

Preview:

MICROBIAL interaction and pathogenesis

Q1: What's parasitism?

**Q2: What's normal flora and its
function?**

**Q3: What's pathogen? How could
they cause illness?**

Microbial interaction and pathogenesis

Mutualism

Cooperation

Commensalism

Predation

Parasitism

Amensalism

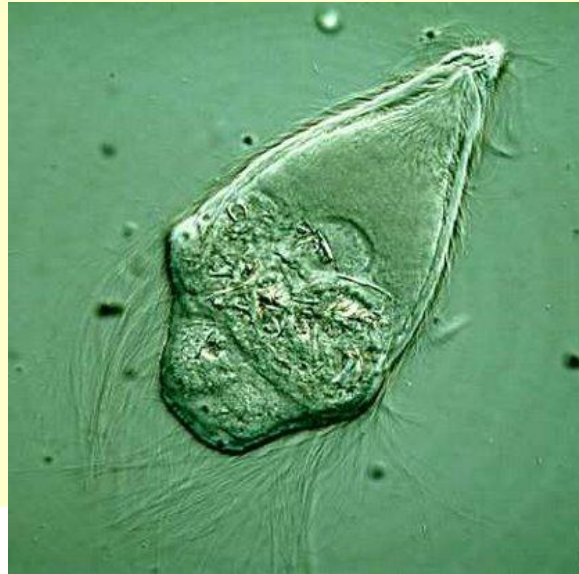
Competition

symbiosis



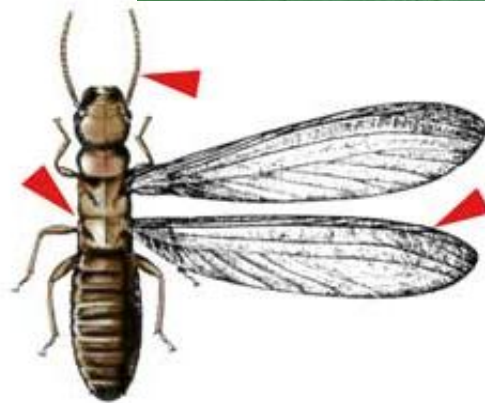
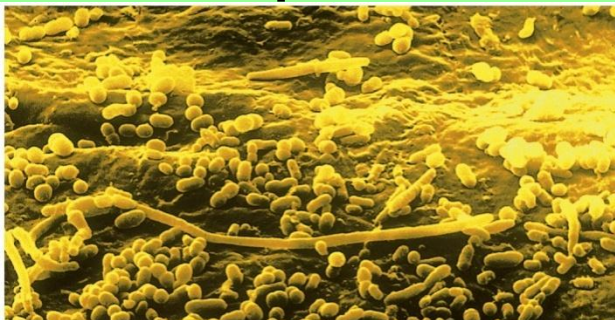
- **Mutualism**
- Cooperation
- Commensalism
- Predation
- Parasitism
- Amensalism
- Competition

biological interaction between organisms of two different species, where both individuals derive a fitness benefit.
Dependent, different species.



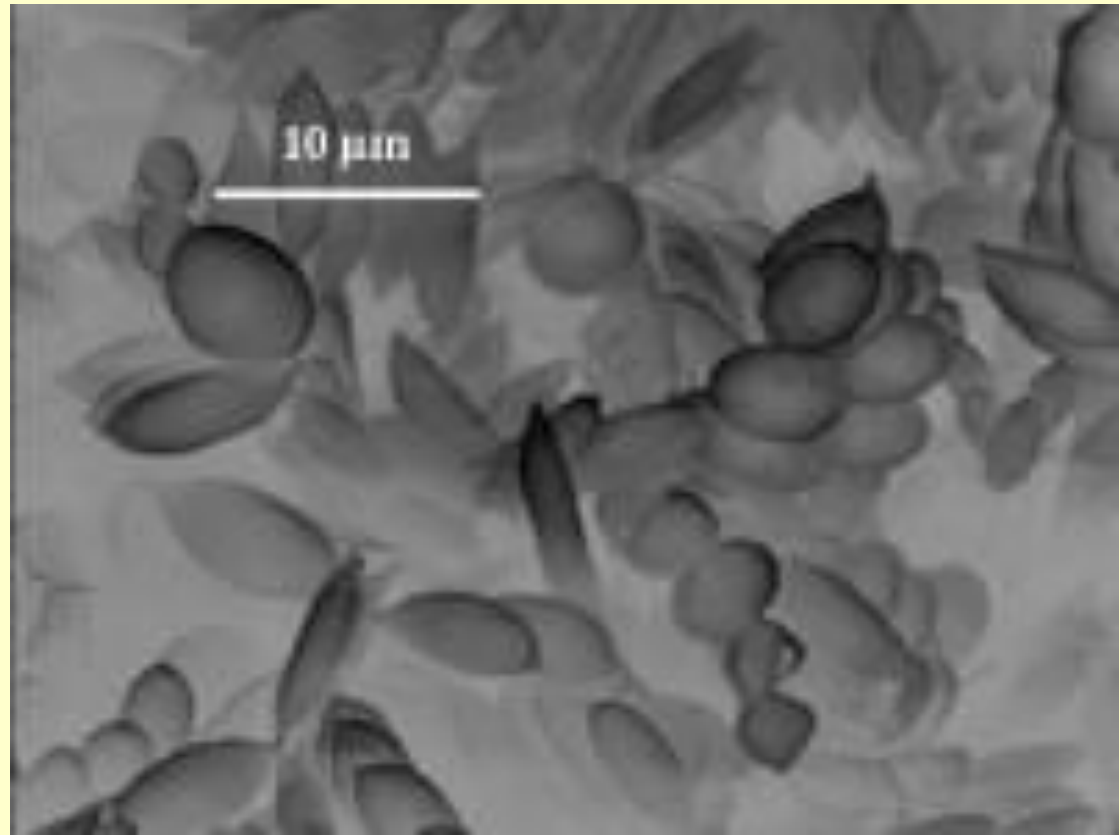
<http://www.youtube.com/watch?v=h0GdTHxQKrs>

Trichonympha



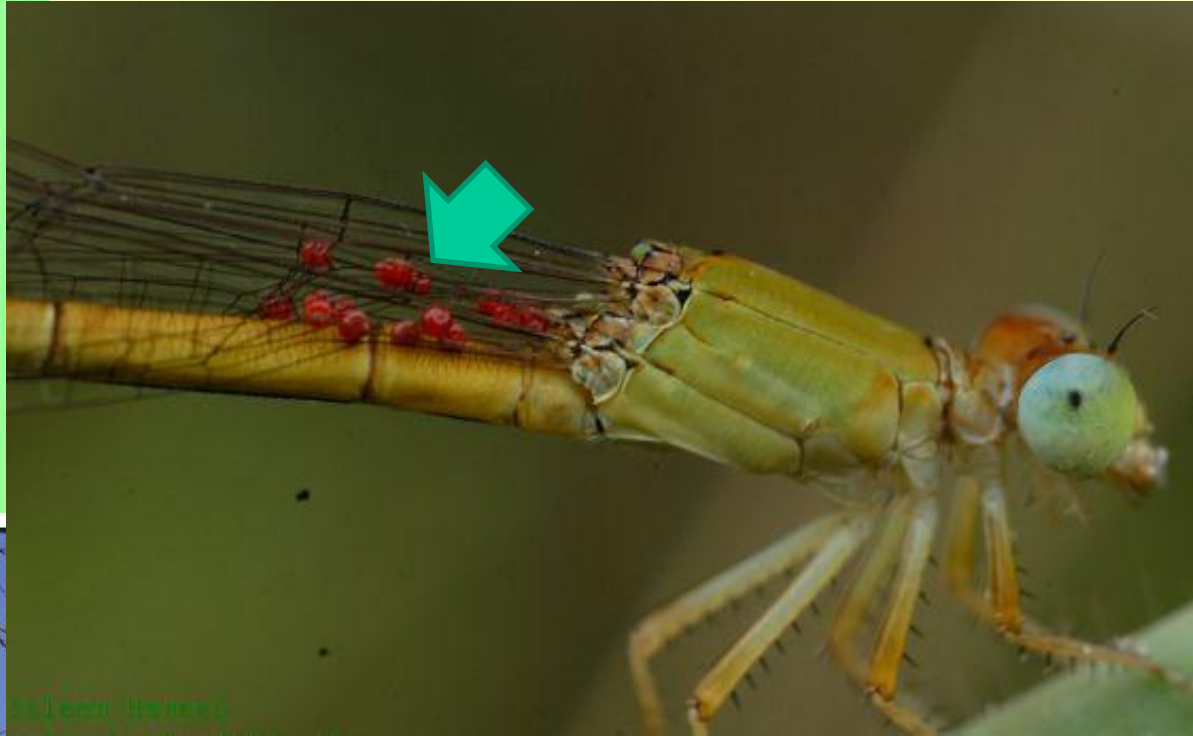
- Mutualism
- **Cooperation**
- Commensalism
- Predation
- Parasitism
- Amensalism
- Competition

biological interaction between individual organisms of two **same or different species**, where both individuals derive a fitness benefit. **Can be independent**



