

Bacteria

Gram positive

Name	Shape	Motility	Features	Structure	Location	Examples	Note
Staphylococci	Spherical Irregular cluster (grape)	Not	Catalase (+)	Peptidoglycan: -activate immune system + complement -chemoattractant For PMN -(endotoxin-like activity Adhesion : MSCRAMM Virulence : Protein A + clumping factor - teichoic acid : Act as antigen	Found in clothing, bed linens, and other fomites	Staphylococcus -aureus -epidermidis -lugdunensis -saprophyticus	
Staphylococcus aureus	Spherical Irregular cluster (grape	Not	Coagulase (+) Pigment: gray to deep golden yellow colonies has different hemolytic activity	Has the clumping factor A : FIBRONEGIN – binding protein which coat the surface of bacteria with it to complicate the recognition process	Anterior nares (nasal carriage)	Methicillin- resistant Staphylococcus aureus (MRSA) : People with compromised immune systems are More susceptible	Higher incidence in the hospitalized patients, medical personnel ‘ eczematous skin diseases.
Staphylococcus epidermidis	Spherical Irregular cluster (grape	Not	Coagulase (-) Pigment: gray to white		Normal microbiota found in the skin and in the GI		

Clinical cases

Staphylococci / Clinical correlations

A localized staphylococcal infection appears as a “**pimple,**” **hair follicle infection, or abscess.** There is usually an intense, localized, painful inflammatory reaction that undergoes central suppuration and heals quickly when the pus is drained.



Impetigo: localized cutaneous infection characterized by pus-filled vesicle on an erythematous base
Folliculitis: impetigo involving hair follicles
Furuncles or boils: large, painful, pus-filled cutaneous nodules
Carbuncles: Coalescence of furuncles with extension into subcutaneous tissues and evidence of systemic disease (fever, chills, bacteremia)

Staphylococci / Clinical correlations / Toxin mediated

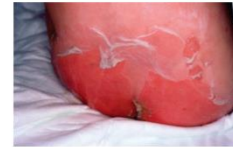
- Staphylococcal food poisoning, one of the most common foodborne illnesses, is an **intoxication** rather than an infection. Disease is caused by **heat stable bacterial toxin** present in food rather than from a direct effect of the organisms on the patient. With a **short incubation period (1–8 hours)**; violent nausea, vomiting, and diarrhea; and **rapid convalescence.**
- Staphylococcal scalded skin syndrome** is a condition which predominantly affects **infants and children** and causes a spectrum of skin lesions.

Toxin-Mediated Diseases

Scalded skin syndrome: Disseminated desquamation of epithelium in infants; blisters with no organisms or leukocytes

Food poisoning: After consumption of food contaminated with heat-stable enterotoxin, rapid onset of severe vomiting, diarrhea, and abdominal cramping, with resolution within 24 hours

Toxic shock: multisystem intoxication characterized initially by fever, hypotension, and a diffuse, macular, erythematous rash; high mortality without prompt antibiotic therapy and elimination of the focus of infection



Staphylococci / Clinical correlations / Coagulase negative

- S epidermidis** infections are difficult to cure because they occur in **prosthetic devices** where the bacteria can sequester themselves in a **biofilm.** staphylococci are a major cause of **endocarditis of artificial valves.**
- More than 50% of all infections of **catheters and shunts** are caused by **coagulase-negative staphylococci.** These infections have become a major medical problem because long-dwelling catheters and shunts are used commonly for the medical management of critically ill patients.

Coagulase-Negative Staphylococcus Species

Wound infections: Characterized by erythema and pus at the site of a traumatic or surgical wound; infections with foreign bodies can be caused by *S. aureus* and coagulase-negative staphylococci

Urinary tract infections: Dysuria and pyuria in young sexually active women (*S. saprophyticus*); in patients with urinary catheters (other coagulase-negative staphylococci), or following seeding of the urinary tract by bacteremia (*S. aureus*)

Catheter and shunt infections: Chronic inflammatory response to bacteria coating a catheter or shunt (most commonly with coagulase-negative staphylococci)

Prosthetic device infections: Chronic infection of device characterized by localized pain and mechanical failure of the device (most commonly with coagulase-negative staphylococci)

streptococcus

streptococcus categorized depending on : 1- serologic properties (: Lancefield) 2- hemolytic activity (β, α, γ) 3- biochemical properties

Name	Shape	motility	Feature	Structure	location	Ways of Transmission	Disease
Streptococcus pyogenes	- Spherical shape (arranged in chains)		- B hemolytic - Group A - produce streptococcal pyrogenic exotoxins (Spe) (erythrogenic toxins) which act as superantigens	By these structures it can avoid the phagocytes: - Hyaluronic capsule: Poor immunogen - M protein: Block the binding of c3b. Other function: - M protein: adhesion - M+F protein : invade the epithelial cells - C5 peptidase	Colonize in the oropharynx of healthy children and young adults	person to person through respiratory droplets day-care facilities especially during winter season	Pharyngitis + pyoderma

