




*Microbial Mechanisms of
Pathogenicity*

Chapter 15



Pathogenicity - ability to cause disease
Virulence - degree of pathogenicity

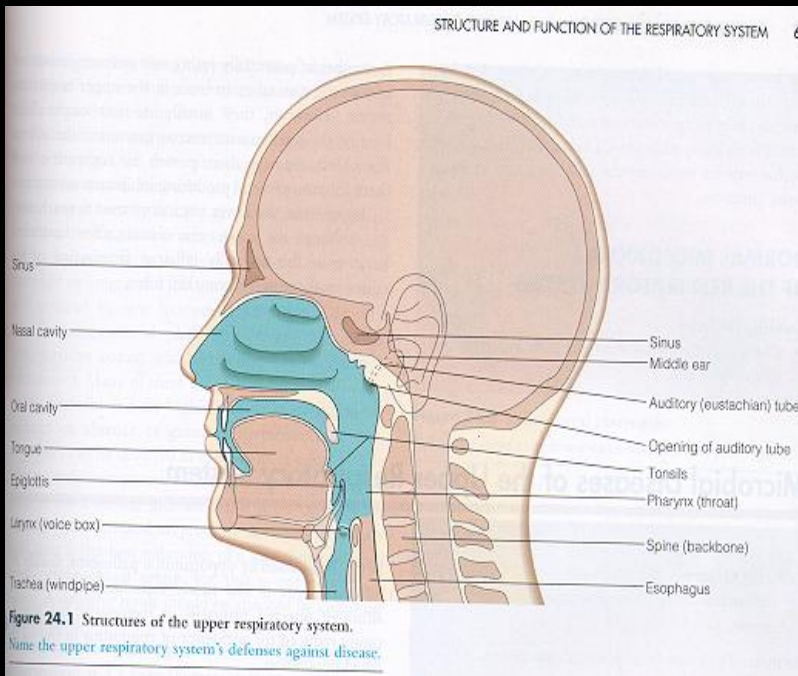
- ◆ Many properties that determine a microbe's pathogenicity or virulence are unclear or unknown
- ◆ But, when a microbe overpowers the host's defenses, disease results!



Portals of Entry

- ◆ 1. Mucus Membranes
- ◆ 2. Skin
- ◆ 3. Parentarel

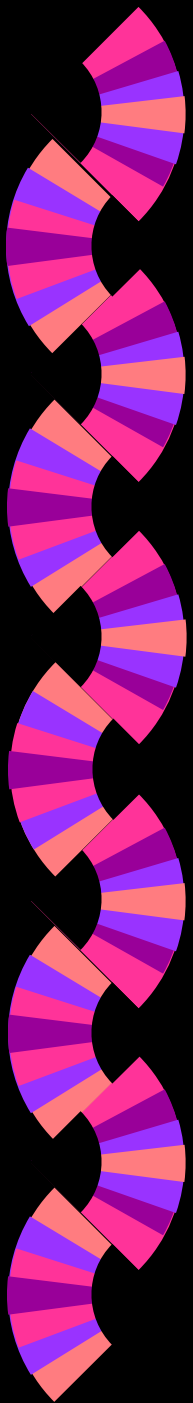
1. Mucus Membranes



- ◆ A. Respiratory Tract
 - microbes inhaled into mouth or nose in droplets of moisture or dust particles
 - Easiest and most frequently traveled portal of entry

Common Diseases contracted via the Respiratory Tract

- ◆ Common cold
- ◆ Flu
- ◆ Tuberculosis
- ◆ Whooping cough
- ◆ Pneumonia
- ◆ Measles
- ◆ Strep Throat
- ◆ Diphtheria



Mucus Membranes

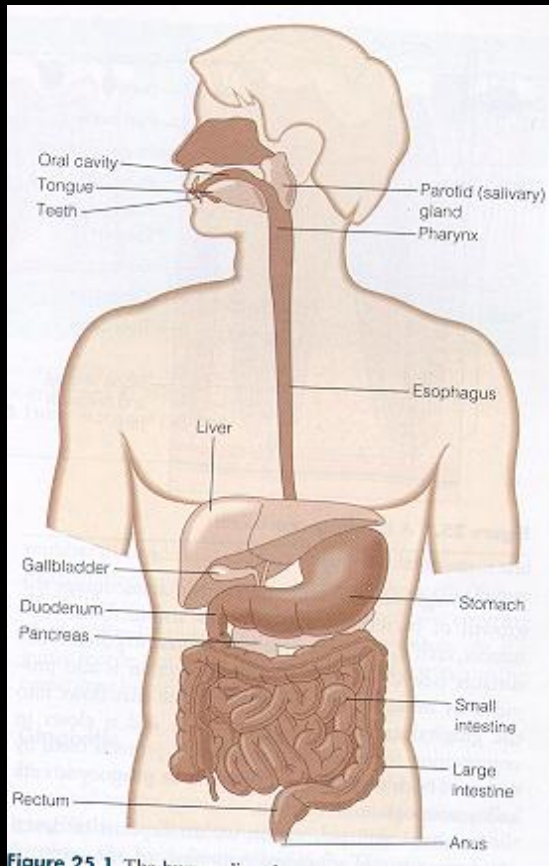
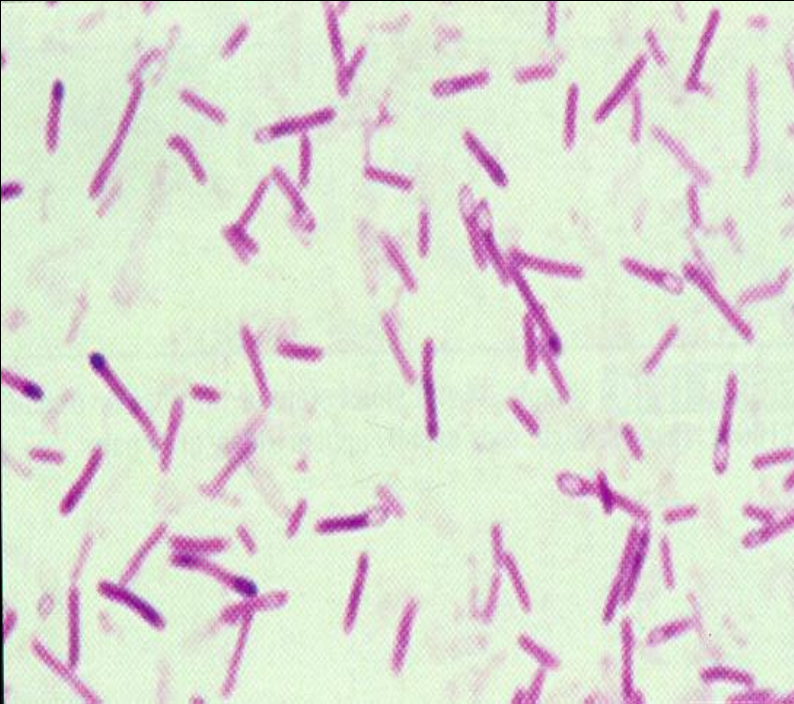