- Mutualism
- Cooperation
- **Commensalism**
- Predation
- Parasitism
- Amensalism
- Competition

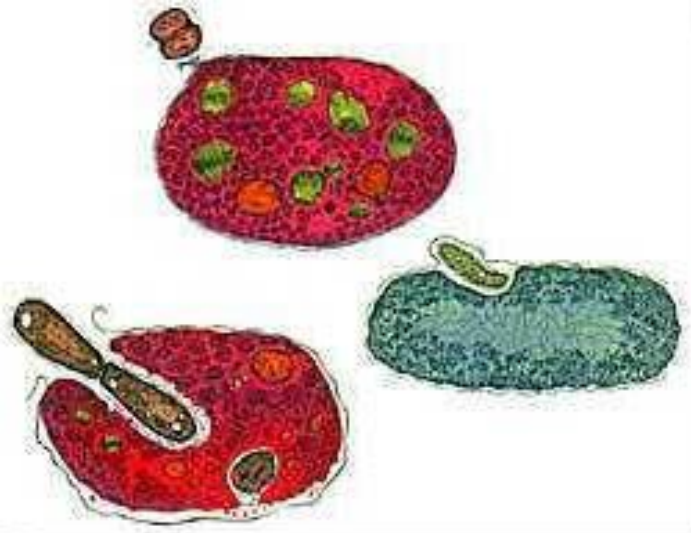
biological interaction that one organism benefits from the host which is not harmed or helped.



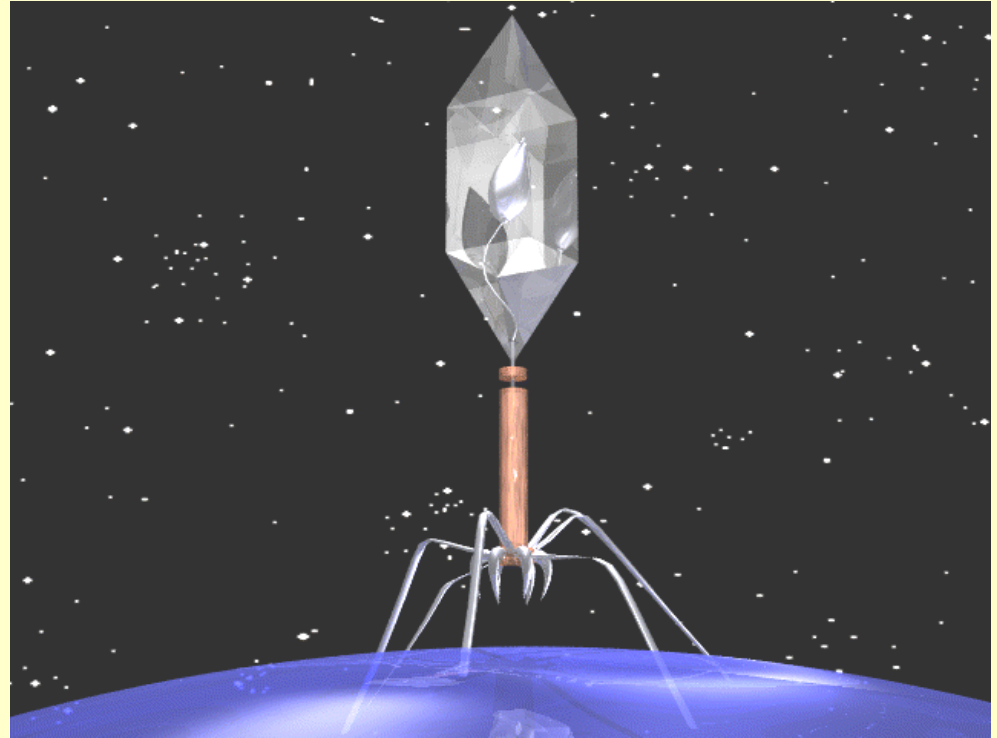
Mites on damselfly



- Mutualism
- Cooperation
- Commensalism
- **Predation**
- Parasitism
- Amensalism
- Competition



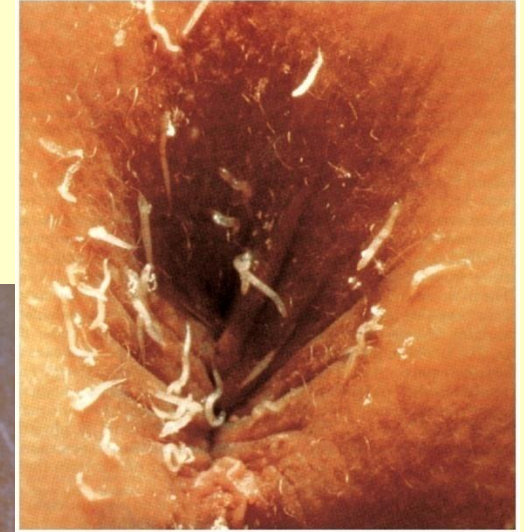
biological interaction that one organism engulfs or attacks another one, which will be harmed or killed. **Predator/prey.**



<http://www.mansfield.ohio-state.edu/~sabadon/virus4.gif>

- Mutualism
- Cooperation
- Commensalism
- Predation
- **Parasitism**
- Amensalism
- Competition

biological interaction that one organism benefits by living inside of another one, which will be harmed in certain degree but coexist for a period. **Parasite/host**

