (50% have eschar), lymphadenopathy, atypical lymphocytes
Spotted fever group[b]	*Rickettsia rickettsii*	Rocky Mountain spotted fever	Western Hemisphere (United States, South America)	Tick[c]	Rodents, dogs	Fever, headache, rash (no eschar); many systemic manifestations
	Rickettsia conorii	Fièvre boutonneuse, Mediterranean spotted fever, Israeli spotted fever, South African tick fever, African (Kenya) tick typhus, Indian tick typhus	Mediterranean countries, Africa, Middle East, India	Tick[c]	Rodents, dogs	Fever, headache, rash, “tache noire” (eschar)

Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e > Rickettsia and Related Genera

	Rickettsia sibirica	Siberian tick typhus (North Asian tick typhus)	Siberia, Mongolia	Tick[c]	Rodents	Fever, rash (eschar)
Transitional group	*Rickettsia akari*	Rickettsial pox	United States; Russia; Korea; South Africa	Mite[c]	Mice	Mild illness, fever, headache, vesicular rash (eschar)
	Rickettsia australis	Queensland tick typhus	Australia	Tick[c]	Rodents, marsupials	Fever, rash of trunk and limbs (eschar)
Q fever	*Coxiella burnetii*	Q fever	Worldwide	Airborne fomites tick	Sheep, cattle, goats, others	Headache, fever, fatigue, pneumonia (no rash); can have major complications
Ehrlichiae	*Erlichia chaffeensis*	Human monocyte ehrlichiosis	South-central, southeastern, and western United States	Tick	Deer, dogs, humans	Fever, headache, atypical white blood cells
	Anaplasma phagocytophilum	Human granulocyte anaplasmosis	Upper midwestern, northwestern, and West Coast United States and Europe	Tick	Mice, other mammals	Fever, headache, myalgia
	Ehrlichia ewingii	Ewingii ehrlichiosis	Midwestern United States	Tick	Dogs	Fever, headache, myalgia

Rickettsia

- Obligate intracellular parasite.
- Giemsa stain
- Yolk sac cultivation
- Require CoA and NAD for growth
- Cell walls are peptidoglycans-containing muramic acid and diaminopimelic acid
- Lipopolysaccharide membrane (toll receptor reacts).
- Invade endothelial cells of microvasculature.
- Replicate, release endotoxic cytotoxins, leading to generalized (obliterative) vasculitis.

Rickettsia

- Response mounted by NK cells
- Sulfonamides enhance replication
- Doxycycline as drug of choice

Rickettsia

- R.prowazekii
- Epidemic typhus
- Louse borne
- Flying squirrel as reservoir in US
- R. typhi
- Endemic typhus
- Flea bite
- Rodent as reservoir
- R. rickettsia
- Rocky Mountain Spotted Fever
- Dermacentor (dog) tick.

Rickettsia

- R. ankari
- Rickettsialpox
- Chiggers
- Orientia tsutsugamushi
- Scrub typhus
- Chiggers
- Only Coxiella burnetti (Q fever) not transmitted by arthropod bite.
- Weil-Felix reaction assays positive for typhus and Rocky Mountain spotted fever
- Negative for Q fever.

Rickettsial disease

- Epidemic typhus and Rocky Mountain spotted fever are characterized by:
- Onset of fever, chills, headache, and myalgia after 8 days incubation (2-30 day range).
- Complications include myocarditis, stupor and delirium.
- Mortality rate 60-70%.
- Brill-Zinsser disease is recrudescent epidemic typhus.
- Occurs decades after the initial infection.
- Similar clinical course but milder

Rocky Mountain spotted fever

- Enter through bite or abrasion.
- Virulence factors and host immunity do not appear to contribute to pathogenesis.
- Infect endothelial cells by stimulating phagocytosis
- Degrade phagosome, enter cytoplasm.
- Replication in endothelial cells causes focal areas of thrombosis and leaking of red cells
- Rash of the spotted fever group usually appears after 3–5 days of illness, first on the extremities, then moves centripetally, and involves the palms and soles.

Other rickettsial diseases

- Scrub typhus
- Occurs in Asia and Pacific Islands.
- Mite is both reservoir and vector and passes the bacteria transovarially.
- Rodents as a reservoir.
- Humans are accidentally infected.
- Onset of fever, chills, headache, myalgias. Centrifugally spreading rash 2 days later.
- Rickettsialpox
- Milder disorder
- Characterized by eschar

Erlichosis

- Obligate, intracellular
- Gram negative
- Able to synthesize ATP
- 5-21 day incubation period
- Leukocyte ingestion leads to infection.
- Proliferates in phagocytic vacuole as fusion of phagosome and lysosome is inhibited.
- Morula is an inclusion body containing organisms.
- Phagosome lyses, releasing organisms.
- Fever, chills, headache.
- Rash is rare.