Figure 25.1 The human gastrointestinal tract.

- ◆ B. Gastrointestinal Tract
 - microbes gain entrance thru contaminated food & water or fingers & hands
 - most microbes that enter the G.I. Tract are destroyed by HCL & enzymes of stomach or bile & enzymes of small intestine

Common diseases contracted via the G.I. Tract



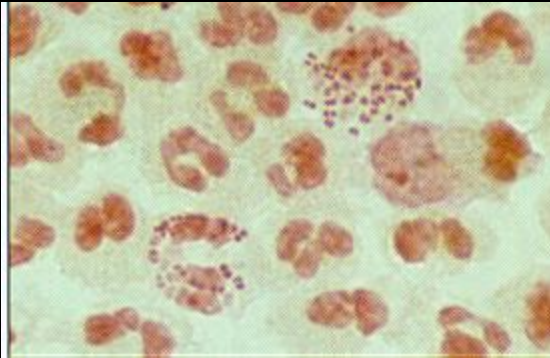
- ◆ Salmonellosis
 - *Salmonella sp.*
- ◆ Shigellosis
 - *Shigella sp.*
- ◆ Cholera
 - *Vibrio cholorea*
- ◆ Ulcers
 - *Helicobacter pylori*
- ◆ Botulism
 - *Clostridium botulinum*



Fecal - Oral Diseases

- ◆ These pathogens enter the G.I. Tract at one end and exit at the other end.
- ◆ Spread by contaminated hands & fingers or contaminated food & water
- ◆ Poor personal hygiene.

Mucus Membranes of the Genitourinary System - STD's



Gonorrhea

Neisseria gonorrhoeae



Syphilis

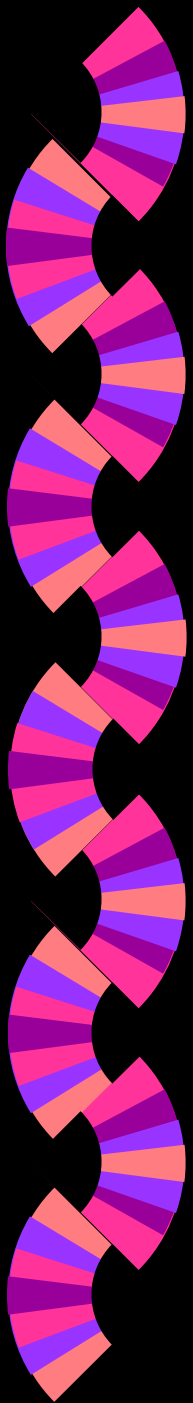
Treponema pallidum

Chlamydia

Chlamydia trachomatis

HIV

Herpes Simplex II



Mucus Membranes



- ◆ D. Conjunctiva –
 - mucus membranes that cover the eyeball and lines the eyelid
- ◆ Trachoma
 - *Chlamydia trachomatis*



2nd Portal of Entry: Skin

- ◆ Skin - the largest organ of the body. When unbroken is an effective barrier for most microorganisms.
- ◆ Some microbes can gain entrance thru openings in the skin: hair follicles and sweat glands



3rd Portal of Entry: Parentarel

- ◆ Microorganisms are **deposited** into the tissues below the skin or mucus membranes
- ◆ Punctures
- ◆ injections
- ◆ bites
- ◆ scratches
- ◆ surgery
- ◆ splitting of skin due to swelling or dryness



Preferred Portal of Entry

- ◆ Just because a pathogen enters your body it does not mean it's going to cause disease.
- ◆ pathogens - preferred portal of entry



Preferred Portal of Entry

- ◆ *Streptococcus pneumoniae*
 - if inhaled can cause pneumonia
 - if enters the G.I. Tract, no disease
- ◆ *Salmonella typhi*
 - if enters the G.I. Tract can cause Typhoid Fever
 - if on skin, no disease



Number of Invading Microbes

- ◆ LD₅₀ - Lethal Dose of a microbes toxin that will kill 50% of experimentally inoculated test animal
- ◆ ID₅₀ - infectious dose required to cause disease in 50% of inoculated test animals
 - Example: ID₅₀ for *Vibrio cholerea* 10⁸ cells (100,000,000 cells)
 - ID₅₀ for Inhalation Anthrax - 5,000 to 10,000 spores ????