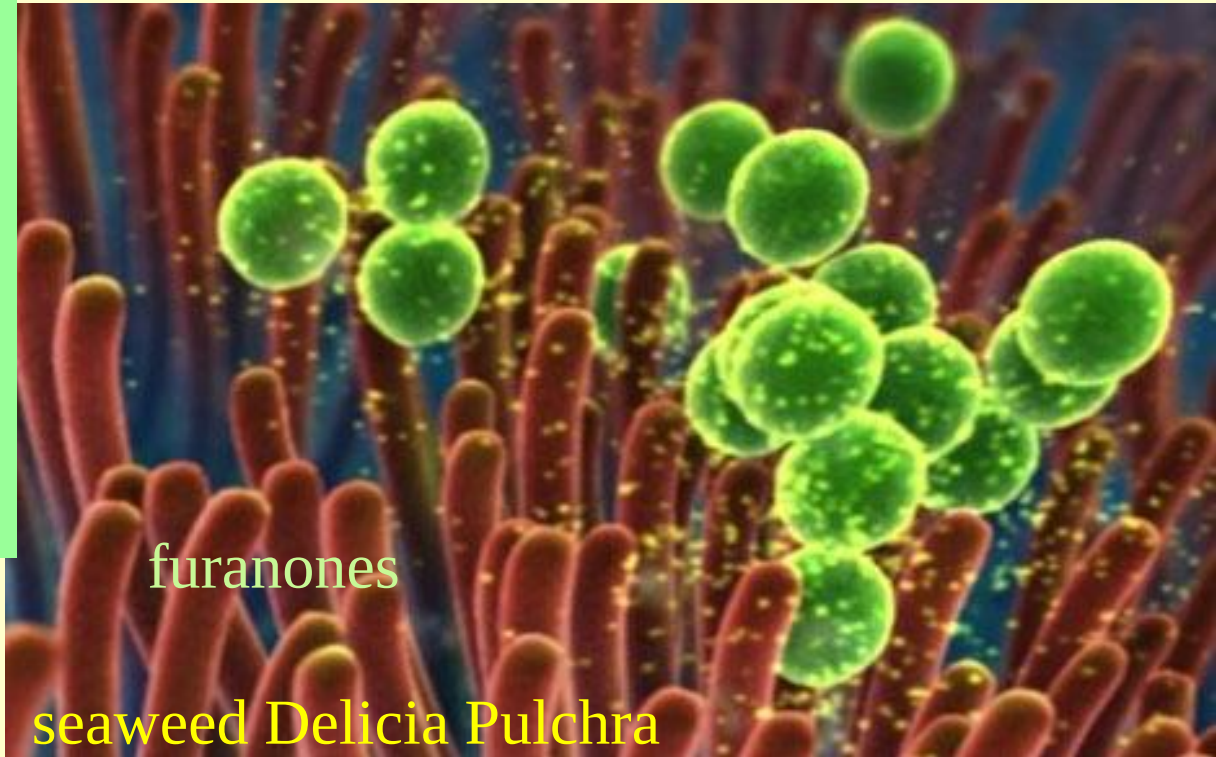


Ringworm fungi (*Dermatophytosis*)

- Mutualism
- Cooperation
- Commensalism
- Predation
- Parasitism
- **Amensalism**
- Competition



biological interaction that one organism produce a special signal to drive away or harm another one.



www.treehugger.com/files/2006/03/biosignal.php

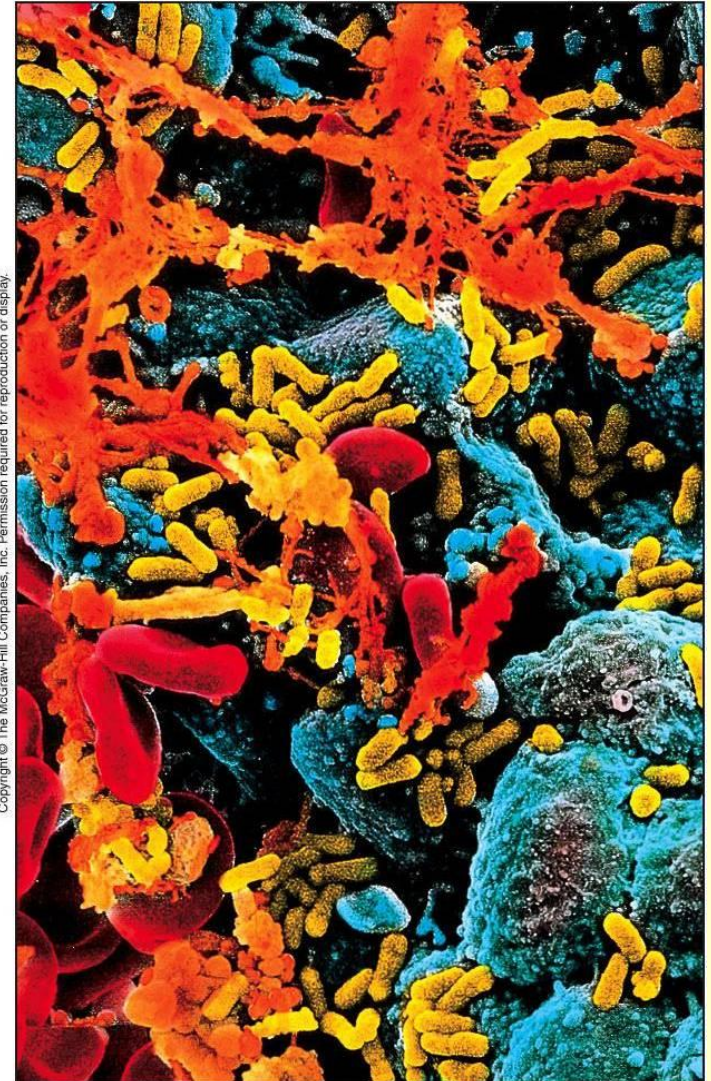
- Mutualism
- Cooperation
- Commensalism
- Predation
- Parasitism
- Amensalism
- **Competition**

biological interaction that different organisms try to acquire the same resources(**nutrients/space**).

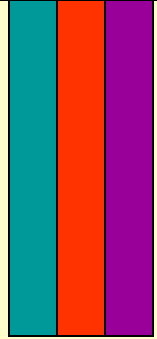


Microbial-human interaction: Ecosystem

- Skin and mucous membranes provide anatomical barriers to infection
 - Also supply foundation for microbial ecosystem
 - Microbial community offers protection from disease-causing organisms
- Intimate interaction between microorganisms and human body is an example of **symbiosis**

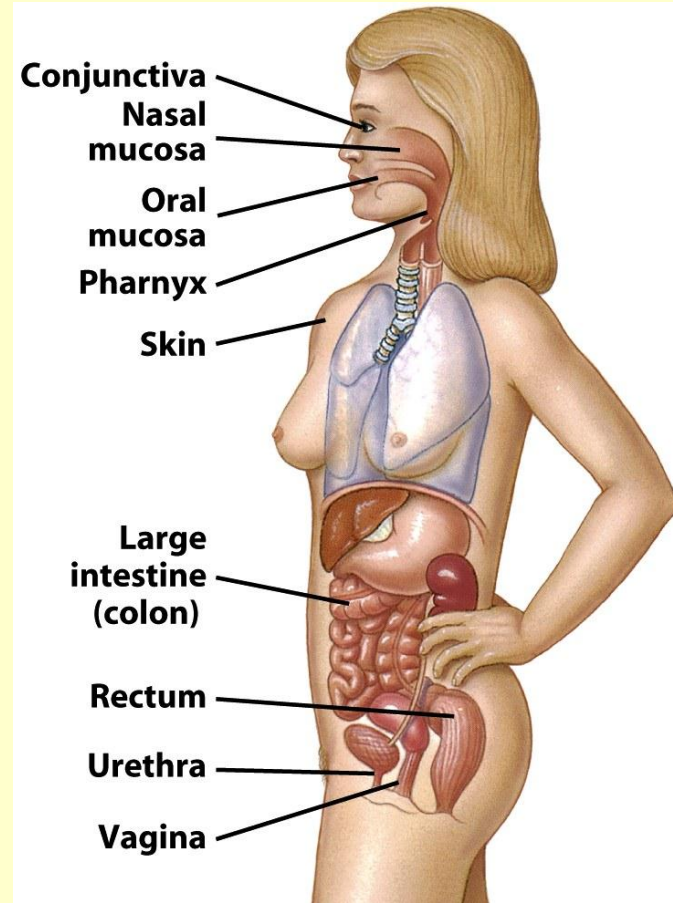


Normal Microflora

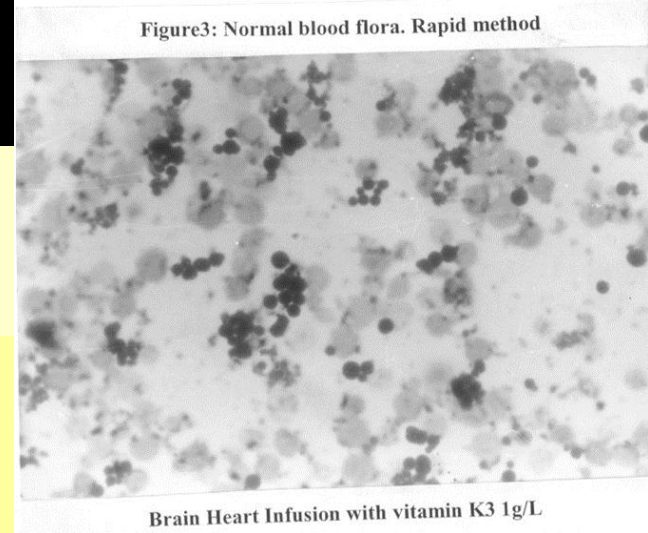
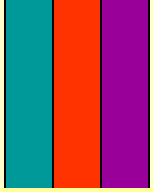