Q fever

- Coxiella burnetii
- Live inside acidic lysozomes.
- Undergoes antigenic variation of lipopolysaccharide cell wall.
- LPS has a complex carbohydrate (phase I antigen) that blocks antibody binding.
- After entry, phase I antigen gene is mutated.
- Phase II antigen produced
- Exposes antibody binding sites.
- Immune complex formation.

Q fever

- Inhalation.
- Acute disease: antibody against phase II antigen
- Flu-like illness is usually self-limited.
- More severe illness may present with cough, dyspnea, and chest pain (atypical pneumonia).
- Myocarditis, hepatitis, headache and confusion, septic thromboembolism may develop.
- Chronic disease: high antibody titers against the phase I and II antigens
- Chronic illness associated with subacute bacterial endocarditis.

Chlamydia

- Obligate intracellular parasite.
- Cannot make own ATP.
- No peptidoglycan.
- Lipopolysaccharide outer cell wall.
- Chlamydia exists in 2 forms during an infection
- Elementary body (EB), small, resistant, the infectious form of the organism.
- MOMP adhesion attaches to the host cell heparin sulfate protoglycan.
- Enters cell via type III mechanism in a process that uses host cell metabolism.

Chlamydia

- Using host ATP, the RB divides within the endocytic vesicle
- The newly formed organisms finally occupy much of the host cell producing large cytoplasmic inclusion bodies that are characteristic of Chlamydia infections.
- After 24-72 hours, the RB reorganize and condense to yield multiple EB.
- EB stains purple with Giemsa
- RB stains blue with Giemsa

Chlamydia

- C. pneumonia lacks glycogen (intracytoplasmic inclusions)
- C. psittaci lacks glycogen (Diffuse intracytoplasmic inclusions)
- C. pneumonia has large intracytoplasmic inclusions
- Respond to macrolides

Atypical pneumonia

- Chlamydia pneumoniae
- Has been linked to atherosclerosis
- Pharyngitis is common
- Cough may persist for weeks.
- Sinusitis and otitis media may occur and be accompanied by lower airway disease.
- Atypical pneumonia in 5%

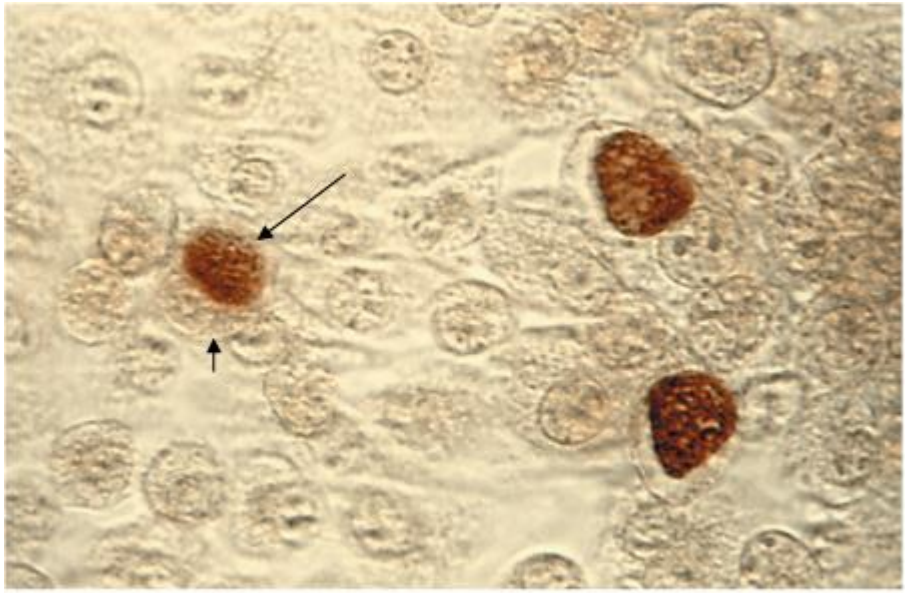
Parrot fever

- Chlamydia psittaci
- Exposure to birds.
- Incubation period is 5-14 days.
- Acute onset of fever, chills, headache, malaise, muscle aches, dry hacking cough.
- Patchy inflammation of the lungs in which consolidated areas are sharply demarcated. (Interstitial pattern)
- The exudates are predominantly mononuclear.
- Only minor changes occur in the large bronchioles and bronchi.

