Course*: Medical Microbiology*

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Subject: Medical Bacteriology

Bacterial Pathogenesis

- **Pathogen** is a microorganism that is able to produce pathology.
- **Pathogenicity** is the ability of a microorganism to cause disease in the host for the pathogen, pathogenicity is a manifestation of a host- parasite interaction.
- **Obligate pathogenic bacteria: bacteria that live only in host and cause diseases.**
- **Opportunistic Pathogens** Bacteria which cause a disease in the immune-compromised such as normal flora; *Staphylococcus aureus* and *E. coli* can cause an opportunistic infection.
- **Determinants of Virulence**: the weapons or characteristics that pathogenic bacteria utilize to produce disease, e.g. toxins, capsules, enzymes …etc.

Pathogenic Bacteria Virulence Factors

1. Bacterial Adherence and Colonization Factors (Surface Antigens):

Bacterial adherence to portal of entry like: Mucosal Surfaces or attachment to a eukaryotic cell or tissue surface requires two factors: a receptor and an adhesin. The receptors are specific carbohydrate or peptide residues on the eukaryotic cell surface (A complementary molecular binding site on a surface that binds specific adhesins). The bacterial adhesin is typically a component of the bacterial cell surface which interacts with the host cell receptor.

Some adhesins are able to act as antigens and induce specific immune response against them. And some are used during infections diagnosis like flagellar H Ag of *Salmonella typhi*. The following table contains the types

of adherence factors are used by pathogenic bacteria for adherence to surfaces or tissues:

Adherence Factor	Role associated with virulence
1. Fimbriae	Filamentous proteins on the surface of bacterial cells that may behave as adhesins for specific adherence
2. Common pili	Same as fimbriae
3. Sex pilus	A specialized pilus that binds mating procaryotes together for the purpose of DNA transfer
4. Type 1 fimbriae	Fimbriae in Enterobacteriaceae which bind specifically to mannose terminated glycoproteins on eukaryotic cell surfaces
5. Glycocalyx	A layer of exopolysaccharide fibers on the surface of bacterial cells which may be involved in adherence to a surface
6. Capsule	A detectable layer of polysaccharide (rarely polypeptide) on the surface of a bacterial cell which may mediate specific or nonspecific attachment
7. Lipopolysaccharide (LPS)	A distinct cell wall component of the outer membrane of Gram-negative bacteria with the potential structural diversity to mediate specific adherence. Probably functions as an adhesion

8. Teichoic acids and lipoteichoic acids (LTA)	Cell wall components of Gram-positive bacteria that may be involved in nonspecific or specific adherence
9. Biofilm formation	Formation of slimy extracellular matrix (polysaccharides) produced by some bacteria for colonization, avoid phagocytosis and resist antibiotics.

Factors affect adherence:

1) Tissue tropism: some bacteria prefer certain tissues e.g. *Streptococcus mutans* is usually found in dental plaques and not on epithelial surfaces of the tongue.
2) Species specificity: some pathogenic bacteria infect only certain species, e.g. *Neisseria gonorrhoeae* infections are limited to humans.
3) **Genetic susceptibility:** some races are genetically immunized to a pathogenic bacteria.

2. Bacterial Invasion Factors:

Invasins are proteins that act locally to damage host cells and facilitating the growth and spread of the pathogen. The damage (break down) to the host as a result of this invasive activity is a major part of the pathology of an infectious disease. Also, these invasins can stop immune response activity against the pathogenic bacteria.

Some bacteria have the ability to survive and multiply inside phagocytic cells. This ability is considered an important virulence factor and escape mechanism from the specific immune response. For example: *Mycobacterium tuberculosis*, *Legionella pneumophila*, *Brucella abortus*, and *Listeria monocytogenes* can remain alive inside phagocytes.

Types of Invasins:

1. Spreading Factors (Enzymes)

They are bacterial enzymes that affect the physical properties of tissue matrices and intercellular spaces, they help in the spread of the pathogen.

1) Hyaluronidase.

It is the original spreading factor produced by *Streptococci*, *Staphylococci*, and *Clostridia*. The enzyme attacks the interstitial cement (ground substance) of connective tissue (hyaluronic acid).

2) Collagenase

It is produced by *Clostridium perfringens*. It breaks down collagen of muscles and cause gas gangrene.

3) Neuraminidase

It is produced by intestinal pathogens such as *Vibrio cholerae* and *Shigella dysenteriae*. It breaks neuraminic acid the intercellular cement of the epithelial cells of the intestinal mucosa.

4) Streptokinase and Staphylokinase

They are produced by streptococci and staphylococci. These Kinase enzymes convert plasminogen to plasmin which digests fibrin and prevents clotting of the blood. The absence of fibrin in spreading bacterial lesions allows more rapid diffusion of the infectious bacteria.

