Pyogenic Cocci - round bacteria that cause pus formation AKA suppurative - Gram positive

Staphylococcus
Streptococcus

Staphylococcus spp. typically occur in grapelike clusters because cell division occurs in 3 planes such that daughter cells stick together

- Grow well on all media
- Facultative anaerobes
- Can grow in the presence of O2 because they produce catalase - catalase (+) + grow best in presence of O2
- Can also grow well in absence of O2

Grow best at temperatures between 25°C and 35°C but can grow at temps as low as 8°C and as high as 48°C

- Are most resistant to heat, light, drying, extreme temperatures and chemicals.
- Staph frequently resist a temp of 80°C for as long as 30 minutes
- Are resistant to drying - can be carried on dust particles and can live for weeks to months in dried pos or dried sputum.

Can grow under high salt conditions. Concentrations (up to 15% NaCl).

Preserved foods can carry Staph - e.g., hams cured with salt - Staph can grow in or on these hams and produce enterotoxin

- Resistant to phenols and other disinfectants. Although they are sensitive to some dyes like crystal violet in MacConkey media.

Tend to become resistant to antibiotics. ~90% of Staph spp are penicillin resistant.
2. Staph species of medical significance

- **Staph aureus** - Staph aureus is coagulase positive
- **Staph epidermidis** - while Staph epidermidis is negative

Staph species produce several toxins:

- Hemolysins
- Leukoceads
- Enterotoxin
- Exfoliative toxin
- Coagulase
- Hyalase
- Nuclease
- Staphyto kinase
- Hyaluronidase

**Virulence**

Staph aureus - has a protein (Protein A) - that is attached to its peptidoglycan - such that its surface is uniformly coated with this protein. It has a strong affinity for the Fc constant region of IgG - such that IgG is unable to clear the pathogen by the use of complement pathway instead of this, complement binding domains are obscured.

Also secretes protein A - which binds free circulating IgG, Abs forms an immune complex that sequesters the complement proteins.
Coagulase - binds fibrinogen that is present in the plasma
and converts it to fibrin (which is insoluble)
- this allows bacteria to clump when confines of fibrin
protects bacteria from attack by phagocytic cells.
- this can easily be observed in the laboratory

Can bind to host cells - by producing binding proteins that
are specific to those cells + tissue
- collagen binding proteins
- elastin binding proteins
- fibrinogen binding proteins - teichoic acids

Produces hyaluronidase
- hyaluronic acids are polysaccharides that make up connective
tissue
- cement cells together
- degrades this
- this aids in freeing the permeability of such tissues
- to Staph + to their toxic substances

Staphylokinase (AKA) fibrinolysin - used to dissolve fibrin
clots that have formed around bacteria by host.
- leads to the spread of bacteria that were initially
confined to a region by the fibrin clot

Lipases - hydrolyze lipids
- 1) to invade cells and tissues such that they can penetrate
   deeper into tissues
- 2) food source for the bacteria

Nuclease - cleaves DNA & RNA of host cell may also be used
as a food source

Penicillinase (β-lactamase) - breaks the β-lactam ring of penicillin
- oxacillin is drug of choice - but vancomycin can be used against
β-lactam drug-resistant strains.
Staphylococcal toxins

Aa toxin - polypeptide
- disrupts the smooth muscle that lines blood vessels
- toxic to RBCs, WBCs, platelets, liver cells
- integrates into the hydrophobic region of host cell membrane

- forming 2 nm pores - thus leads to the efflux of K+ (protonated) and influx of Na^+ and Ca^2+ + other molecules
- leads to osmotic swelling and cell lysis.

S toxin (delta toxin) - small 3000 D peptide that lyases a broad # of cells - not specific & believed to serve as a detergent.

X toxin + P.V. leukocidin - produced together form a 6 subunit structure - this forms pores in host cells that lead to leakage of cytoplasmic components & cell lysis - acts on 1 neutrophiles (PMN-leukocytes) 2 macrophages.

Exfoliative toxins - cause staphylococcal scalded skin syndrome - mostly affects neonates & young children by possibly binding to special glycolipids only found in these hosts.