S. pyogenes disease is caused by recently acquired strains that can establish an infection of the pharynx or skin before specific antibodies are produced or competitive organisms are able to proliferate

Examples of the toxins :

- **Streptolysin S** is an oxygen-stable, nonimmunogenic, cell-bound hemolysin that can lyse erythrocytes, leukocytes, and platelets, and is responsible for the characteristic β -hemolysis seen on blood agar media.
- **Streptolysin O** is an oxygen-labile hemolysin capable of lysing erythrocytes, leukocytes, platelets, and cultured cells. Antibodies are readily formed against streptolysin O (**antistreptolysin O [ASO] antibodies**), and are useful for documenting recent group A streptococcal infection (**ASO test**). patients with **cutaneous infections do not develop ASO** antibodies.
- **Streptokinase** lyse blood clots and fibrin deposits and facilitate the rapid spread of *S. pyogenes* in infected tissues.
- **DNases A to D** can depolymerize free deoxyribonucleic acid (DNA) present in pus.

Name	Example	location	Diseases	Susceptable
Group B streptococcus (GBS)	Streptococcus agalactiae	- lower GI tract - genitourinary tract (10-30% Transient vaginal carriage)	- pneumonia - bone + joint infection - skin + soft tissue infection - bacteremia	older and have debilitating underlying conditions

Note: GBS detected by : 1- GBS antigen

2- resistance to bacitracin

- neonatal infection to Streptococcus agalactiae:

Early infection (7 days >)

Late infection (7 days ≤)

Both are characterized by bacteremia or meningitis.

Name	Shape	Features	Structure	location	Disease	Suspectable
Streptococcus pneumoniae	-Encapsulated - oval bacteria with (0.5-1.2 µm in diameter) - appear as pairs (diplococci)	- α-hemolytic by (pneumolysin which degrade hemoglobin into green product)	-Virulent factor : polysaccharide capsule - IgA protease - pneumolysin - Amidase -Phosphorylcholine	inhabitant of the throat and nasopharynx in healthy people	Can spread to : 1-lungs (pneumonia) 2-paranasal sinuses (sinusitis) 3-ears (otitis media) 4-meninges (meningitis)	common in children + adults living in a household with children

Note : The most commonly isolated serotypes are used in a polyvalent vaccine which decrease the incidence of pneumonia

Pathogenesis :

The disease happened primarily by the host response to infection rather than the production of organism-specific toxic factors

Let's explain it :


The bacteria migrate to the lower respiratory tract " so it attached to IgA and to the mucus , but the bacteria has the IgA protease which degrade IgA , pneumolysin which destroy the ciliated epithelial cells and phagocytic cells , Amidase enhances release of the cell wall components (Teichoic acid and the peptidoglycan fragments) which can activate complement and initiate an immune response, Phosphorylcholine bind to receptors for platelet-activating factor , helps in host cell invasion , important for amidase function

Name	Shape	Features	Location	Disase	Suspectable						
Viridans	-	Variable hemolytic activity : 1- α-hemolytic (green color) 2- non hemolytic	Oropharynx gastrointestinal tract genitourinary tract	<table border="1"> <tr> <td>Mitis</td> <td><i>S. mitis</i>, <i>S. pneumoniae</i>, <i>S. oralis</i></td> <td>Subacute endocarditis; sepsis in neutropenic patients; pneumonia; meningitis</td> </tr> <tr> <td>Mutans</td> <td><i>S. mutans</i>, <i>S. sobrinus</i></td> <td>Dental caries; bacteremia</td> </tr> </table>	Mitis	<i>S. mitis</i> , <i>S. pneumoniae</i> , <i>S. oralis</i>	Subacute endocarditis; sepsis in neutropenic patients; pneumonia; meningitis	Mutans	<i>S. mutans</i> , <i>S. sobrinus</i>	Dental caries; bacteremia	
Mitis	<i>S. mitis</i> , <i>S. pneumoniae</i> , <i>S. oralis</i>	Subacute endocarditis; sepsis in neutropenic patients; pneumonia; meningitis									
Mutans	<i>S. mutans</i> , <i>S. sobrinus</i>	Dental caries; bacteremia									
Enterococci	- pairs or short chains	Grow in : 1- aerobically and anaerobically 2- broad temperature range (10° C to 45° C) 3- wide pH range (4.6 to 9.9) 4- presence of high concentrations of sodium chloride (NaCl) and bile salts - Variable hemolysis pattern. Virulence is mediated by two general properties: (1) ability to adhere to tissues and form biofilms and (2) antibiotic resistance	<i>E. faecalis</i> is found in the large intestine in high concentrations (e.g., 10 ⁵ to 10 ⁷ organisms per gram of feces) and in the genitourinary tract - urinary tract is the most common site of enterococcal		-nosocomial infection frequently associated with urinary catheterization or instrumentation						