- Populations
- Resident
- Transient

- **Normal flora** defined as populations of microorganisms routinely found growing on the body of healthy individual
- Resident flora typically inhabit body sites for extended periods
- Transient flora are temporary
 - They form associations for a short time and are replaced



Normal Flora



■ Protective role of normal flora

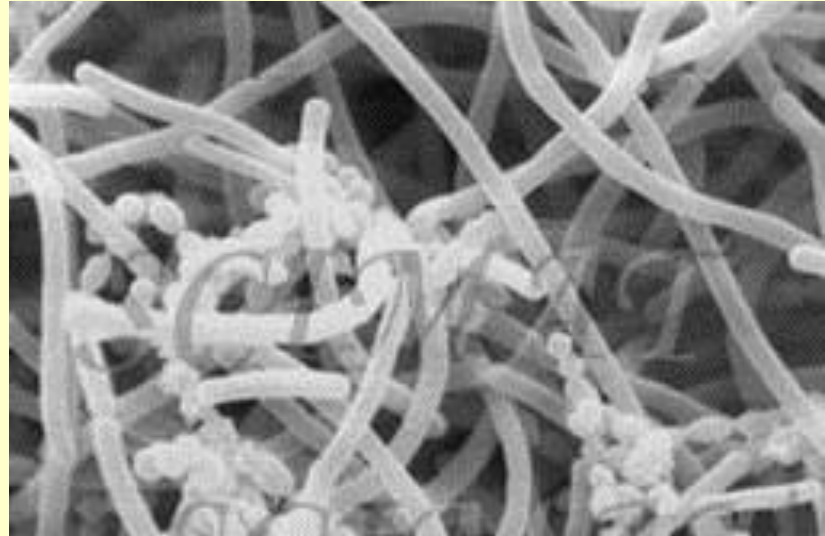
– Contributions include

- **Protection** against potentially harmful organisms
 - **Stimulate** immune system
 - Response mounted against normal flora that breaches body's anatomical barriers
 - May cross-react with pathogen encountered later
- If normal flora are killed or growth suppressed pathogens may colonize and cause disease

Normal Flora

Dynamic nature of normal flora

- Normal flora established during birth process
- Once established, composition of flora is **dynamic**
 - Changes in response to physiological variation within the host
 - Each member of flora ecosystem influenced by presence and condition of other members



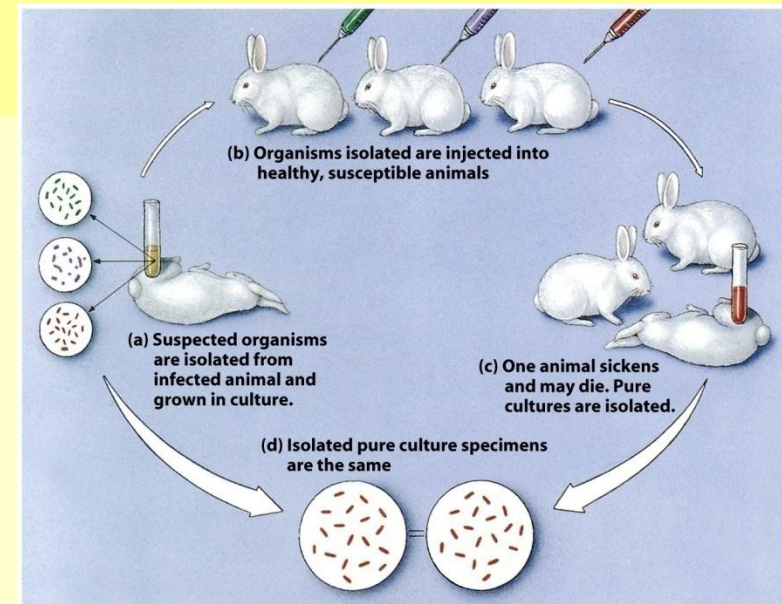
Infection and Disease

- **Pathogenicity:** the ability of a pathogenic agent to produce a disease
 - **Pathogens** are organisms that can cause disease in otherwise healthy people
 - That pathogen termed primary pathogen
 - Microbes that cause disease when the body's defenses are down termed opportunistic pathogen
 - May be part of normal flora or common in environment
 - **Virulence** is quantitative term referring to pathogen's disease-causing ability
 - Highly virulent organisms have high degree of pathogenicity
 - These organisms more likely to cause disease
 - Example: *Streptococcus pyogenes*
 - » Causes disease from strep throat to necrotizing fasciitis

avirulence

Koch's Postulates

- 1. specific causative agent must be observed
 - 2. The agent must be isolated and grown in pure culture.
 - 3. Hosts must get the same disease when inoculated.
 - 4. The agent must be reisolated and show to be the same causative agent.
-
- One infectious disease may leave individual predisposed to developing new disease
 - Initial disease is termed **primary infection**
 - Additional infections resulting from primary infection are termed **secondary infection**

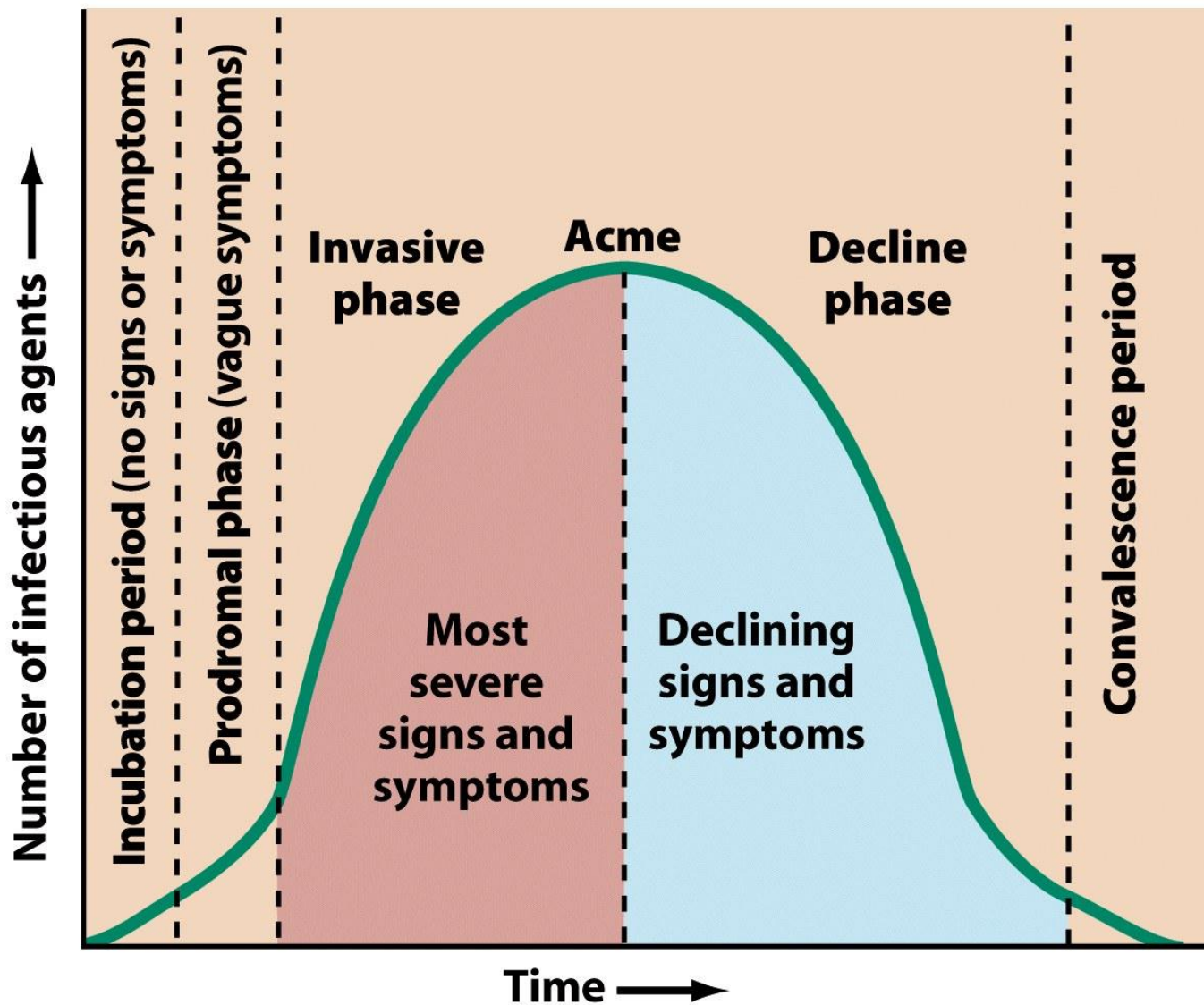


Kinds of Disease

■ Characteristics of infectious disease

- Disease that spreads from host to host termed communicable or **contagious/infectious**
- Ease of spread partly determined by infectious dose
 - **Infectious dose** is number of organisms required to establish infection
 - Diseases with small infectious dose more easily spread than those requiring large numbers