5) Enzymes that Cause Hemolysis and/or Leucolysis

These enzymes usually act on the animal cell membrane by forming a pore that results in cell lysis through enzymatic attack on phospholipids.sometmes thay are called lecithinases or phospholipases, and if they lyse red blood cells they are sometimes called hemolysins. Leukocidins, produced by staphylococci and streptolysin produced by streptococci specifically lyse phagocytes and their granules (these enzymes are also considered as bacterial exotoxins).

6) Phospholipases

They are produced by *Clostridium perfringens* (i.e., alpha toxin), cause lysis of phospholipids in cell membranes.

7) Lecithinases

They also produced by *Clostridium perfringens*, able to destroy lecithin (phosphatidylcholine) in cell membranes.

8) Hemolysins

They are produced by staphylococci (i.e., alpha toxin), streptococci (i.e.,streptolysin) and many clostridia, may be channel-forming proteins or phospholipases or lecithinases that destroy red blood cells and other cells (i.e., phagocytes) by lysis.

9) Staphylococcal coagulase

Coagulase, formed by Staphylococcus aureus, it is an enzyme that converts fibrinogen to fibrin which causes clotting. Coagulase activity is associated with pathogenic *S. aureus* and never produced by *S. epidermidis*. The action of coagulase is to provide an antigenic disguise if it clotted fibrin on the cell surface.

10) Extracellular Digestive Enzymes

Heterotrophic bacteria produce a wide variety of extracellular enzymes including proteases, lipases, nucleases, etc., which have a role in invasion or pathogenesis. These enzymes have other functions more than bacterial nutrition or metabolism and help in invasion either directly or indirectly.

2. Toxins:

They are bacterial products that promote bacterial invasion, Toxigenesis is the ability to produce toxins. Toxic substances, both soluble and cell-associated, may be transported by blood and lymph and cause cytotoxic effects at tissue sites remote from the original point of invasion or growth. There are two types of these toxins:

A. Endotoxins

Endotoxin is the LPS layer of Gram-negative bacteria. Endotoxin biological effects on the host may be lethal because it is released after lysis of bacteria causing toxic effects include pyrogenicity, leukopenia followed by leukocytosis, complement activation (alternative pathway), depression in blood pressure (hypotension), mitogenicity, induction of prostaglandin synthesis, and hypothermia; cause disseminated intravascular coagulation DIC leading to thrombosis; inhibits inflammatory responses and kinin system; some patients suffer from sepsis and lethal shock. In general it is not good antigen and heat stable.

Some effects of endotoxin are beneficial to the host. These include:

1. Mitogenic effects on B lymphocytes that increase resistance to viral and bacterial infections

2. Induction of gamma interferon (IFN-γ) production by T-lymphocytes, which may enhance the antiviral state, promotes rejection of tumor cells, and activates macrophages and natural killer cells

3. Activation of the complement cascade with the formation of C3a and C5a (anaphylotoxin)

4. Induction the production of interleukin-1 by macrophages and interleukin-2 and other mediators by T-lymphocytes.

B. Exotoxins

Exotoxins are bacterial metabolic products; unlike the lipopolysaccharide endotoxin, the general properties are:

1. Proteins with toxic effects released from viable bacteria.
1. Immunogenic, they are protective antigen due to high molecular weight and complex composition, induce specific antibodies (called antitoxins), resulting in complete inhibition of the toxic activity (this immunological Ag-Ab reaction is called neutralization).
2. Poisonous in low doses (very low concentrations per unit weigh).

3. Most of the higher molecular exotoxin proteins are heat labile; while, low molecular exotoxins are heat-stable peptides.
4. They are produced by both Gram-positive and Gram-negative bacteria.
5. Chemical composition of exotoxins contains mainly two types of polypeptides**; Type A and Type B**; type A polypeptides are responsible for the toxic effect (toxogenic part of the toxin); while B polypeptides are responsible for delivering the part A to the target cell or tissue. Part B do not enter target cell. Toxins are different in their composition of both parts types, some contain (A2B) meaning one Aand two polypeptides of B; while (2A5B) meaning two A polypeptides and five B polypeptides.