Clinical cases

Streptococcus pyogenes / Clinical correlations

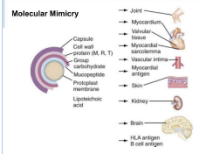
Streptococcus pyogenes (Group A)
 Suppurative Infections
Pharyngitis: reddened pharynx with exudates generally present; cervical lymphadenopathy can be prominent
Scarlet fever: diffuse erythematous rash beginning on the chest and spreading to the extremities; complication of streptococcal pharyngitis
Pyoderma: localized skin infection with vesicles progressing to pustules; no evidence of systemic disease
Erysipelas: localized skin infection with pain, inflammation, lymph node enlargement, and systemic symptoms
Cellulitis: infection of the skin that involves the subcutaneous tissues
Necrotizing fasciitis: deep infection of skin that involves destruction of muscle and fat layers
Streptococcal toxic shock syndrome: multiorgan systemic infection resembling staphylococcal toxic shock syndrome; however, most patients are bacteremic and with evidence of bacteria



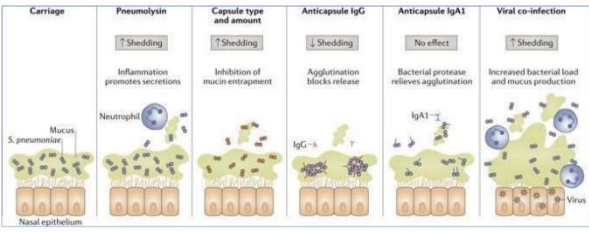
Streptococcus pyogenes / Clinical correlations

- **Post-streptococcal glomerulonephritis (PSGN)** is an immunologically-mediated sequela of pharyngitis or skin infections caused by nephritogenic strains of *Streptococcus pyogenes*.
- **Rheumatic fever (RF)** is an inflammatory disease that can involve the heart, joints, skin, and brain. The disease typically develops two to four weeks after a streptococcal throat infection.

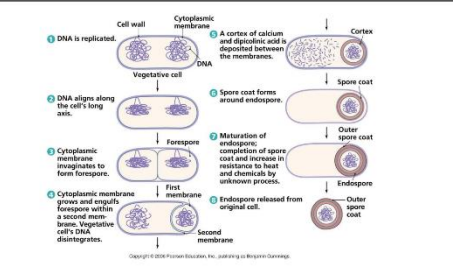
Molecular Mimicry



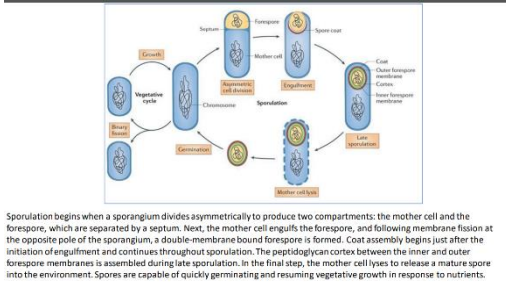
Non-suppurative Infections
Rheumatic fever: characterized by inflammatory changes of the heart (pancarditis) joints (arthritis), blood vessels, and subcutaneous tissues
Acute glomerulonephritis: acute inflammation of the renal glomeruli with edema, hypertension, hematuria, and proteinuria



Endospore



- Endospores**
- When faced with harsh environmental conditions, like depletion of any of several nutrients (carbon, nitrogen, or phosphorous), **some gram positive bacteria** undergo a cycle of differentiation called **sporulation**.
 - Sporulation involves the production of many new structures, enzymes, and metabolites along with the disappearance of many vegetative cell components.
 - The spore contains a complete copy of the chromosome, the bare minimum concentrations of essential proteins and ribosomes, and a high concentration of **calcium bound to dipicolinic acid**
 - The **spore** is a resting cell, highly resistant to desiccation, heat, and chemical agents, can exist for centuries as viable spores.
 - When returned to favorable nutritional conditions, the spore **germinates** to produce a single vegetative cell.
 - The location of the spore within a cell can assist in identification of the bacterium.
 - The ultra structure and formation process of spores can vary from one species to another. (exact detailed structure is not exam material).



Spore-Forming Gram-Positive rods

Name	shape	Structure	Features	Location	Disease	Source	Transmission
Bacillus anthracis	Single or pair or long chain appearance	Capsules consist of poly-D-glutamic acid	-aerobic - virulence factors: 1- capsule (inhibit phagocyte) 2- edema toxin 3- lethal toxins (cause inflammation)	Spores germinate at the site of entry	- growth of the vegetative organisms results in formation of gelatinous edema and congestion. - shock and death within 3 days of initial symptoms unless treatment is initiated immediately	-Through herbivores (contaminated animal or its product) - biological warfare	Inoculation (95%) Inhalation Ingestion
Bacillus cereus	Spores retain the malachite green dye.		- aerobic		Cause food poisoning: 1- emetic (vomiting) Caused by eating contaminated rice (enterotoxin)	Found in environment	