Disease Stages and Microbe Populations



Principles of Infectious Disease

■ Course of infectious disease

– Disease course follows several stages

• Incubation

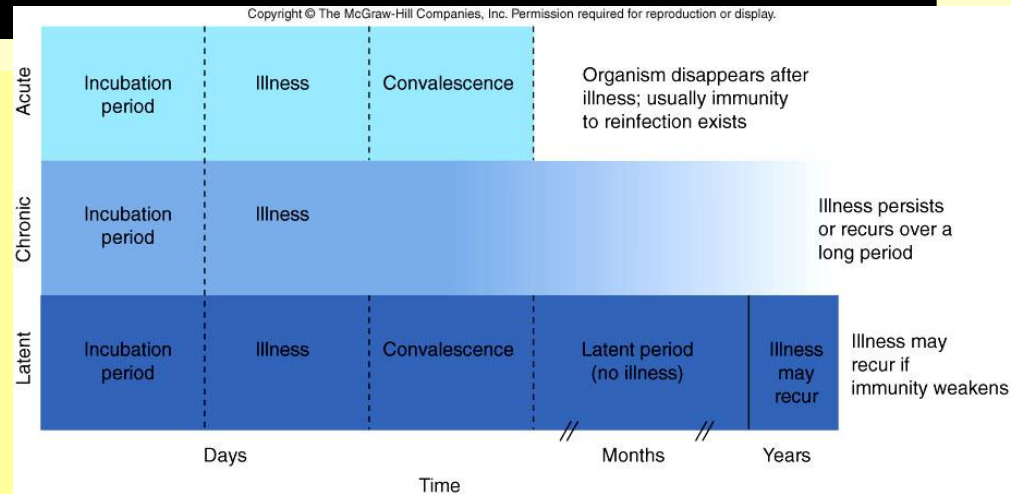
- Time between introduction of organism to onset of symptoms
- Incubation period depends on numerous factors

• Illness

- Follows incubation
- Individual experiences signs and symptoms of disease

• Convalescence

- Period of recuperation and recovery
- Infectious agents may still be spread



■ Duration of symptoms

– Acute

- Symptoms have rapid onset and last only short time

– Chronic

- Symptoms develop slowly and persist

– Latent

- Infection never completely eliminated
- Infection becomes reactive

Principles of Infectious Disease

■ If colonized organisms have parasitic relationship with host, the term infection applies

- Infection does not always lead to noticeable adverse effects
 - Termed subclinical or inapparent
 - Symptoms do not appear or are mild enough to go unnoticed
- Infection that results in disease is termed infectious disease
 - Disease causes characteristic signs and symptoms
 - Symptoms are effects experienced by patient
 - » Pain and nausea
 - Signs are effects that can be observed through examination
 - » Rash, puss formation, and swelling

Principles of Infectious Disease

■ Distribution of pathogen

- Infections often described according to distribution within the body

- **Localized**

- Infection limited to small area
- Example = boil

- **Systemic or generalized**

- Agent has spread or disseminated throughout the body
- Example = measles

- **Toxemia**

- Toxins circulating in blood

- **Viremia**

- Viruses circulating in blood

- **Septicemia**

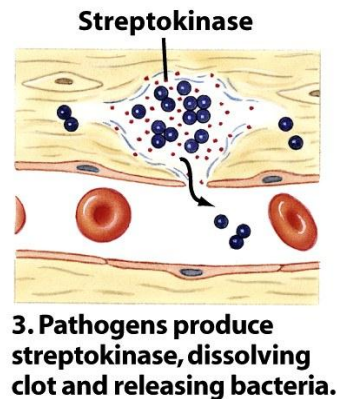
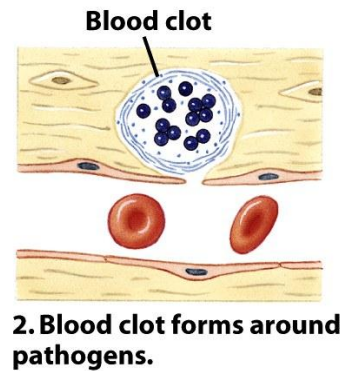
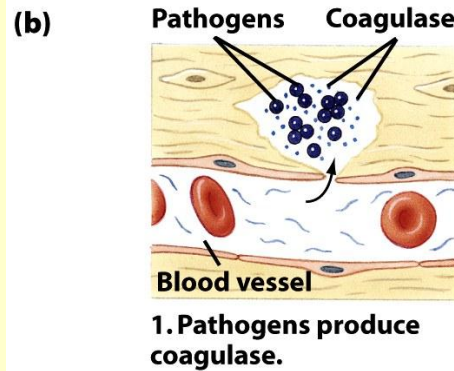
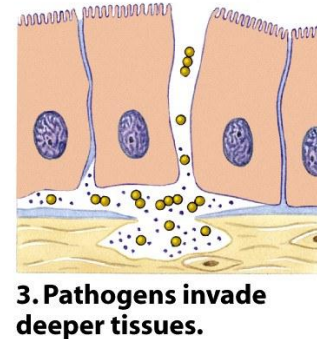
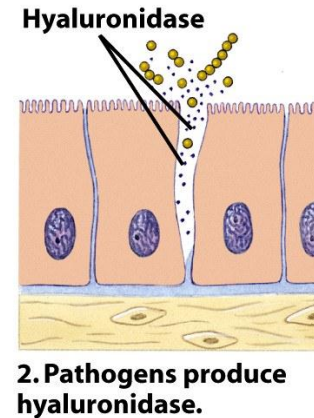
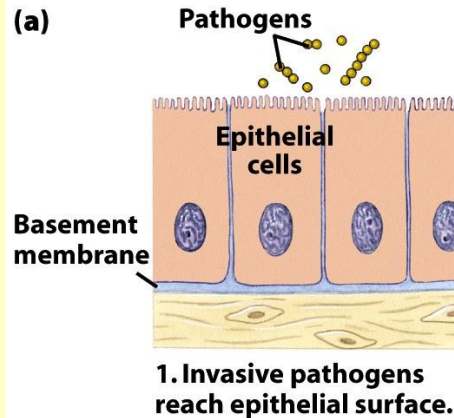
- Acute life-threatening illness caused by infectious agent or its products circulating in blood