Exotoxins can be grouped into several categories:

1. Neurotoxins like Botulin of *Clostridium botulinum*.

2. Cytotoxins, like diphtheria toxin of *Corynebacterium diphtheriae*.

3. Enterotoxins which are responsible of many types of watery diarrhea like shigatoxin of *Shigela sp.*

4. Hemolysins, cause blood hemolysis like Streptolysin of *Streptococcus pyogens.* Include three types α, β and γ.

5. Erythrogenic toxin which cause bleeding under skin, like *Streptococcus pyogens* erythrogenic toxin.

6. Leucocidin cause WBCs lysis like leucocidin of *Staphylococcus aureus*.

Bacteria Invasins		
Invasin	**Bacteria**	**Activity**
Hyaluronidase	*Streptococci, staphylococci and clostridia*	Degrades hyaluronic of connective tissue
Collagenase	*Clostridium species*	Dissolves collagen framework of muscles
Neuraminidase	*Vibrio cholera and Shigella dysenteriae*	Degrades neuraminic acid of intestinal mucosa
Coagulase	*Staphylococcus aureus*	Converts fibrinogen to fibrin which causes clotting
Kinases	*Staphylococci and Streptococci*	Converts plasminogen to plasmin which digests fibrin
Leukocidin	*Staphylococcus aureus*	Disrupts neutrophil membranes and causes discharge of lysosomal granules
Streptolysin	*Streptococcus pyogenes*	Repels phagocytes and disrupts phagocyte membrane and causes discharge of lysosomal granules
Hemolysins	*Streptococci, staphylococci and clostridia*	Phospholipases or lecithinases that destroy red blood cells (and other cells) by lysis
Lecithinases	*Clostridium perfringens*	Destroy lecithin in cell membranes
Phospholipases	*Clostridium perfringens*	Destroy phospholipids in cell membrane

Anthrax toxin	*Bacillus anthracis*	One component (EF) is an adenylate cyclase which causes increased levels of intracellular cyclic AMP
Pertussis toxin	*Bordetella pertussis*	One toxin component is an adenylate cyclase that acts locally producing an increase in intracellular cyclic AMP

Pyrogenic Bacteria

These bacteria are pus forming bacteria, they include the following genera:

1. Staphylococci and Streptococci (Gram + cocci).
2. Neisseria (Gram - cocci).
3. Hemophilus (Gram - coccibacilli).

Staphylococci Genus

Staphylococci are Gram-positive spherical bacteria that found in clusters like grapes. Although more than 20 species of *Staphylococcus* are described in Bergey's Manual (2001), only *Staphylococcus aureus* and *Staphylococcus epidermidis* are of medical importance to humans. *S. aureus* colonizes mainly the nasal passages and *S. epidermidis* is normal flora of the skin. Taxonomically, the genus ***Staphylococcus*** is in the Bacterial family ***Staphylococcaceae.***

Staphylococcus Species That Affect Humans Most Frequently Species Parameter

Species	**Special Character**	**Infections**
S. aureus	Coagulase-positive; colonies golden yellow. Can grow at 45 C ˚ and NaCl 15%	Local purulent infections: furuncles, carbuncles, bullous impetigo, wound infections, sinusitis, otitis media, mastitis puerperalis, ostitis, postinfluenza pneumonia, sepsis. Toxin-caused illnesses: food poisoning, dermatitis exfoliativa, toxic shock syndrome
S. epidermidis	Coagulase-negative; sensitive to novobiocin	most frequent coagulase negative Staphylococci pathogen; opportunist; infection requires host predisposition;

		foreign body infections with discrete clinical symptoms
S. saprophyticus	Coagulase-negative; resistant to novobiocin	Urinary tract infections in young women (10–20%); occasional nonspecific urethritis in men