	vegetative cells are gray or colorless.				Incubation → short (1 to 6 hours Illness → 24 hours > 2- Diarrheal form true infection from bacteria in contaminated meat, vegetables, or sauces. With longer incubation period. - ocular infections (traumatic) → contaminated soil		
Clostridium difficile			-obligate anaerobes - Developed in people taking antibiotic, alter the normal enteric flora by : 1- permitting overgrowth 2- making the patient more susceptible to exogenous acquisition of C. difficile		Pseudomembranous colitis an inflammatory condition of the colon characterized by elevated yellow-white plaques that coalesce to form pseudomembranous on the mucosa		
Clostridium perfringens	- large rectangular - spores rarely observed - Colonies are distinctive, with their rapid, spreading growth -complete hemolysis (caused by the theta toxin) and a wider zone of partial hemolysis(caused by the alpha toxin		- obligate anaerobes		-soft-tissue infections including cellulitis, fasciitis or suppurative myositis, and myonecrosis - gas gangrene : caused by the metabolic activity of the rapidly dividing bacteria (which contain α -toxin that disrupt plasma membrane of cells. - Clostridial food poisoning, an intoxication : 1: incubation → 8-12 hours 2- illness : <24 hr 3- abdominal cramps	- type A : inhabits the intestinal tract of humans and animals + widely distributed in nature, particularly in soil and water contaminated with feces types B -E : do not survive in soil but colonize the intestinal tracts of animals and	

occasionally humans

Some notes about Clostridium perfringens : enterotoxin produced when vegetative cells transformed to spores in the alkaline environment of the small intestine (sporulation)

- Treatment is usually debridement and excision, with amputation necessary in many cases. Water soluble antibiotics (such as penicillin) alone are not effective because they do not penetrate ischemic muscles sufficiently to be effective.

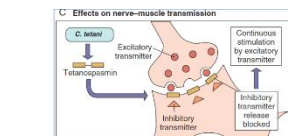
Name	Shape	Features	Disease	Source
Clostridium tetani	produces round, terminal spores (drumstick)	- motile - obligate anaerobes - produces two toxins, an oxygen-labile hemolysin (tetanolysin) and a plasmid-encoded, heat-labile neurotoxin (tetanospasmin)	spastic paralysis: caused by Tetanospasmin inactivates proteins that regulate release of the inhibitory neurotransmitters. (GABA) - sardonic smile	found in fertile soil and transiently colonizes the GI tracts of many animals, including humans
Clostridium botulinum		- etiologic agents of botulism are a heterogeneous - fastidious - anaerobic - Seven antigenically distinct botulinum toxins (A to G), human disease is associated with types A, B, E, and F .	foodborne botulism : become weak and dizzy 1 to 3 days after consuming the contaminated food. Bilateral descending weakness of the peripheral muscles develops in patients with progressive disease (flaccid paralysis), and death is most commonly attributed to respiratory paralysis . Infant botulism : , this disease is caused by neurotoxin produced in vivo by C. botulinum colonizing the GI tracts of infants. (The botulinum neurotoxin remains at the neuromuscular junction, The botulinum endopeptidase then inactivates the proteins that regulate release of acetylcholine, blocking neurotransmission at peripheral cholinergic synapses. The resulting clinical presentation of botulism is a flaccid paralysis)	- soil and water - home – canned food (foodborne botulism) - honey, infant milk powder contaminated with botulinum spores and ingestion of spore-contaminated soil and dust. (Infant botulism

Clinical

Clostridium tetani



Involvement of the masseter muscles (trismus or lockjaw) is the presenting sign in most patients. The characteristic **sardonic smile** that results from the sustained contraction of the facial muscles.

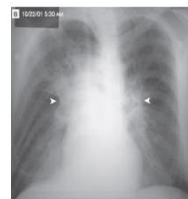


unregulated excitatory synaptic activity in the motor neurons, resulting in **spastic paralysis**. **Generalized tetanus** is the most common form.

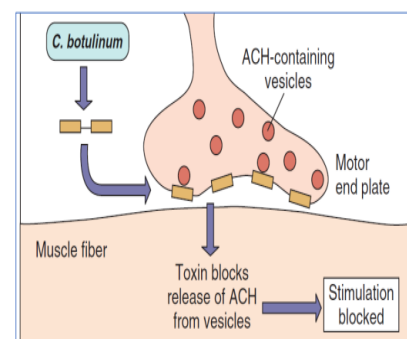
Bacillus anthracis



Typically, **cutaneous anthrax** starts with the development of a painless papule at the site of inoculation that rapidly progresses to an ulcer surrounded by vesicles and then to a necrotic eschar.



Inhalation anthrax can be associated with a **prolonged latent period** (2 months or more), during which the infected patient remains asymptomatic. Spores phagocytosed in the lungs; and transported by the lymphatic drainage to the **mediastinal lymph nodes, where germination occurs**. Hemorrhagic necrosis and edema of the mediastinum are early manifestations, Sepsis occurs and spread to other organs (GI ulcerations, meningitis) can take place.