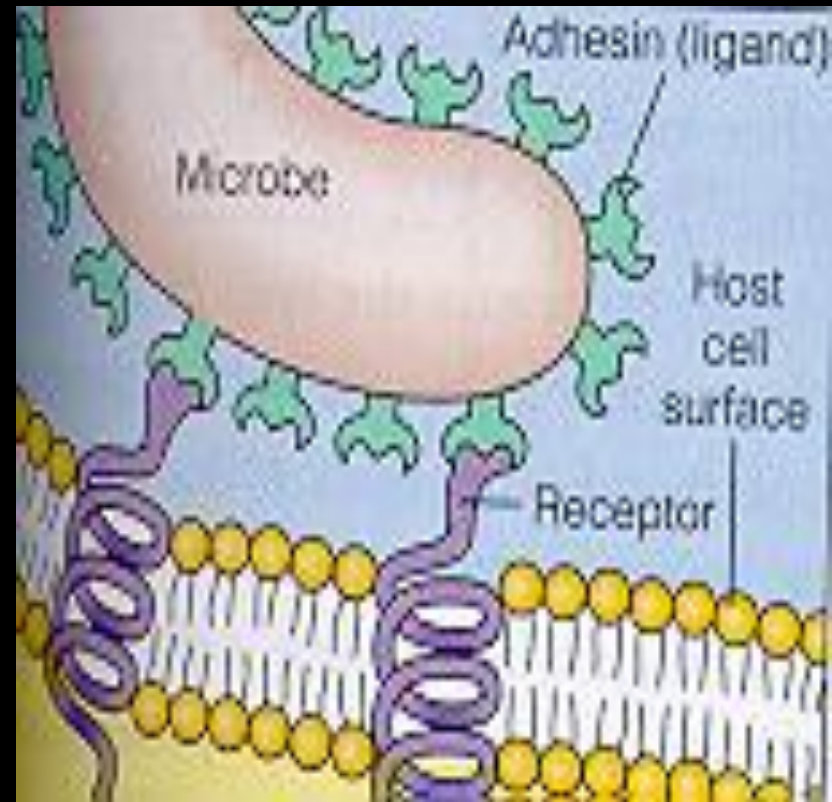
How do Bacterial Pathogens penetrate Host Defenses?