- produce severe proteases - that split intercellular linkages between epidermal cells

\[ \text{desmosomes} \quad \text{intercellular bridges} \]
Enterotoxins - involved in food poisoning

- Heat stable - 100°C, 30 minutes
- Resistant to acids and enzymes found in the stomach and enzymes found in small intestines
- Once food has been contaminated, Staph and that Staph has produced enterotoxin, cooking or digestive processes can't help
- Mechanism by which enterotoxins work are unknown because there are no suitable animal models

Enterotoxins are superantigens

- Induce nonspecific activation of T cells - leading to a lot of cytokine release & mass activation of macrophages
- This greatly act as toxins & damages - the epithelial cells of the stomach & small intestine, thus is believed to cause diarrhea

Toxic shock syndrome toxin - resistant to heat & proteolytic
TSST - is also a superantigen

TSST - is able to penetrate mucosal epithelium

- Such that although the bacteria remain at the site of the injection
- The toxin can travel everywhere in the body,

This causes the systemic effects of TSS

Death is caused by extremely low blood pressure that leads to the failure of many organs
Staphylococcal Disease

1. All people have staph epidermidis associated with their skin.
2. Staphaureus found sporadically - associated with most regions of body (skin, feet).
3. Also can be found in mucosa: pharynx, G-I tract, urogenital tract.

Found in a # of hospital acquired infections - nosocomial because they are hard to eradicate.
Can be transferred to susceptible person by direct contact or by contact with inanimate surfaces.

Causes disease in 2 ways - Staph aureus:
1. Direct invasion and destruction of tissue.
2. Production of toxin.

Toxin activity leads to 

Scalded Skin Syndrome - Focal Peumony - enterococcal - usually of tissues.
Cutaneous infections - impetigo & boils.
Endocarditis - heart infection (50% die).
Pneumonia - aspiration of St. aureus.
Osteomyelitis - in adults occurs in the vertebrae.
Children
- in bone found in long bones - where bones are actually growing.

Bacteremia - enters blood stream via superficial infection.
Staph epidemnus is usually introduced via hospital procedures

1) Artificial heart valves
2) Catheters
3) Artificial joints
Streptococci

Streptococcus pyogenes
- Agalactiae
- Strept pyogenes

Pneumonia (Jim Henson died of this)
Meningitis
Sinusitis, otitis media, bacteremia

Pharyngitis, scarlet fever, pyoderma
Cellulitis, necrotizing fasciitis
(Flesh-eating bacteria), streptococcal
TSS, bacteremia, rheumatic fever
Glomerulonephritis

Neonatal infections (meningitis
Pneumonia, Bacteremia)
Urinary tract infections, pneumonia
Bacteremia in adults

Gram +/diploid or in chains, facultative anaerobic but unlike Staph is catalase negative, do not ferment carbohydrates
Nutritional requirements are complex ⇒ usually one must use blood or serum based media to isolate the organisms
High levels of fatty acid produced kills cells

Classification of medically relevant Strept. spp.
1) Based on hemolytic qualities (ability to lyse RBC)
2) Based on carbohydrates found on cell wall = surface antigens (Lancefield group)

Streptococci

Non-hemolytic

Group A
Strept pyogenes

Group B
Strept agalactiae

Group D
Enterococcus spp

Group C
cocci, S. faecalis

BLOOD AGAR
B-hemolytic = clear zones around bacteria - partial clear zones around bacteria
O-hemolytic = no hemolysis (no coloration of hemoglobin)

X-hemolytic = no clearance zone
Virulence factors

M-protein - embedded in cell wall of bacteria.
- Surrounds the bacteria like pilo-like structures.
- Lends to mutate at a high rate - leading to a great deal of antigenic variability.

M-protein prevents phagocytosis in two manners:
1) M-protein binds fibrinogen - thus reducing access of complement proteins to bacteria.
2) A conserved region of M-protein binds to a protein called Factor H.

Such that when a complement protein binds (C3b) to the bacteria, which is important in the complement cascade that ultimately leads to phagocytosis, it is degraded by Factor H.

Binding to cells:
Lipoteichoic Acids - teichoic acids associated with cell wall & cytoplasmic membrane.
- Help S. pyogenes to bind to fibronectin on most cells.

The association between the lipoteichoic acids & fibronectin is initially weak.
M proteins, M-like proteins & F proteins strengthen the interaction.

Furthermore, M-proteins & F proteins are involved in the internalization of S. pyogenes into epithelial cells.
1) This leads to recurrent persistent pharyngitis.
2) Invasion of S. pyogenes into deeper tissues.