NON-SPORE-FORMING Anaerobic gram-positive rods

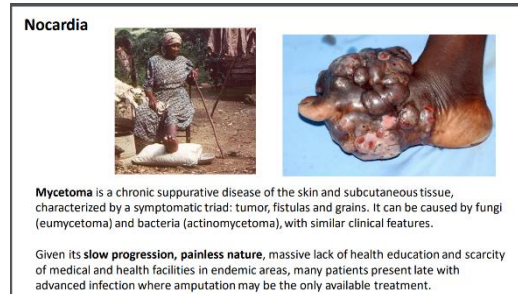
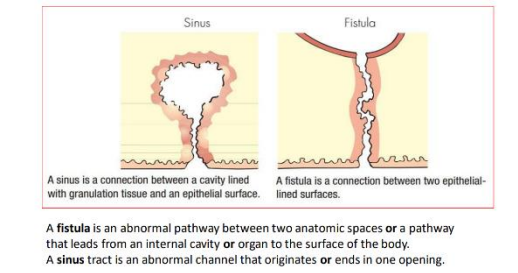
Name	Shape	Features	Location	Sources	Disease	Treatment
Actinomyces	-delicate filamentous forms or hyphae fastidious and grow slowly (>2weeks)	- facultatively anaerobic or strictly anaerobic	<p>In healthy man : colonize the upper respiratory, GI, and female genital tracts but are not normally present on the skin surface</p> <p>In infections 1- cervicofacial (following invasive dental procedure or oral trauma) 2- abdominopelvic (associated with abdominal surgery, tuboovarian abscess, ruptured appendicitis, and intrauterine contraceptive devices (IUCD) 3- thoracic</p>	endogenous	Actinomycosis: chronic granulomatous lesions that become suppurative and form abscesses connected by sinus tracts	drainage of a localized abscess or surgical debridement of the involved tissues, and prolonged administration of antibiotics
Nocardia	-branched filaments - weakly acid-fast (This distinguish it from the similar Actinomyces) - Growth is slow, requiring 3 to 5 days of incubation	- strict aerobic rods ability of pathogenic strains to avoid phagocytic killing by : 1- catalase 2- superoxide dismutase 3- cord factor : preventing fusion of the phagosome-lysosome		Exogenous: (not normally part of the normal human flora) soil rich with organic matter	1- Bronchopulmonary disease colonization of the upper respiratory tract by inhalation and then aspiration of oral secretions into the lower airways, occurs almost always in immunocompromised patients. 2- Primary cutaneous nocardiosis: Mycetoma 3- one third of all patients with Nocardia infections	

					have dissemination to the brain, most commonly involving the formation of single or multiple brain abscesses.	
Lactobacillus	-ferment to yield lactic acid	-facultatively anaerobic or strictly anaerobic - found in probiotics -starter cultures in industry for controlled fermentation	normal flora of the mouth, stomach, intestines, and genitourinary tract - 70% of women in the female genital tract	Invasion into blood through : 1- transient bacteremia from a genitourinary source (e.g., after childbirth or a gynecologic procedure) (2) endocarditis (3) opportunistic septicemia in an immunocompromised patient	- Rarely cause infections	
Propionibacterium	arranged in short chains or clumps	- facultatively anaerobic or strictly anaerobic		Skin , conjunctiva, and external ear, and in the oropharynx and female genital tract.	Propionibacterium acnes which cause : 1- acne vulgaris 2- opportunistic infections in patients with prosthetic devices or intravascular lines	
Mobiluncus	-obligate anaerobic - gram-variable or gram-negative - curved rods with tapered ends	classified as gram positive. because they (1) have a gram-positive cell wall (2) lack endotoxin (3) are susceptible to vancomycin, clindamycin, erythromycin, and ampicillin but resistant to colistin	rarely found in the vaginas of healthy women but is abundant in women with bacterial vaginosis			

Note : P. acnes apparently only triggers the disease (acne vulgaris) when it meets favorable dermatophysiological terrain; **P. acnes colonization of the skin is therefore necessary but not sufficient for the establishment of the pathology.**

-Bifidobacterium and Eubacterium : commonly found in the oropharynx, large intestine, and vagina. Usually represent clinically insignificant contaminants

Clinical



Non-spore forming Aerobic Gram-Positive Rods

- human pathogens (e.g., *Listeria monocytogenes*, *Corynebacterium diphtheria*)
- primarily animal pathogens that can cause human disease (e.g., *Erysipelothrix rhusiopathiae*)
- opportunistic pathogens that typically infect hospitalized or immunocompromised patients (e.g., *Corynebacterium jeikeium*)