1. Adherence - almost all pathogens have a means to attach to host tissue

Binding Sites

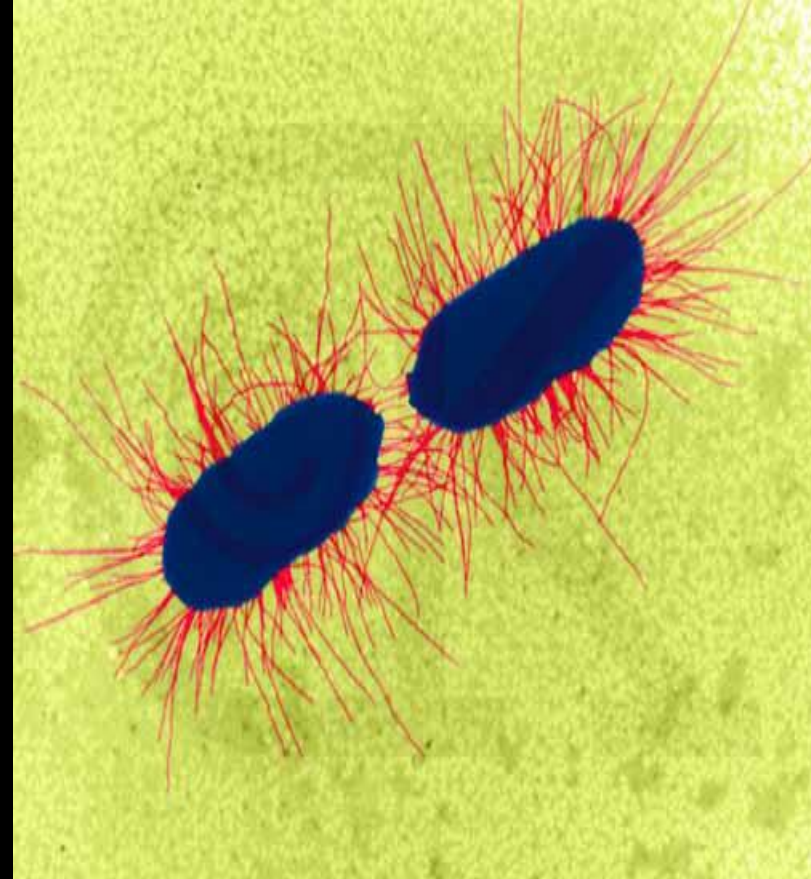
adhesins

ligands

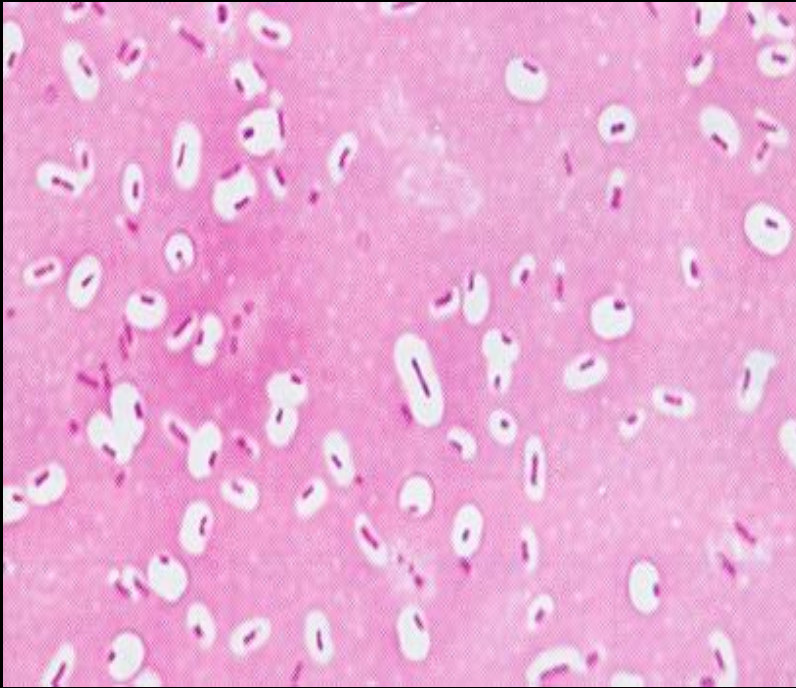


Adhesins and ligands are usually on Fimbriae

- ◆ *Neisseria gonorrhoeae*
- ◆ *ETEC*
(*Enterotoxigenic E. coli*)
- ◆ *Bordetello pertussis*



2. Capsules



K. pneumoniae

- ◆ Prevent phagocytosis
- ◆ attachment
- ◆ *Streptococcus pneumoniae*
- ◆ *Klebsiella pneumoniae*
- ◆ *Haemophilus influenzae*
- ◆ *Bacillus anthracis*
- ◆ *Streptococcus mutans*
- ◆ *Yersinia pestis*