Staphylococcus aureus

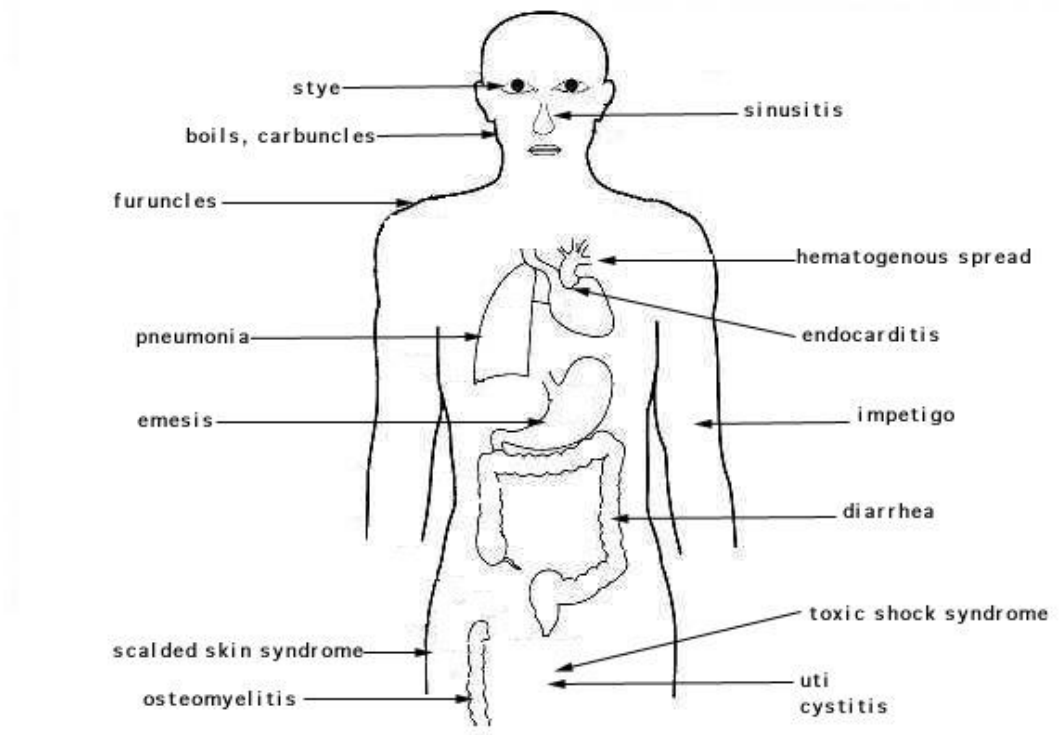
Gram-positive, cluster-forming coccus
nonmotile, nonsporeforming facultative anaerobe
fermentation of glucose produces mainly lactic acid
ferments mannitol (distinguishes from *S. epidermidis)*
catalase positive
coagulase positive
golden yellow colony on agar
normal flora of humans found on nasal passages, skin and mucous membranes
pathogen of humans, causes a wide range of suppurative infections, as well as food poisoning and toxic shock syndrome

Pathogenesis of *S. aureus* infections

Staphylococcus aureus causes suppurative (pus-forming) infections and toxinoses in humans. It causes superficial skin lesions such as **boils**; more serious infections such as **pneumonia**, **mastitis**, **meningitis**, and **urinary tract infections UTI**; and deep infections, such as **osteomyelitis** and **endocarditis**.

S. aureus is a major cause of **hospital acquired (nosocomial) infection** of surgical wounds and infections associated with contaminated medical devices. *S. aureus* causes **food poisoning** by releasing enterotoxins into food, and **toxic shock syndrome** by release of superantigens into the blood stream.

Portals for entry: Staphylococcus produce local infection as a start after entry. The portal may be a hair follicle, but usually it is a break in the skin, scratches, trauma or surgical wound. Another portal for entry is the respiratory tract. Staphylococcal pneumonia is a common complication of influenza.



Sites of infection and diseases caused by *Staphylococcus aureus*

Adherence to Host Cell Proteins

S. aureus have **surface proteins** that promote attachment to host proteins such as laminin and fibronectin that form the extracellular matrix of epithelial and endothelial surfaces. In addition, most strains express a fibrin/fibrinogen binding protein (clumping factor) which promotes attachment to blood clots and traumatized tissue. Most strains of *S. aureus* express both fibronectin and fibrinogen-binding proteins. In addition, an adhesin that promotes attachment to collagen has been found in strains that cause osteomyelitis and septic arthritis. Interaction with collagen may also be important in promoting bacterial attachment to damaged tissue where the underlying layers have been exposed.

Invasion Factors

The invasion of host tissues by staphylococci involves the production of a huge amount of invasion factors (extracellular proteins). These proteins are described below with some possible explanations for their role in invasive process.

1) Membrane-damaging toxins

1. **α-toxin (α -hemolysin)**: The most effective membrane-damaging toxin of *S. aureus*, mainly platelets and monocytes are sensitive to **α** -toxin. Susceptible cells have a specific receptor for **α** -toxin which allows the toxin to bind then form small pores and cause osmotic lysis.
2. **ß-toxin**: is a sphingomyelinase which damages membranes rich in this lipid, usually lyse RBCs. A lysogenic bacteriophage is known to encode the toxin. Found rare in human isolates.
3. **γ-toxin** is a very small peptide toxin produced by most strains of *S. aureus*. It is also produced by *S. epidermidis*. The role of **γ** -toxin in pathogenisity is unknown.
4. **Leukocidin** is a multicomponent protein toxin act together to damage membranes, it is hemolytic, but less than alpha hemolysin. The strains isolated from severe dermonecrotic lesions produce this toxin, it is an important factor in necrotizing skin infections.
5. **Coagulase and clumping factor:** Coagulase is an extracellular protein which binds to prothrombin in the host to form a complex called staphylothrombin. It has protease activity and cause conversion of fibrinogen to fibrin. Coagulase is a marker for identifying *S. aureus* in the clinical microbiology laboratory. Helps the bacteria to protect themselves from phagocytic and immune defenses by causing localized clotting.
6. **Staphylokinase:** it is a plasminogen activator, this factor lyses fibrin. The genetic code found in the lysogenic bacteriophages. It causes dissolution of fibrin clots, hence it is used in medicine to treat patients suffering from coronary thrombosis. It is bacterial spreading factor.
7. **Other extracellular enzymes:** *S. aureus* can produce proteases, a lipase, a deoxyribonuclease (DNase) and a fatty acid modifying enzyme (FAME). The first three provide nutrients for the bacteria, and have a