How Microbes Cause Disease

- Direct Action

- Bacterial Toxins

- Cytopathic Effects



Establishing Cause of Infectious Disease



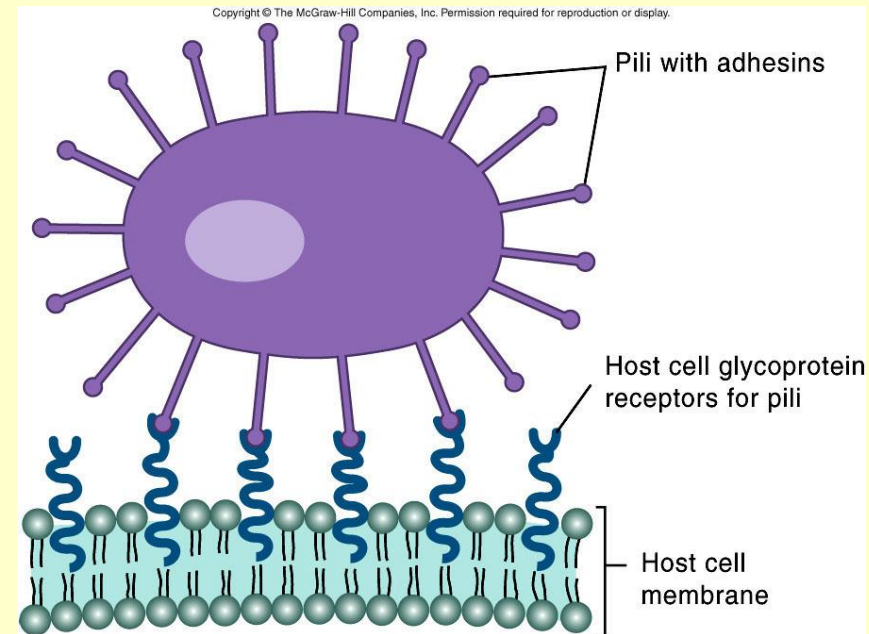
■ Mechanisms of pathogenesis

- Mechanisms of disease follow several patterns
 - Production of toxins that are ingested
 - Foodborne intoxication
 - » *Clostridium botulinum* and *Staphylococcus aureus*
 - Colonization of surface of host followed by toxin production
 - Organism multiplies to high numbers on host surface then produces toxin that interferes with cell function
 - » *E. coli* O157:H7 and *Vibrio cholerae*
 - Invasion of host tissue
 - Microbes penetrate barriers and multiply in tissues
 - Generally have mechanism to avoid destruction by macrophages
 - » *Mycobacterium tuberculosis* and *Yersinia pestis*
 - Invasion of host tissues followed by toxin production
 - Penetration of host barriers with addition of toxin production
 - » *Streptococcus pyogenes*

Establishment of Infection

■ Adherence

- Pathogen must adhere to host cells to establish infection
- Bacteria use adhesins
 - Often located at the top of pili or fimbriae
- Binding of adhesins to host cell receptors is highly specific
 - Often dictates type of cell to which bacteria can attach





Establishment of Infection



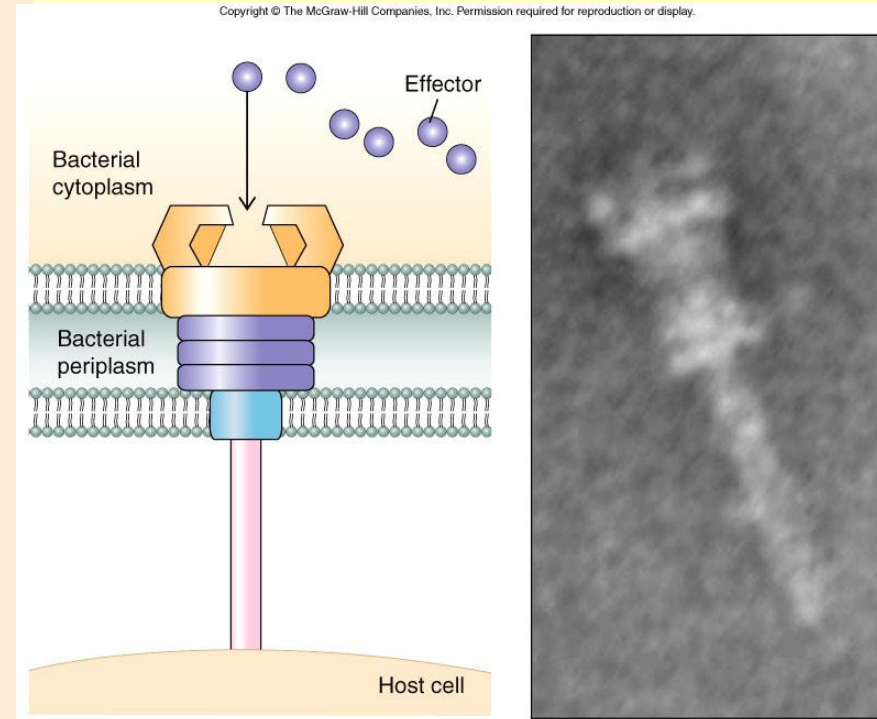
■ Colonization

- Organism must multiply in order to colonize
- New organisms must compete with established organisms for nutrients and space
 - New organism must also overcome toxic products produced by existing organisms as well as host immune responses
- Microbes have developed counterstrategies, including rapid turnover of pili
 - Some organisms produce iron-binding molecules called siderophores
 - Compete with host proteins for circulating iron

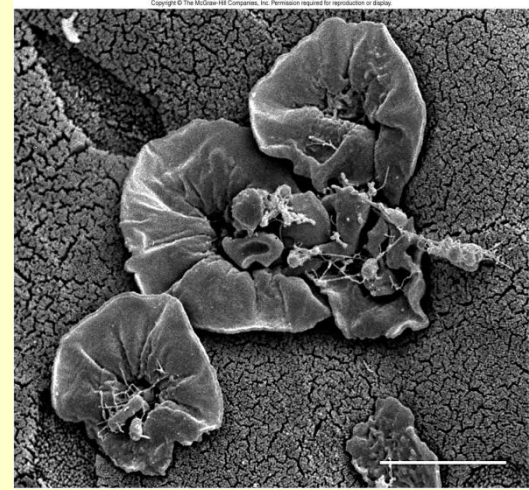
Establishment of Infection

■ Delivery of effector molecules to host cells

- After colonization some bacteria are able to deliver molecules directly to host
 - Induce changes to recipient cell that include
 - Loss of microvilli
 - Directed uptake of bacterial cells
 - » Type III secretion system

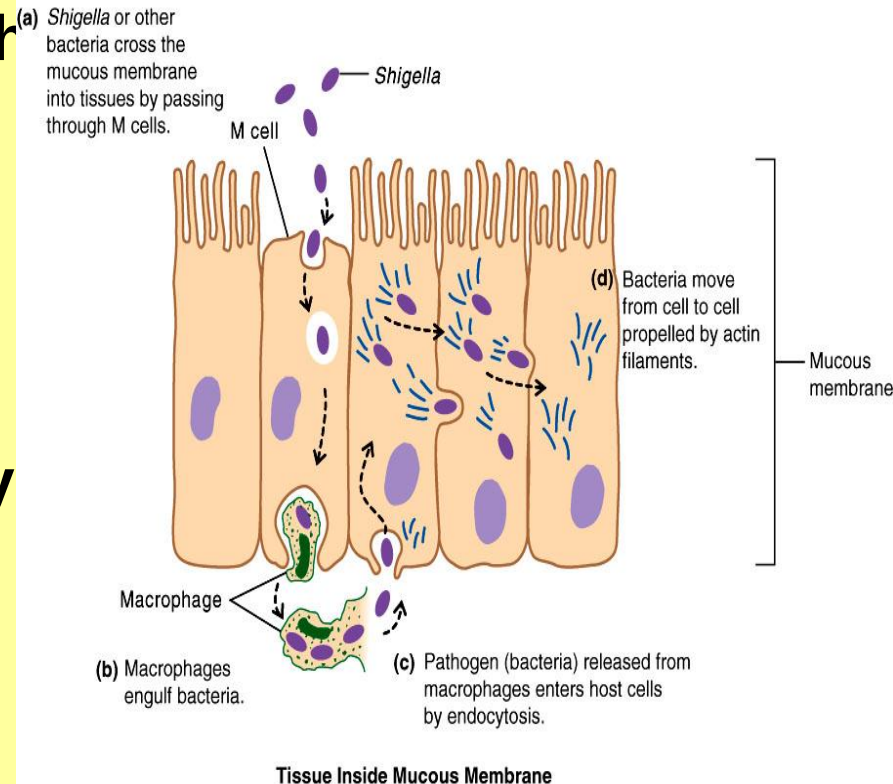


Invasion – Breaching Anatomical Barriers



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Intestinal Space



■ Penetration of skin

- Skin is most difficult barrier to penetrate
- Bacteria that penetrate via the route rely on trauma that destroys skin integrity