3. Enzymes

- ◆ Many pathogens secrete enzymes that contribute to their pathogenicity

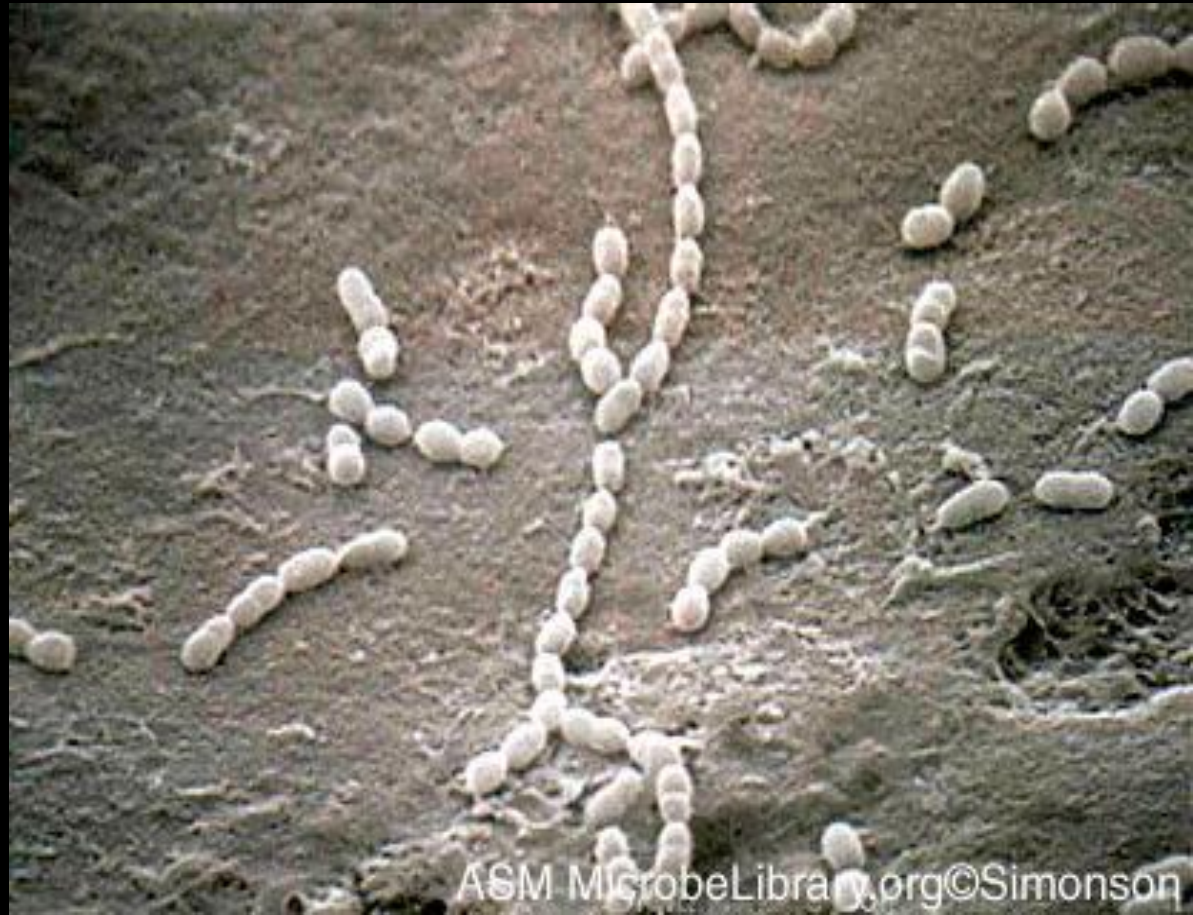


A. Leukocidins

- ◆ Attack certain types of WBC's
 - ◆ 1. Kills WBC's which prevents phagocytosis
 - ◆ 2. Releases & ruptures lysosomes
 - lysosomes - contain powerful hydrolytic enzymes which then cause more tissue damage

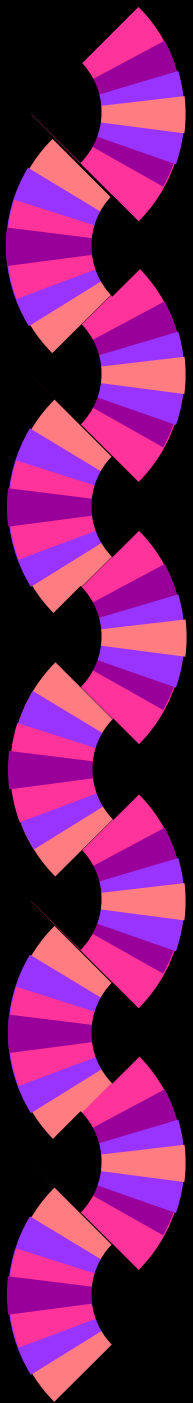
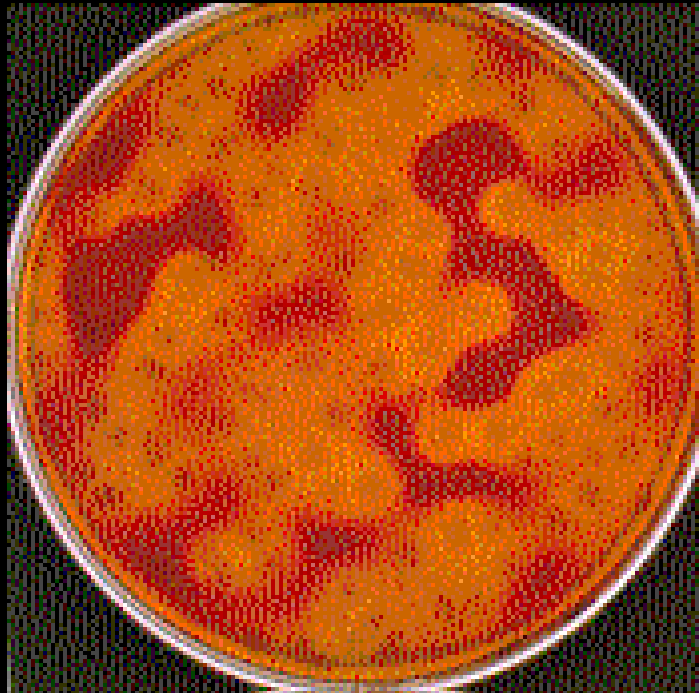
B. Hemolysins - cause the lysis of RBC's