Name	Shape	Feature	Structure	Source	Disease	Susceptable
<i>Listeria monocytogenes</i>	-Non branching -appear singly in pairs, or in short chains	- facultatively anaerobic - can be mistaken for Streptococcus pneumonia - motile at room temperature (end-over-end tumbling motion) - weak β -hemolysis - facultative intracellular pathogen. - can replicate in macrophages	- internalin A : adhere to host cells (glycoprotein receptors (e.g., epithelial cadherin) ActA : coordinates assembly of actin (movement) After penetration into the cells : 1- listeriolysinO (bacterial pore-forming cytolysin) 2- phospholipase C (2 types) 1+2: release of the bacteria into the cell cytosol (both are activated by acid pH of the phagolysosome)	- widely distributed in nature - contaminated food; causing Foodborne Listeriosis - mother to child in utero or at birth	- human disease is uncommon - Healthy Adults is self limited and asymptomatic or in the form of a mild influenza-like illness	- neonates - elderly - pregnant women (mostly during the third trimester) - patients with defective cellular immunity not in humoral immunity , are particularly susceptible to severe infections

Note : Neonatal Disease (1) early-onset disease, acquired transplacentally in utero can result in abortion, stillbirth, or premature birth

(2) late-onset disease, acquired at or soon after birth occurs 2 to 3 weeks after birth in the form of meningitis or meningoencephalitis with septicemia

Name	Shape	Feature	Structure	Source	Disease	Susceptable
Corynebacterium diphtheriae	- irregularly staining - pleomorphic rod	- aerobic or facultatively anaerobic - non motile - catalase (+)	Virulence factor A-B exotoxin : A subunit : catalytic region B subunit : receptor-binding region and a translocation region -	- ubiquitous in plants and animals - normally colonize the skin, upper respiratory tract, gastrointestinal tract, and urogenital tract in humans	Respiratory droplets or skin contact transmits it from person to person - Respiratory Diphtheria	Humans are the only known reservoir Respiratory droplets or skin contact transmits it from person to person

- mechanism of the exotoxin : The toxin binds to heparin-binding epidermal growth factor precursor (HB-EGF) present on many epithelial membranes. And is endocytosed by the cell. **A subunit** is translocated to the cytosol. **A subunit** ADP-ribosylates host eEF-2. eEF-2 is required for protein synthesis; when it is inactivated by the toxin, the host cannot make protein and thus dies

Clinical

Corynebacterium diphtheriae

Respiratory Diphtheria
The onset is sudden, with malaise, sore throat, exudative pharyngitis, and a low-grade fever. The exudate evolves into a thick pseudomembrane composed of bacteria, lymphocytes, plasma cells, fibrin, and dead cells that can cover the tonsils, uvula, and palate and can extend up into the nasopharynx or down into the larynx.

Diphtheria has become uncommon in the United States because of an active immunization program, as shown by the fact that more than 700,000 cases were reported in 1921 but no cases have been reported since 2003.


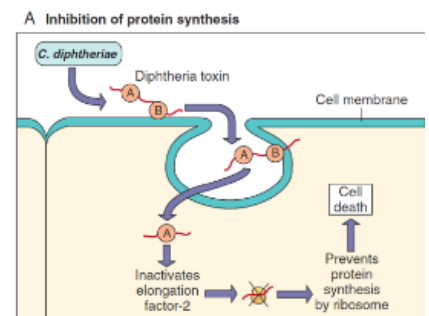


FIGURE 21-5 Pharynx of a 39-year-old woman with bacteriologically confirmed diphtheria. The photograph was taken 4 days after the onset of fever, malaise, and sore throat. Inevitably caused by removal of the membrane by swabbing appears as a dark area on the left. (From Mandell G, Resnet F, Dolin R. Principles and practice of infectious diseases, ed 8, Philadelphia, 2015; Elsevier.)



Anaerobic Gram-Positive Cocci

- normally colonize the oral cavity, gastrointestinal (GI) tract, genitourinary tract, and skin. They produce infections when they spread from these sites to normally sterile sites.
- can be isolated from infections at all body sites, a predisposition for certain sites has been observed.
- **Peptostreptococcus** species have been recovered more often from subcutaneous and soft tissue abscesses and diabetes-related foot ulcers than from intra-abdominal infections. Peptostreptococcus infections occur more often in chronic infections. Many infections caused by peptostreptococcus bacteria are synergistic.

ENTEROBACTERIACEAE

Name	Feature	Structure	Source
ENTEROBACTERIACEAE	-non-spore-forming - gram-negative rods - facultative anaerobes that share a common antigen enterobacterial common antigen - Resistance to Serum Killing and Antimicrobial Resistance. - grow in the MacConkey's agar (pink color)	- Endotoxin: depends on the lipid A component of LPS, released at cell lysis. - Capsule (hydrophilic) repel the hydrophobic phagocytic but anticapsular antibodies diminish the capsule role. <ul style="list-style-type: none"> • Antigenic Phase Variation: <ol style="list-style-type: none"> 1- somatic O antigens 2- capsular K antigens 3-flagellar H antigens alternately expressed or not expressed (phase variation). - Type III Secretion Systems. - The bacteria counteract iron sequestration by producing their own competitive siderophores or iron-chelating compounds (e.g., enterobactin, aerobactin). Or from Iron released from lysed cells. 	- ubiquitous : oil, water, and vegetation - part of the normal intestinal flora of most animals, including humans In human it can be : -normal intestinal flora -always associated with human disease - opportunistic infections - normally commensal organisms that become pathogenic when they acquire virulence genes