minor role in pathogenesis. But, the FAME enzyme is important in abscesses, where it could modify anti-bacterial lipids and help bacterial survival.

2) Avoidance of Host Defenses

S. aureus expresses a number of factors that interfere with host defense mechanisms. This includes both **structural** and **soluble elements** of the bacterium.

1. **Capsule**

The majority of clinical isolates of *S aureus* express a surface polysaccharide of either serotype 5 or 8. Usually called a microcapsule because it can be seen only by electron microscopy unlike the true capsules of other bacteria. The function of the capsule is to resist phagocytosis.

2. **Protein A**

Protein A is a surface protein of *S. aureus* which binds to IgG molecules by their Fc region (in the wrong region), which disrupts opsonization and phagocytosis.

3. **Leukocidin**

This toxin acts on polymorphonuclear leukocytes (PMNs).

4. **Exotoxins**

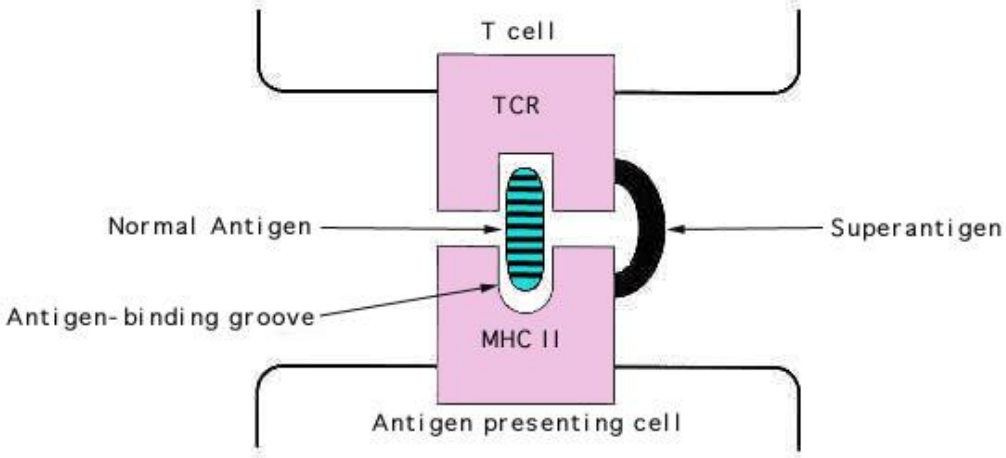
Include several toxic proteins which are responsible for symptoms during infections:

- **Enterotoxins and toxic shock syndrome toxin**

S. aureus secretes two types of toxin that are superantigens, **enterotoxins** (have six types SE-A, B, C, D, E and G), and **toxic shock syndrome toxin** (**TSST-1**). Enterotoxins cause diarrhea and vomiting when ingested and are responsible for staphylococcal food poisoning and Toxic shock. TSST-1 is expressed systemically and is the cause of toxic shock syndrome (TSS). When produced systemically.

Superantigens mode of action is to stimulate T-cells non-specifically without normal antigenic recognition, see figure below, up to one in five T-cells will be activated, whereas only 1 in 10,000 are stimulated during the usual

antigen presentation. Cytokines are released in large amounts, causing the symptoms of TSS. Superantigens bind directly to class MHCII major histocompatibility complexes of antigen-presenting cells.



Superantigens and the non-specific stimulation of T cells.