Streptococci



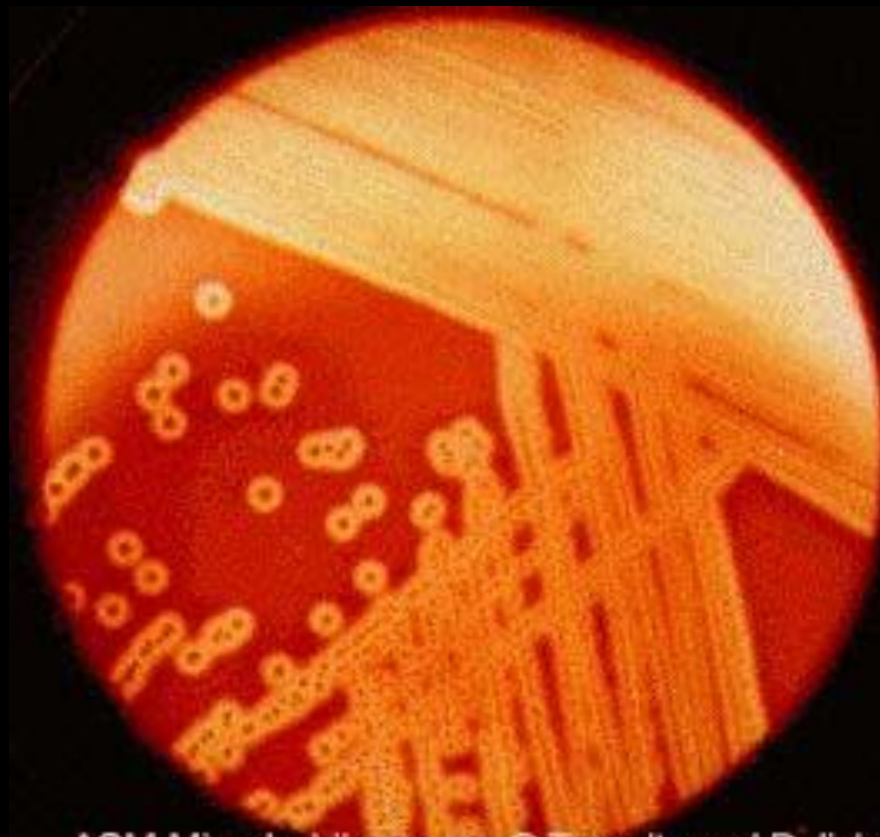
1. Alpha Hemolytic Streptococci

- secrete hemolysins that cause the incomplete lysis of RBC's

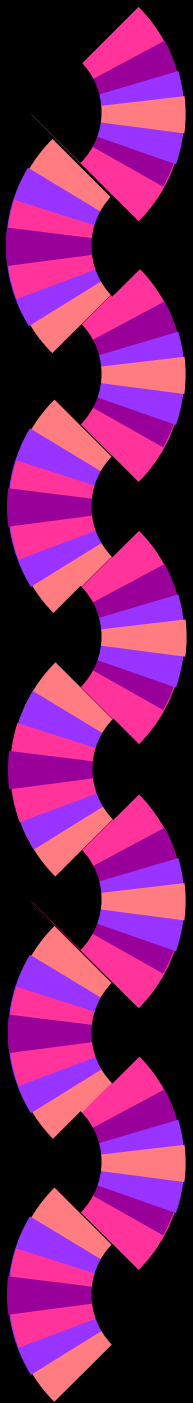


2. Beta Hemolytic Streptococci

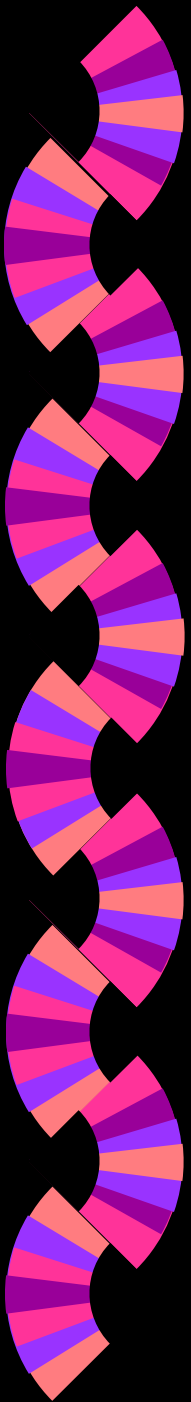
- secrete hemolysins that cause the complete lysis of RBC's

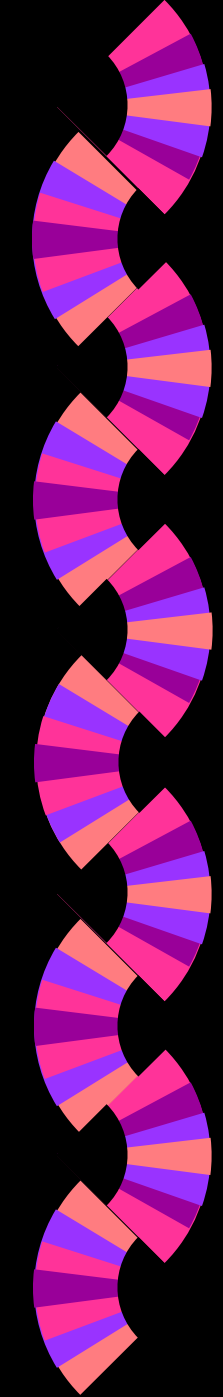


ASM MicrobeLibrary.org © Tomalty and Delisle



3. Gamma Hemolytic Streptococci - do not secrete any hemolysins





C. Coagulase - cause blood to coagulate

- ◆ Blood clots protect bacteria from phagocytosis from WBC's and other host defenses
- ◆ Staphylococci - are often coagulase positive
 - boils
 - abscesses



D. Kinases - enzymes that dissolve blood clots

- ◆ 1. Streptokinase - Streptococci
- ◆ 2. Staphylokinase - Staphylococci

- ◆ Helps to spread bacteria - **Bacteremia**

- ◆ **Streptokinase** - used to dissolve blood clots in the Heart (Heart Attacks due to obstructed coronary blood vessels)



E. Hyaluronidase

- ◆ Breaks down Hyaluronic acid (found in connective tissues)
- ◆ “Spreading Factor”
- ◆ mixed with a drug to help spread the drug thru a body tissue



F. Collagenase

- ◆ Breaks down collagen (found in many connective tissues)
- ◆ *Clostridium perfringens* - Gas Gangrene
 - uses this to spread thru muscle tissue

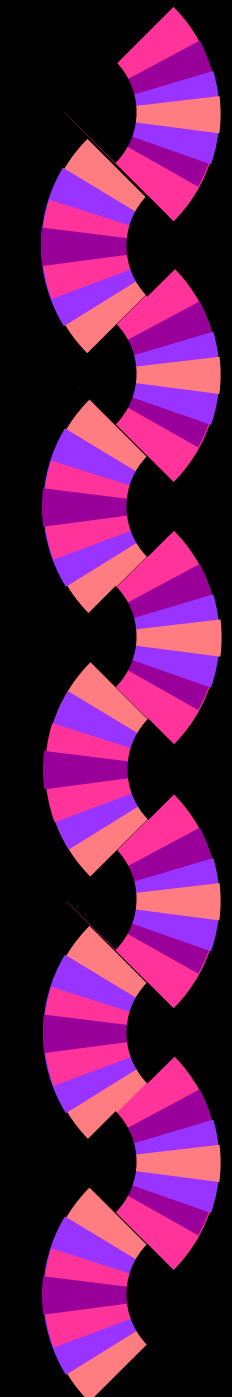
G. Necrotizing Factor

- causes death (necrosis) to tissue cells



“Flesh Eating Bacteria”