MacConkey's agar : contains bile salts (to inhibit most Gram-positive bacteria), crystal violet dye (which also inhibits certain Gram-positive bacteria), neutral red dye (which turns pink if the microbes are fermenting lactose)

ENTEROBACTERIACEAE/ Antibiotic resistance

- Resistance of the Enterobacteriaceae to antibiotics, especially of the β lactam type, is increasingly dominated by the mobilization of continuously expressed single genes that encode efficient drug modifying enzymes.
- **Multi drug resistant (MDR)** Enterobacteriaceae has been frequently reported from different parts of the world as an emergence of treatment problem. Antibiotics given empirically without proper antibiotic susceptibility testing are one of the major causes for the development of MDR.
- There is a shift of the "natural" resistance, such as **membrane impermeability** and **drug efflux**, to the modern paradigm of **mobile gene pools** that transmit resistance between bacteria.

Name	Feature	Examples
E.coli	Common : 1- commensal inhabitant of the GIT 2- one of the most important pathogens (diarrheal) 3- most frequent cause of bloodstream infection and urinary tract infections (UTIs) among <u>Gram-negative bacteria</u>	Commensal strains innocuously colonize the colon of healthy hosts, causing extraintestinal disease only in the presence of a large inoculum (e.g., with penetrating abdominal trauma) and/or significant host compromise. <ul style="list-style-type: none"> • Diarrhoeagenic strains cause diarrhea syndromes that vary in clinical presentation and pathogenesis according to the strain's distinctive virulence traits • Extra intestinal pathogenic E. coli (ExPEC) often innocuously colonize the human gut. However, they have a unique ability to enter and survive within normally sterile extraintestinal body sites, and to cause disease when they do so

Name	Feature	Disease	Transmission
Enterotoxigenic E. coli (ETEC)	<p>Produces 2 classes of toxins:</p> <p>1- Heat stable toxin leads to increase in (cGMP) and subsequent hypersecretion of fluids well as inhibition of fluid absorption</p> <p>2- heat labile toxins leads to increase in (cAMP) levels, resulting in enhanced secretion of chloride and decreased absorption of sodium and chloride</p> <p>- 1- to 2-day incubation period and persists for an average of 3 to 5 days</p>	<p>- causes of bacterial diarrheal disease in developing countries, and 30% of traveler's diarrhea</p> <p>- Secretory diarrhea (watery, non-bloody diarrhea) and abdominal cramps; less commonly nausea and vomiting. Can be fatal in undernourished individuals</p>	<p>consumption of fecally contaminated food or water(Person-to-person spread does not occur)</p>
Shiga toxin-producing E. coli (STEC)	<p>- Ingestion of fewer than 100 bacteria can produce disease</p> <p>- 3 to 4 days of incubation, Within 2 days of onset, disease in 30% to 65% of patients progresses to a bloody diarrhea with severe abdominal pain, Complete resolution of symptoms typically occurs after 4 to 10 days in most untreated patients</p>	<p>- ranges from mild uncomplicated diarrhea to hemorrhagic colitis with severe abdominal pain and bloody diarrhea (severe : associated with STEC O157:H7)</p> <p>- Hemolytic uremic syndrome (HUS), a disorder characterized by acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia, is a complication in 5% to 10% of infected children younger than 10 years</p>	<p>- consumption of undercooked meat products, water, unpasteurized milk or fruit juices uncooked vegetables, and fruits</p> <p>- person-to-person spread occurs</p>
Salmonella	<p>- highly adapted to humans and do not cause disease in nonhuman hosts</p> <p>- Virulence dependent on pathogenicity island on the bacterial chromosome</p> <p>- large inoculum (e.g., 10^6 to 10^8 bacteria) is required for symptomatic disease</p> <p>- can persist for 2 to 7 days before spontaneous resolution</p>	<p>- Asymptomatic Colonization : The strains of Salmonella responsible for causing typhoid and paratyphoid fevers are maintained by human colonization</p> <p>- Gastroenteritis is a common form of salmonellosis, nausea, vomiting, and nonbloody diarrhea</p> <p>- Septicemia All Salmonella species can cause bacteremia, although infections with Salmonella Typhi, Salmonella Paratyphi more commonly lead to a bacteremic phase</p> <p>- Salmonella Typhi produces a febrile illness called typhoid fever. Other Salmonella (e.g paratyphi) produce a milder form of this disease, referred to as paratyphoid fever.</p>	<p>- colonize virtually all animals (especially poultry , eggs, dairy products,</p> <p>- foods prepared on contaminated work surface (person to person)</p> <p>- person-to-person spread is common because The infectious dose for Salmonella Typhi infections is low</p>
Shigella : (dysenteriae, flexneri, boydii sonnei)	<p>- analysis of DNA show that these four species are actually biogroups within the species E. coli</p>	<p>- damage to the intestinal epithelium; however, in a small subset of patients, the Shiga toxin</p>	<p>- transmitted person to person by the fecal-oral route Because as few as</p>