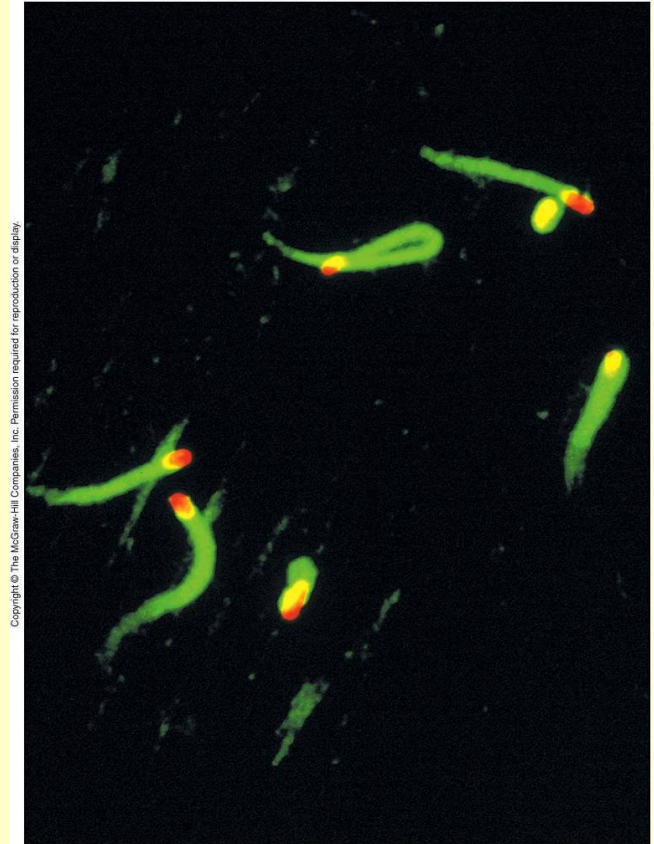
■ Penetration of mucous membranes

- Most common route of entry
- Two general mechanisms
 - **Directed uptake**
 - **Exploitation of antigen sampling**

Avoiding Host Defenses

■ Hiding within the host

- Some organisms evade host defenses by remaining within host
 - Out of reach of phagocytosis
- Once inside certain bacteria orchestrate transfer from cell to cell
 - Actin tails
 - Propels bacteria within cell
 - » Can propel with such force that it drives microbe through membrane into neighboring cell



Avoiding Host Defenses

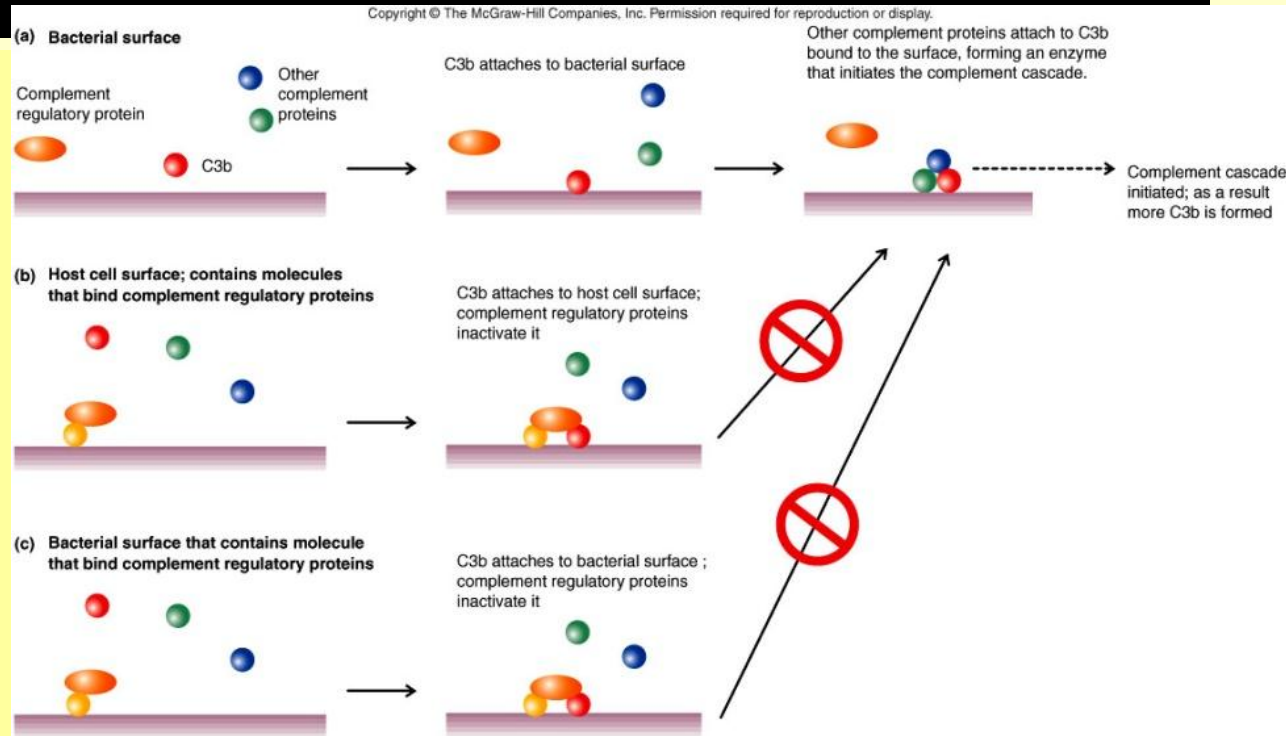
Avoiding being killed by complement proteins

- Gram negative cells susceptible to MAC attack
 - MAC has little effect on gram positive cells

Certain bacteria can circumvent killing by complement (MAC)

Termed **serum resistant**

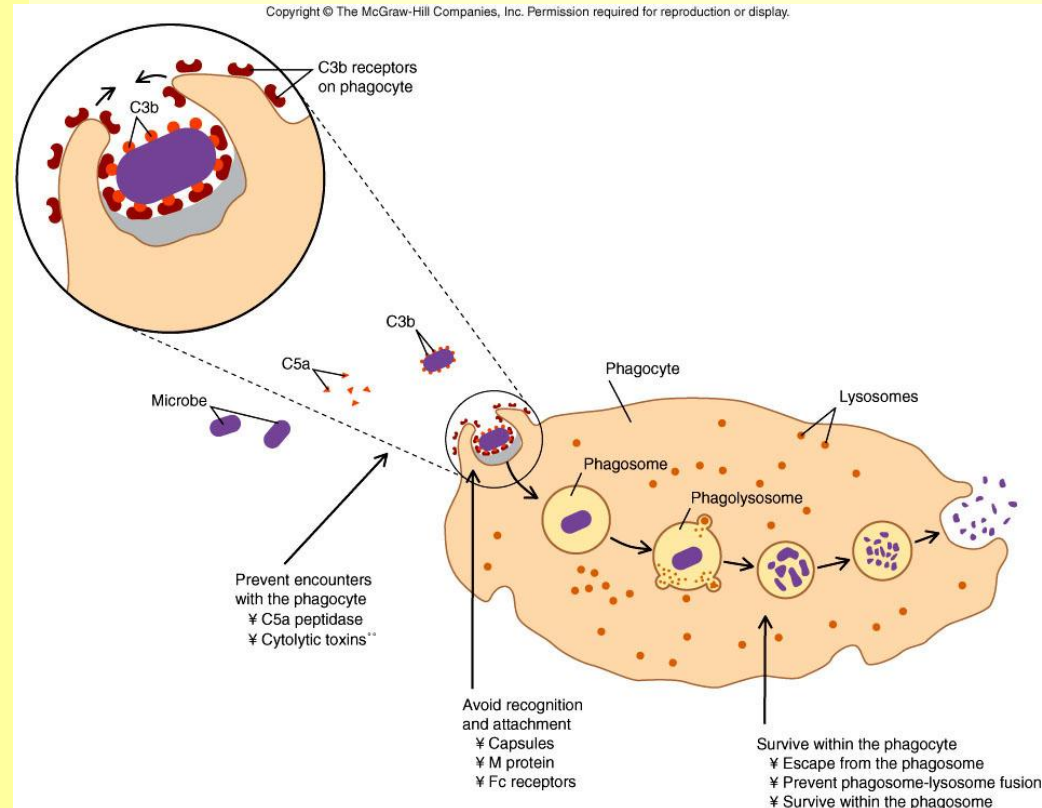
Bacterial cells hijack protective mechanism used by host cells Inhibits formation of MAC