Necrotizing fasciitis



Summary of How Bacterial Pathogens Penetrate Host Defenses

- ◆ 1. Adherence
- ◆ 2. Capsule
- ◆ 3. Enzymes
 - A. leukocidins
 - B. Hemolysins
 - C. Coagulase
 - D. Kinases
 - E. Hyaluronidase
 - F. Collagenase
 - G. Necrotizing Factor



4. *Toxins*

- ◆ Poisonous substances produced by microorganisms
- ◆ toxins - **primary factor** - pathogenicity
- ◆ 220 known bacterial toxins
 - 40% cause disease by damaging the Eukaryotic cell membrane
- ◆ Toxemia
 - Toxins in the bloodstream



2 Types of Toxins

- ◆ 1. Exotoxins
 - secreted outside the bacterial cell
- ◆ 2. Endotoxins
 - part of the outer cell wall of Gram (-) bacteria



Exotoxins

- ◆ Mostly seen in Gram (+) Bacteria
- ◆ Most gene that code for exotoxins are located on **plasmids** or **phages**



3 Types of Exotoxins

- ◆ 1. Cytotoxins
 - kill cells
- ◆ 2. Neurotoxins
 - interfere with normal nerve impulses
- ◆ 3. Enterotoxins
 - effect cells lining the G.I. Tract



Response to Toxins

- ◆ If exposed to exotoxins: antibodies against the toxin (**antitoxins**)
- ◆ Exotoxins inactivated (heat, formalin or phenol) no longer cause disease, but stimulate the production of antitoxin
 - altered exotoxins - **Toxoids**
- ◆ Toxoids - injected to stimulate the production of antitoxins and provide immunity



Example: DPT Vaccine


- ◆ D - Diphtheria
 - *Corynebacterium diphtheriae*
- ◆ P - Pertussis
 - *Bordetello pertussis*
- ◆ T - Tetanus
 - *Clostridium tetani*

DPT - Diphtheria Toxoid

Pertussis Antigen

Tetanus Toxoid

Required Immunizations in Illinois

- 
- ◆ 1. Diphtheria
 - ◆ *Corynebacterium diphtheriae*
 - ◆ 2. Pertussis
 - ◆ *Bordetello pertussis*
 - ◆ 3. Tetanus
 - ◆ *Clostridium tetani*
 - ◆ 4. Measles
 - ◆ Measles virus
 - ◆ 5. Mumps
 - ◆ Mumps virus
 - ◆ 6. Rubella
 - ◆ Rubella virus
 - German Measles
 - ◆ 7. Polio
 - ◆ Polio virus
 - ◆ 8. Hib
 - ◆ *Haemophilus influenzae*
 - ◆ 9. Hepatitis B
 - ◆ Hepatitis B Virus
 - ◆ 10. Chicken Pox
 - ◆ Varicella-zoster virus

Type of Vaccines



- ◆ D
- ◆ P
- ◆ T
- ◆ M
- ◆ M
- ◆ R
- ◆ Polio
 - Salk
 - Sabin
- ◆ Hib
- ◆ HBV
 - Capsid produced by genetically engineered yeast
- ◆ Chicken Pox
- ◆ Toxoid
- ◆ Antigen
- ◆ Toxoid
- ◆ Attenuated
- ◆ Attenuated
- ◆ Attenuated
- ◆ IPV — Inactivated Polio virus (Killed) 1953
- ◆ OPV — Oral Polio vaccine (attenuated) 1964
- ◆ Conjugated vaccine
- ◆ Recombinant vaccine (antigen) yeast
- ◆ Attenuated



*Most genes that code for exotoxins -
plasmids or phages*

- ◆ Lysogenic convergence
- ◆ Diphtheria
- ◆ Cytotoxin inhibits protein synthesis - resulting in cell death
- ◆ Pseudomembrane
 - fibrin, dead tissue, bacterial cells





Lysogenic Convergence

- ◆ Scarlet Fever
- ◆ *Streptococcus pyogenes*
 - lysogenic convergence
- ◆ prophage
 - **cytotoxin** - damages blood capillaries and results in a skin rash
 - Strep Throat with a rash



Diseases caused by Neurotoxins

◆ Botulism

- *Clostridium botulinum*
 - Gram (+), anaerobic, spore-forming rod, found in soil
- works at the neuromuscular junction
- prevents impulse from nerve cell to muscle cell
- results in muscle paralysis

AFRICA'S CHILD SOLDIERS THE REAL BARBARA BUSH

Newsweek

May 13, 2002 : \$3.95

newsweek.msnbc.com

A Once-Feared
Poison Could
Become the Next
Billion-Dollar Drug.
Is It Safe? And Why
Are We So Vain?