Parrot fever

- The liver and spleen are often enlarged.
- Complications include myocarditis, encephalitis, hepatitis, coma and death.
- GI symptoms can also occur.
- Incubation period is 5-14 days.

Chlamydia trachomatis



Light microscopy of cell culture. Long arrow points to cytoplasmic inclusion body of Chlamydia trachomatis; short arrow points to nucleus of cell.

Provider: CDC/Dr. E. Arum and Dr. N. Jacobs.

Color plate 14
Accessed 08/01/2010

Chlamydia trachomatis

- Types A, B, Ba, C cause trachoma
- Types D-K cause sexually transmitted disease
- Non-gonococcal urethritis
- 3-10 day incubation
- Type L causes lymphogranuloma venereum
- Responds to azithromycin or doxycycline

Trachoma

- Chlamydia trachomatis
- The first exposure results in acute conjunctivitis which usually resolves.
- Lacrimation, mucopurulent discharge, conjunctival hyperemia, and follicular hypertrophy
- Epithelial keratitis, subepithelial infiltrates, and extension of limbal vessels into the cornea (pannus)
- Chronic inflammation of the eyelids and scarring of conjunctiva cause the eyelids to turn inward and the eyelashes can abrade the cornea.
- Visual loss can occur 15-20 years after initial infection.

Lymphogranuloma venereum

- Caused by serotypes L1, L2 and L3.
- Acquired by abrasions.
- Characterized by transient papules on external genitalia followed by 1-2 months by painful swelling of inguinal and peri-rectal lymph nodes.
- The affected lymph nodes are those that drain the primary site of infection.
- The lesions that develop become necrotic and attracts granulocytes.
- Responds to azithromycin.

Inclusion conjunctivitis

- Most common form of neonatal conjunctivitis in US effecting 2-6% of newborns.
- 30–50% of infants of infected mothers acquire the infection
- 15–20% of infected infants manifesting eye symptoms
- 10–40% manifesting respiratory tract involvement.
- Begins as a mucopurulent conjunctivitis 5–12 days after delivery.

Inclusion conjunctivitis

- Infection in the adult can result from direct contact with infected cervical secretions during delivery or by autoinoculation from individuals with genital infections.
- Peak incidence 18-30 years of age.

Non-specific urethritis
Non-gonococcal urethritis

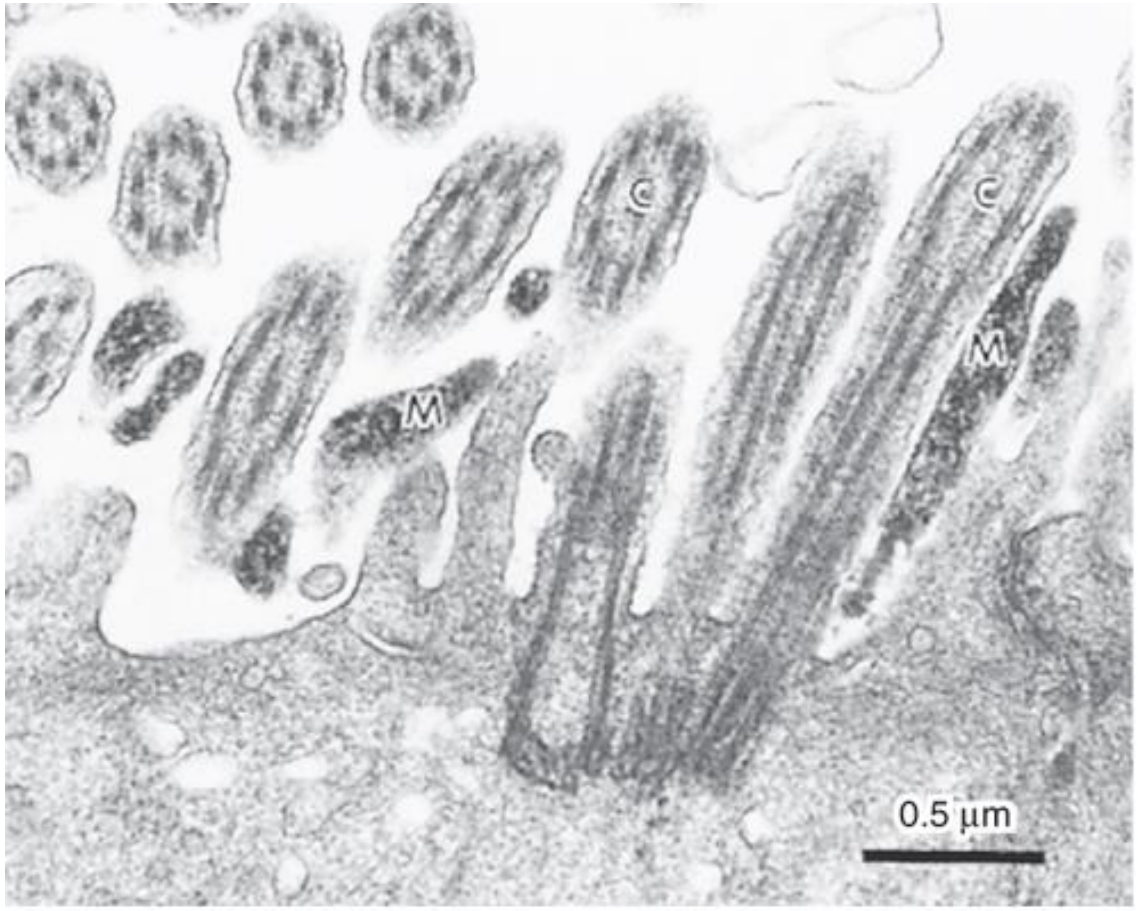
- Most common STD in US.
- Highest prevalence among sexually active teens
- Rate exceeds 5% in men and 10% women
- One third to one half of all male contacts of females with cervicitis develop urethritis after 2-6 weeks
- Penile discharge, dysuria, itch
- Gram stain with 5 or more WBC's per high power field
- AND no organism identified on culture.
- Responds to single dose azithromycin or use of doxycycline for 7 days