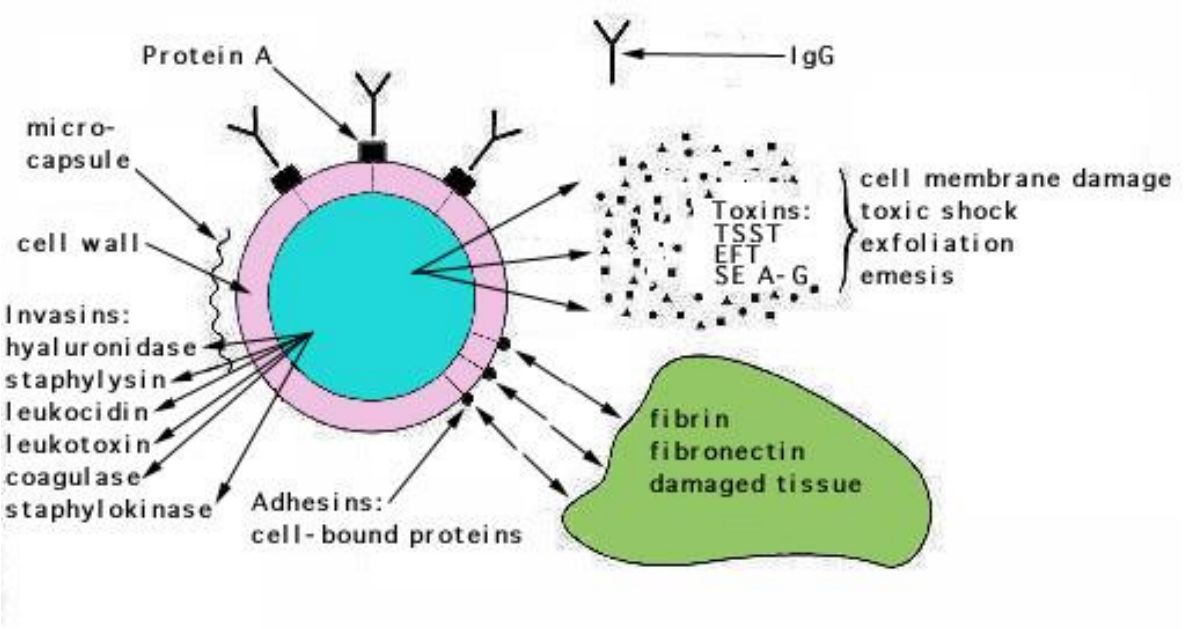
- **Exfoliatin toxin (ET)**

The exfoliatin toxin, associated with scalded skin syndrome (SSS), causes separation within the epidermis, between the living layers and the superficial dead layers. The separation is through the stratum granulosum of the epidermis leading to the risk of fluid loss and secondary infections.

5. Biofilm formation ability

Biofilm is the slim growing of *Staphylococcus aureus* as group of bacterial cells forming layer upon layer of bacterial growth, during colonization process of infection. The biofilm matrix components, contain polysaccharides polymer, protein (teichoic acid), and DNA, they play a major role in pathogenicity because biofilm help to share nutrients, shield from immune system of hosts and avoid antibiotics effect.

Pathogenic *Staphylococcus epidermidis* is able to show plastic interaction and able to colonize catheters devices by forming of biofilm. This ability to form a biofilm on the surface of a prosthetic device is a significant problem.



Virulence determinants of *Staphylococcus aureus*

Resistance of Staphylococci to Antimicrobial Drugs

Hospital strains of *S. aureus* are usually resistant to many antibiotics except vancomycin, usually called as **MRSA** refers to **Methicillin resistant *Staphylococcus aureus***. Methicillin resistance is widespread and most methicillin-resistant strains are also multi-antibiotics resistant. The antibiotics resistance is due to the plasmids (extrachromosomal genes) associated with resistance ability or by chromosomal mutation.

S. aureus shows resistance to antiseptics and disinfectants, such as quaternary ammonium compounds, which may aid its survival in the hospital environment hence these bacteria is a significant problem in the hospital environment causing **nosocomial infection** especially in surgical wounds.

Host Defense against Staphylococcal Infections

- Phagocytosis is the major mechanism against staphylococcal infection. But they are difficult to be killed after phagocytic engulfment because they produce catalase which neutralizes oxygen and superoxide and avoid killing mechanisms inside the phagolysosome.
- Specific Antibodies are produced which neutralize toxins and induce opsonization.

The localized host response to staphylococcal infection is inflammation, characterized by an elevated temperature at the site, swelling, the accumulation of pus, and necrosis of tissue. Around the inflammation area, a fibrin clot help to form pus-filled boil or abscess.

Epidemiology and Control

Staphylococci are widespread human parasites. The main sources of infection are shedding human lesions, fomites contaminated from such lesions, and the human respiratory tract and skin. Contact spread of occurs in hospitals, where the staff and patients carry antibiotic-resistant staphylococci MRSA in their nose or on the skin.

The areas at highest risk for severe staphylococcal infections in hospitals are newborn nurseries, intensive care units, operating rooms, and cancer chemotherapy wards.

Hygiene, and aseptic management of lesions can control the spread of staphylococci from lesions, ultraviolet irradiation of air have little effect in prevent staphylococci spreading from carriers.