THE BUSINESS OF

BOTOX

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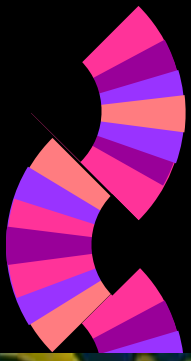
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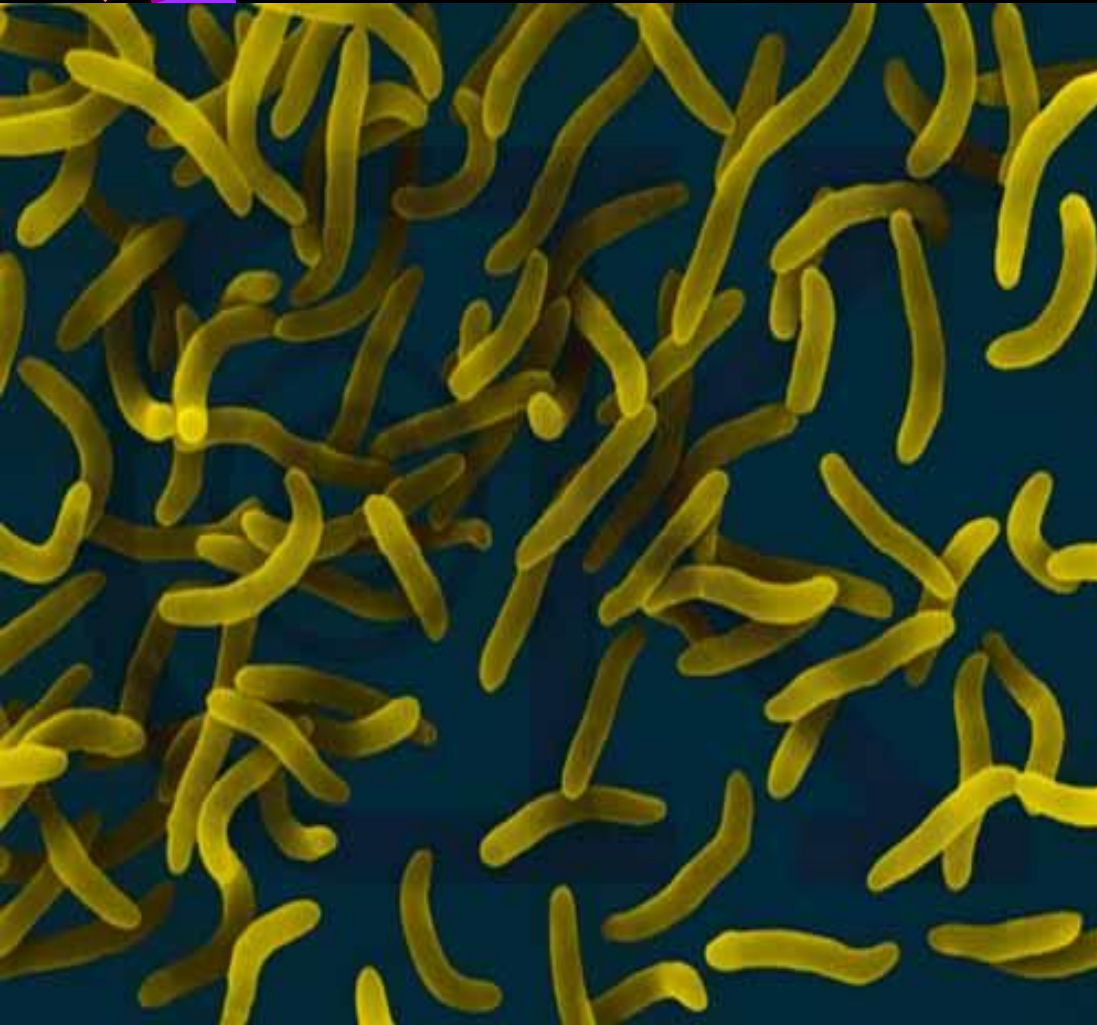
Tetanus (Lock Jaw)

- ◆ *Clostridium tetani*
- ◆ Gram (+), spore-forming, anaerobic rod
- ◆ neurotoxin acts on nerves, resulting in the inhibition of muscle relaxation
- ◆ tetanospasmin - “spasms” or “Lock Jaw”





Diseases caused by Enterotoxins



- ◆ Cholera
 - *Vibrio cholerae*
 - Gram (-) comma shaped rods



Cholera toxin

- ◆ Converts ATP into cAMP
- ◆ causes cells to excrete Cl^- ions and inhibits absorption of Na^+ ions
 - ◆ Electrolyte imbalance
 - ◆ H_2O leaves by osmosis
 - ◆ H_2O Loss (Diarrhea)



*Severe cases, 12 - 20 liters of liquid lost
in a day*

- ◆ Untreated cases - Mortality Rate about 50%
- ◆ Mortality may be reduced to about 1%
 - administering fluids and electrolytes



EHEC (Enterohemorrhagic E. coli)

- ◆ *E. coli* (O157:H7)
- ◆ enterotoxin causes a hemolytic inflammation of the intestines
- ◆ results in bloody diarrhea
 - Toxin
 - alters the 60S ribosomal subunit
 - inhibits Protein Synthesis
 - Results in cell death
 - lining of intestine is “shed”
 - Bloody Diarrhea (Dysentary)



Endotoxins - part of the Gram (-) Bacterial cell wall

- ◆ LPS (Lipopolysaccharides)
 - O Antigen
 - Lipid A
- ◆ Lipid A - Toxin portion of the LPS
 - responsible for Fever that is associated with many Gram (-) Bacterial infections
 - Gram (-) cells are “digested” endotoxins are released - fever
 - Antibiotics