	<ul style="list-style-type: none"> - S. dysenteriae strains produce an exotoxin, Shiga toxin. Similar to Shiga toxin produced by STEC - A subunit in the toxin cleaves the 28S rRNA in the 60S ribosomal subunit, thereby preventing the binding of aminoacyl-transfer RNA and disrupting protein synthesis - Humans are the only reservoir - infection is generally self-limited, although antibiotic treatment is recommended to reduce the risk of secondary spread to family members and other contacts 	<ul style="list-style-type: none"> can mediate damage to the glomerular endothelial cells, resulting in renal failure (HUS) - S. sonnei is responsible for almost 85% of U.S. infections, whereas S. flexneri predominates in developing countries. Epidemics of S. dysenteriae infections occur periodically, most recently in West Africa and Central America - Shigellosis(Shigella infection) (is primarily a pediatric disease, with 60% of all infections in children younger than 10 years (characterized by abdominal cramps, diarrhea, fever, and bloody stools. The clinical signs and symptoms of the disease appear 1 to 3 days after the bacteria are ingested) 	<p>100 to 200 bacteria can establish disease, shigellosis spreads rapidly in communities where sanitary standards and the level of personal hygiene are low .</p>
Klebsiella	<ul style="list-style-type: none"> - found in the human nose, mouth, and gastrointestinal tract as normal flora - 	<ul style="list-style-type: none"> - K. pneumoniae, which can cause community- or hospital-acquired primary lobar pneumonia. These bacteria also cause wound and soft-tissue infections and UTIs 	<ul style="list-style-type: none"> - colonize the hospital environment (hospital-acquired infections)
Proteus (P. mirabilis)		<ul style="list-style-type: none"> - Infections of the urinary tract 	
Yersinia	<ul style="list-style-type: none"> - best-known human pathogen within the genus Yersinia is Y. pestis - infections are zoonotic : 1- urban plague, for which rats are the natural reservoirs 2- sylvatic plague, which causes infections in squirrels, rabbits, field rats, and domestic cats 3- Bubonic plague 	<ul style="list-style-type: none"> Bubonic plague : s characterized by an incubation period of no more than 7 days after a person has been bitten by an infected flea. Patients have a high fever and a painful bubo (inflammatory swelling of the lymph nodes) in the groin or axilla. Bacteremia develops rapidly if patients are not treated, and as many as 75% die. - 	<ul style="list-style-type: none"> The patients are highly infectious; person-to-person spread occurs by aerosols in case of pneumonic plague.

Mechanism of action of the salmonella : After ingestion and passage through the stomach, salmonellae attach to the mucosa of the small intestine and invade into the M (microfold) cells located in Peyer patches, as well as into enterocytes. The bacteria remain in endocytic vacuoles, where they replicate. The bacteria can also be transported across the cytoplasm and released into the blood or lymphatic circulation. The inflammatory response confines the infection to the GI tract, mediates the release of prostaglandins, and stimulates cAMP and active fluid secretion + The bacteria responsible for enteric fever pass through the cells lining the intestines and are engulfed by macrophages. They replicate after

being transported to the liver, spleen, and bone marrow. Ten to 14 days after ingestion of the bacteria, patients experience gradually increasing fever, with nonspecific complaints of headache, myalgias, malaise, and anorexia).

Mechanism of Shigella : passes the epithelial cell (EC) barrier by transcytosis through M cells and encounters resident macrophages. The bacteria evade degradation in macrophages by inducing an apoptosis-like cell death, which is accompanied by proinflammatory signaling. Free bacteria invade the EC from the basolateral side, move into the cytoplasm by actin polymerization, and spread to adjacent cells. Proinflammatory signaling by macrophages and EC further activates the innate immune response and attracts PMN. The influx of PMN disintegrates the EC lining, which initially exacerbates the infection and tissue destruction by facilitating the invasion of more bacteria. Ultimately, PMN phagocytose and kill Shigella, thus contributing to the resolution of the infection

P. mirabilis mechanism : P. mirabilis produces large quantities of urease, which splits urea into carbon dioxide and ammonia. This process raises the urine pH, precipitating magnesium and calcium in the form of struvite and apatite crystals, respectively, and results in the formation of renal (kidney) stones. The increased alkalinity of the urine is also toxic to the uroepithelium

ENTEROBACTERIACEAE/ Antibiotic resistance

- **Carbapenem-resistant Enterobacteriaceae (CRE)** or carbapenemase-producing Enterobacteriaceae (CPE) are Gram-negative bacteria that are resistant to the carbapenem class of antibiotics, considered the drugs of last resort for such infections.
- They are resistant because they produce an enzyme called a carbapenemase that disables the drug molecule. The resistance can vary from moderate to severe.
- Experts fear CRE as the new “superbug”. The bacteria can kill up to half of patients who get bloodstream infections.
- The main risk factors for CRE acquisition in the United States include **exposure to healthcare and exposure to antibiotics.**

The end

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