Treatment

Hospital acquired infection is often caused by antibiotic resistant strains and can only be treated with vancomycin or Rifampin coupled with a second oral antistaphylococcal drug sometimes provides long-term suppression and possibly cure of nasal carriage. Many of the community acquired Staphylococcal infections are now methicillin resistant and only be treated with combination therapy using sulfa drugs and minocycline or rifampin.

Vaccines

No vaccine is yet available that stimulates active immunity against staphylococcal infections in humans.

Infections and involved Virulence factors in the pathogenesis of *Staphylococcus aureus*

(1) Boils, pimples and carbuncle (folliculitis)

Colonization: cell-bound (protein) adhesins

Invasion: **Invasins**: staphylokinase

Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)

Resistance to phagocytosis: coagulase, leukocidin

Resistance to immune responses: coagulase

Toxigenesis: cytotoxic toxins (hemolysins and leukocidin)

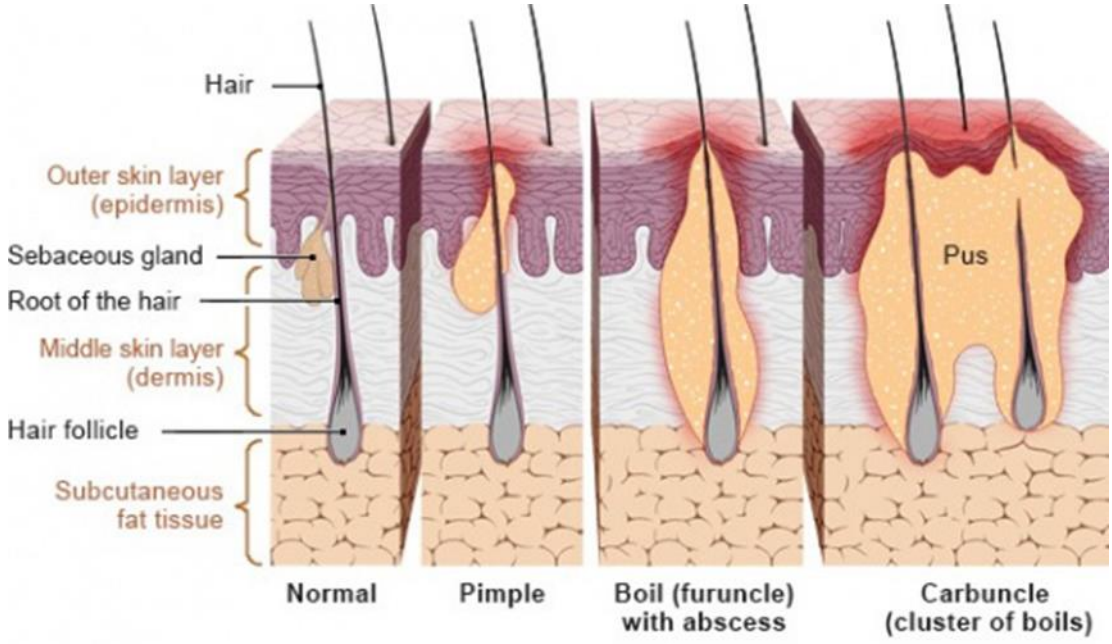
Pathogenesis:

It is a pus-filled bump in the skin that is caused by the bacterial infection. It's a bit like a very big yellow pimple, but it's deeper in the skin and hurts a lot more.

Boils develop when a hair follicle and the surrounding tissue become infected. Hair follicles consist of one hair, the root of the hair, a sebaceous gland and a small muscle that can pull the hair up, making it stand on end. Hair follicle inflammations are sometimes also referred to as "deep folliculitis" or "perifolliculitis."

The infection cause the death of skin tissue inside the boil, creating a pus-filled space (an abscess). Skin abscesses can develop from boils, but also from other things like infected insect bites or injections with dirty needles. If several boils merge into a larger bump, it's called a carbuncle (a cluster of boils)..

Sometimes boils heal without causing any problems, but it is better to get medical treatment for quick cure, relieve the pain and prevent complications. Because sometimes boils develop into carbuncle.



(2) Pneumonia

Colonization: cell-bound (protein) adhesins

Invasins: staphylokinase, hyaluronidase

Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)

Resistance to phagocytosis: coagulase, leukocidin, hemolysins, carotenoids, superoxide dismutase, catalase, growth at low pH

Resistance to immune responses: coagulase, antigenic variation

Toxigenesis: Cytotoxic toxins (hemolysins and leukocidin)

(3) Food poisoning (emesis or vomiting)

Toxigenesis: Enterotoxins A-G (superantigens).