C5A peptidase - produced by Str. pyogenes
- involved in the attraction of PMN-lymphocytes and mononuclear phagocytes
- the peptidase clears this C5A complement protein

Streptococcal pyrogenic exotoxins (SpeS) - Sound in Str. pyogenes (an exotoxin) nonspecifically to cause superantigens to interact with a broad range of NKs & T-helper cells - leading to cytokine production

\( \text{(severely producing)} \)

A) Caused the red rash associated with streptococcus
B) Causes organ failure & shock - seen in people suffering from strept TSS

STOPPED HERE w/ SpeS - streptococcal pyrogenic exotoxins

2) Streptolysins (Strept. S) is bound to the cell
   - it lysed RBC, leukocytes, platelets
   - can kill a phagocytic cell after it has been engulfed

Streptolysin S is only produced if the bacteria is exposed to serum

\( \Rightarrow \) Leads to B-hemolytic activity seen on Blood Agar Plates

3) Streptokinases A + B - lyse blood clots or fibrin clots surrounding bacteria - such that bacteria can spread from the original source of infection
Epidemiology - St. Pyogenes - mostly school aged children
1. Spread from person - person due to respiratory droplets
   (cover mouth + nose when you sneeze or cough)
2. Caused when 1st defenses are down
   - Competitive bacteria in nasopharynx etc.
   - Patient cannot mount an immediate immune response
   to M-Bacterial
   - Pharyngitis + resulting diseases
3. Skin diseases - pyoderma, cellulitis, fasciitis - caused
   when staph on skin can get into cut or scratch.

Diseases
Pharyngitis - sore throat, fever, malaise (hard to distinguish
from viral based pharyngitis - only bacteriological test can tell if this is a Staphylococcal infection.
Scarlet Fever - complication of pharyngitis - when bacteria
produce pyrogenic exotoxin

Skin & deep tissue diseases
Necrotizing Fasciitis - in deep tissue, extensive destruction
of muscle & fat, appears 1st as cellulitis (which can be
treated w/ antibiotics - but develops into gangrene
disease systemic. - 50% of people die from ascending
infection, organ failure. Fasciitis must be treated surgically
to remove dead tissue, usually end up w/ Staphylococcal

Staphylococcal - responds very well to penicillin + its derivatives
Streptococcus pneumoniae - Pneumonia, sinusitis, otitis media, meningitis, bacteremia

- Present in throat & naso pharynx of healthy people
- Disease occurs when these organisms travel from throat & nasopharynx to other regions of body

Pneumonia - When bacteria enter lungs and alveoli.

- Treatable with antibiotics
- Some serotypes e.g. S. pneumoniae Type 3 can kill.
- Non-Type 3 can kill patients who are immunocompromised

How does strep enter the lungs?

1) Secretory IgA protease (sIgA) - Traps bacteria in mucin by binding to bacteria to the mucin

- Bacteria

Ciliated epithelial cells in the airways are removed, remove the bacteria trapped in mucin.

- The protease prevents sIgA from trapping the bacteria.

- Bacteria can move to the lower respiratory tract.

2) Pneumolysin - Bacteria can bind cholesterol via pneumolysin which can also create pores in these cells.

- Cholesterol

- Pneumolysin, this action kills phagocytic cells and kills ciliated epithelial cells which could remove bacteria.
Treatment
3) passive immunity - using Abs to capsule on Strept pneumoniae - enhanced attraction of phagocytic cells to the bacteria

2) penicillin & erythromycin, chloramphenicol
   a) Today, 33% of all Strept pneumoniae are resistant to penicillin and analogues
   b) because these strains have a reduced affinity to penicillin
      (Pen. binding proteins don't bind antibiotic as well)

   PBP
   Reduced affinity
   PBP →
   Bact. cell wall

3) prevention - vaccines using 23 different capsular antigens
   a) body mounts additional immune response & produces Abs to the capsular antigens
      - doesn't appear to cause an emergence of new serotypes with different capsular antigens
      - can affect people who have encountered bacteria

Enterococcus faecalis + E. faecium
   - paws or short chains, can grow on most lab media, can tolerate 6.5% NaCl & CAN TOLERATE 40% bile salts
   - DOES NOT PRODUCE TOXIN - but can cause serious disease

   why a problem?
   1) can attach to cell surfaces
   2) produces bacteria lysis that kills
   3) are naturally resistant to antibiotics (staphylococal, penicillin, cephalosporins) or have acquired antibiotic resistance genes

   endocarditis - high mortality rate
   affects immunocompromised people in hospital - those undergoing broad-spectrum antibiotic treatment