Mycoplasma

- Smallest free living bacteria.
- Do not have murein cell wall.
- Only bacterial membrane that contains cholesterol.
- Coccal to filamentous shape.
- Fried egg appearance of colony on mycoplasma media.
- High titer of cold agglutinins.

Mycoplasma

- Proline rich P1 adhesins
- Interacts specifically with a glycoprotein receptor at the base of cilia on the epithelial cell surface.
- Ciliostasis, then ciliated epithelial cell death.
- Loss of ciliated epithelial cells interferes with normal airway clearance (persistent cough).
- Produces peroxides.
- M.pneumoniae can function as a superantigen.
- Chemotaxic.
- TNF-α, IL-1 and IL-6 contribute to symptoms and recovery from disease.



Source: S. Riedel, J.A. Hobden, S. Miller, S.A. Morse, T.A. Mietzner, B. Detrick, T.G. Mitchell, J.A. Sakanari, P. Hotez, R. Mejia Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e

Electron micrograph of M. pneumoniae attached to ciliated respiratory epithelial cells in a sputum sample from a patient with culture-proved M. pneumoniae pneumonia. The organisms (M) are seen on the luminal border attached between cilia (C). (Courtesy AM Collier, Department of Pediatrics, University of North Carolina.)

Mycoplasma pneumoniae

- Spread by droplets.
- 20% of all cases of pneumonia in US.
- Infections in children under 6 months of age is uncommon.
- Most common age effected are children between ages of 5-15.
- One-third of all cases of pneumonia in teenagers.
- No seasonal activity
- Often appears as sporadic, endemic, illness is families because of 2-15 day incubation and prolonged shedding of organism.

Mycoplasma pneumoniae

- The presence of non-purulent otitis media and lower respiratory tract illness in a teenager suggests M.pneumoniae infection.
- Mild Upper Respiratory tract infection
- Low grade fever, malaise, headache, dry, non productive cough.
- Mild tracheobronchitis
- Fever, cough, headache and malaise.

Mycoplasma pneumoniae

- Atypical pneumonia
- Fever, headache, and malaise 2-4 days before onset of respiratory symptoms
- Non-or-minimally productive cough.
- Chest X-ray shows unilateral or patchy pneumonia usually in lower lobes.
- Reticulo-nodular pattern.
- Interstitial pneumonitis.
- Pharyngitis with fever and sore throat may occur.
- Non-purulent otitis-media occurs in 15%.
- Tetracyclines and fluoroquinolones lead to improvement but no clinical cure

Ureaplasma urealyticum

- No murein cell wall.
- Distinct from Mycoplasma because of the urease activity.
- Main reservoir is the genital tract of sexually active men and women.
- Rarely found before puberty.
- Occurs in 80% of individuals who have had >3 sexual partners.
- Estimated that half of the cases of Non Gonococcal Urethritis in men are caused by Ureaplasma.
- In women Ureaplasma and Mycoplasma hominis are associated with chorioamnionitis and postpartum fever.