Pathogenesis:

Staph food poisoning is characterized by a sudden start of nausea, vomiting, and stomach cramps. Most people also have diarrhea. Symptoms usually develop within 30 minutes to 8 hours after eating or drinking an item containing Staph toxin, and last no longer than 1 day. Severe illness is rare. The illness cannot be passed from one person to another with Fast cure. The enterotoxins are heat stable and resistant to the action of gut enzymes. Important cause of food poisoning, enterotoxins are produced when *S. aureus* grows in carbohydrate and protein foods. Ingestion of 25 μg of enterotoxin B results in vomiting and

diarrhea. The emetic effect of enterotoxin is the result of central nervous system stimulation (vomiting center) after the toxin acts on neural receptors in the gut.

(4) Septicemia (invasion of the bloodstream):

Invasins: staphylokinase, hyaluronidase
Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)
Resistance to phagocytosis: coagulase, protein A, leukocidin, hemolysins, carotenoids, superoxide dismutase, catalase, growth at low pH
Resistance to immune responses: coagulase, protein A, antigenic variation
Toxigenesis: cytotoxic toxins (hemolysins and leukocidin)

(5) Osteomyelitis (invasion of bone)

Colonization: cell-bound (protein) adhesins
Invasins: staphylokinase, hyaluronidase
Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)
Resistance to phagocytosis: coagulase, protein A, leukocidin, hemolysins, carotenoids, superoxide dismutase, catalase, growth at low pH
Resistance to immune responses: coagulase, protein A, antigenic variation
Toxigenesis: cytotoxic toxins (hemolysins and leukocidin)

(6) Toxic shock syndrome

Colonization: cell-bound (protein) adhesins
Resistance to immune responses: coagulase, antigenic variation
Toxigenesis: TSST-1 toxin, Enterotoxins A-G

Pathogenesis:

Staphylococcal toxic shock syndrome (TSS) is a life-threatening illness characterized by fever, rash (similar to sunburns), hypotension, multi-organ failure or dysfunction (involving at least 3 or more vital organs), and shock. Typically syndrome starts with the infection of the palms and soles and develops after 1-2 weeks from the onset of acute illness. The clinical syndrome can also include severe myalgia, vomiting, diarrhea, headache, and neurologic abnormalities. The gene encoding for this toxin found in 20% of *S. aureus* isolates including MRSA.

(7) Surgical wound infections

Colonization: cell-bound (protein) adhesins
Invasins: staphylokinase, hyaluronidase
Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)
Resistance to phagocytosis: coagulase, protein A, leukocidin, hemolysins, carotenoids, superoxide dismutase, catalase, growth at low pH
Resistance to immune responses: coagulase, protein A, antigenic variation
Toxigenesis: cytotoxic toxins (hemolysins and leukocidin)

(8) Scalded skin syndrome (analogous to scarlet fever) (Called SSS)

Colonization: cell-bound (protein) adhesins
Invasins: staphylokinase, hyaluronidase
Other extracellular enzymes (proteases, lipases, nucleases, collagenase, elastase. etc.)
Resistance to phagocytosis: coagulase, leukocidin, hemolysins
Resistance to immune responses: coagulase, antigenic variation
Toxigenesis: Exfoliative toxins A and B (superantigens)

Pathogenesis:

Exfoliative toxins of *S. aureus* are two types of proteins of the same molecular weight and have epidermolytic activity. Exfoliative toxin A is encoded by gene in a bacteriophage and is heat stable (resists boiling for 20 minutes). Exfoliative toxin B is carried by plasmid and heat labile. These epidermolytic toxins act by dissolving the mucopolysaccharide matrix of the epidermis.

Syndrome occurs commonly in newborns typically following an erythematous cellulitis. Severity of staphylococcal scalded skin syndrome varies from a few blisters localized to the site of infection to a severe exfoliation affecting almost the entire body.

Pathogenesis of these toxins by breaking down the desmosomes of epidermal layer due to protease effect of the exotoxins lead to the separation of the superficial layer of the epidermis due to cleave desmoglein (which normally

holds the granulosum and spinosum layers together), like in the case of the autoimmune skin disease pemphigus vulgaris.

Diagnostic Laboratory tests:

1) **Specimens:**
Surface swab for pus or aspirates from abscess, blood, tracheal aspirate or spinal fluid, are used for culture depending on infection location.

2) **Smear:**
Staphylococci appear Gram + cocci in clusters in gram stained smears of pus or sputum; it is not possible to distinguish between *S. aureus* and *S. eipermidis* in smear only.

3) **Culture:**
On blood agar give typical colonies, on mannitol salt agar only *Staphylococcus aureus* are able to ferment mannitol and it is used as differential media during diagnosis.

4) **Catalase Test**
5) **Coagulase Test**
6) **Antibiotic sensitivity test (susceptibility testing).**
7) **Serologic and typing test.**