Avoiding Host Defenses

Avoiding destruction by phagocytosis

- Preventing encounters with phagocytes
 - Some pathogens prevent phagocytosis by avoiding phagocytic cells
 - Some cells destroy complement components that attract phagocytes through
 - » C5a peptidase – degrades component C5a
 - » Producing membrane-damaging toxins – kills phagocytes by forming pores in membrane



Avoiding Host Defenses

Avoiding destruction by phagocytosis

– Mechanisms include

- Capsule

- Interfere with alternative pathway of complement activation

- » Bind host regulatory protein to inactivate C3b

- M protein

- Binds complement regulatory protein

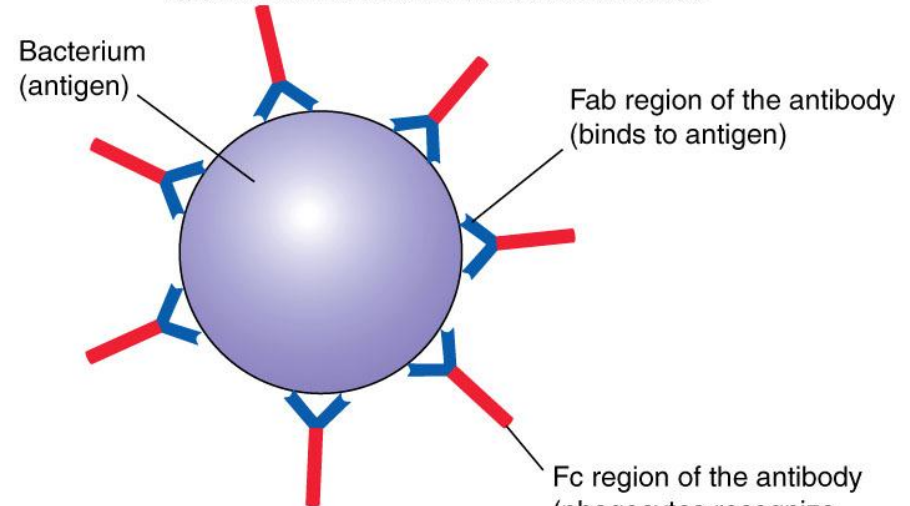
- » Inactivates C3b

- Fc receptors

- Foil opsonization

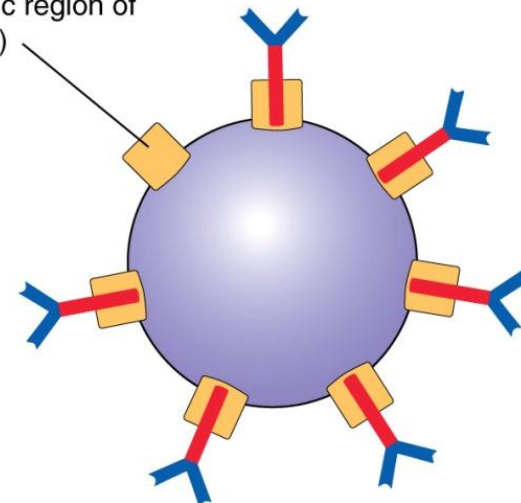
- » Bind Fc region of antibodies interferes with binding to bacteria

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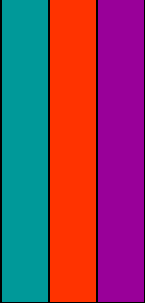
Diagram (b) illustrates a bacterium (antigen) with antibodies bound to its surface. The Fc region of the antibody is bound to the Fc receptor on the bacterium, which interferes with the phagocyte's ability to recognize and bind the Fc region of the antibody.



(b)



Damage to the Host



- In order to cause disease, pathogen must cause damage
 - Damage facilitates dispersal of organisms
 - *Vibrio cholerae* causes diarrhea
 - *Bordetella pertussis* causes coughing
 - Damage can be direct result of pathogen, such as toxin production, or indirect via immune response
 - Exotoxins are secreted by bacterium or leak into surrounding fluids following cell lysis

Damage to the Host



■ Exotoxins

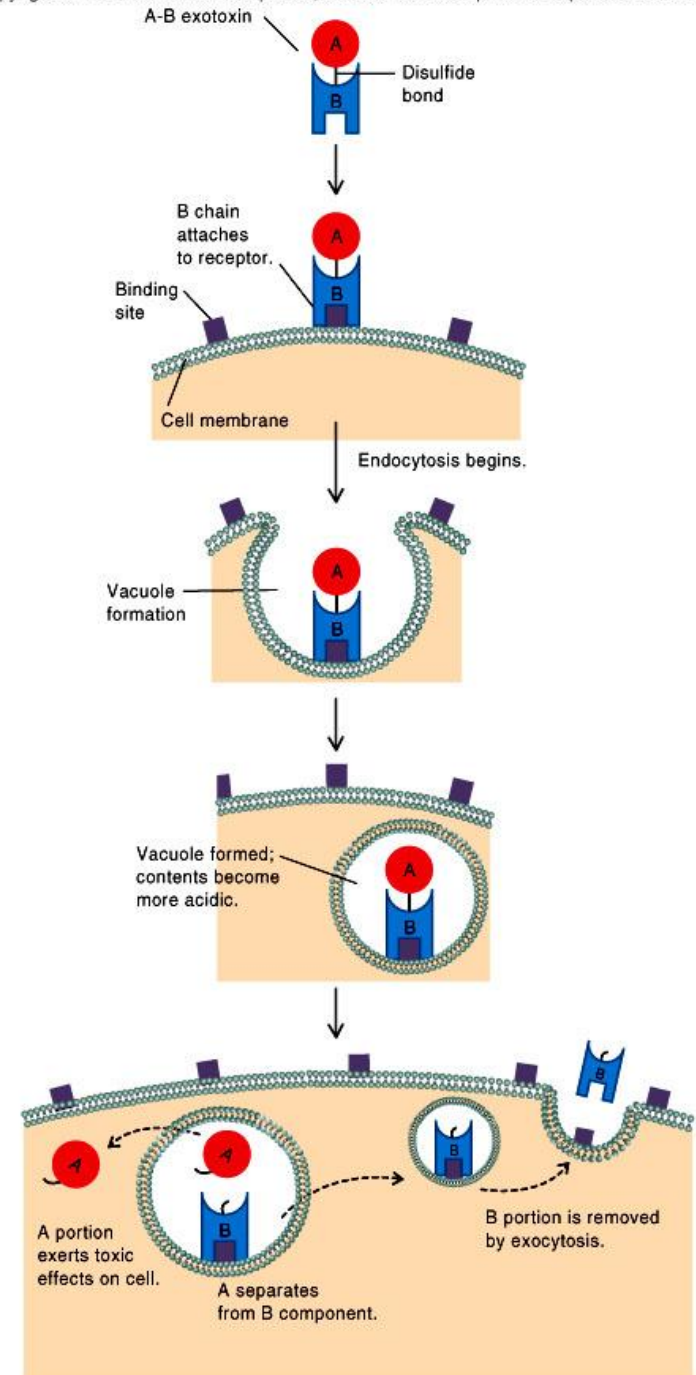
- Can be grouped into functional categories
 - Neurotoxins
 - Cause damage to nervous system
 - Major symptom is paralysis
 - Enterotoxins
 - Damage to intestines and tissues of digestive tract
 - Major symptom is vomiting and diarrhea
 - Cytotoxins
 - Damage to variety of cells
 - Damage caused by interference with cell function or cell lysis

Damage to the Host

A-B toxins

- Toxins consist of two parts
 - A subunit
 - Toxic or active part
 - B subunit
 - Binding part
 - » Binds to specific host cell receptors
- Structure offers novel approaches to development of vaccine and other therapies
 - Use toxin structure as binding a delivery system

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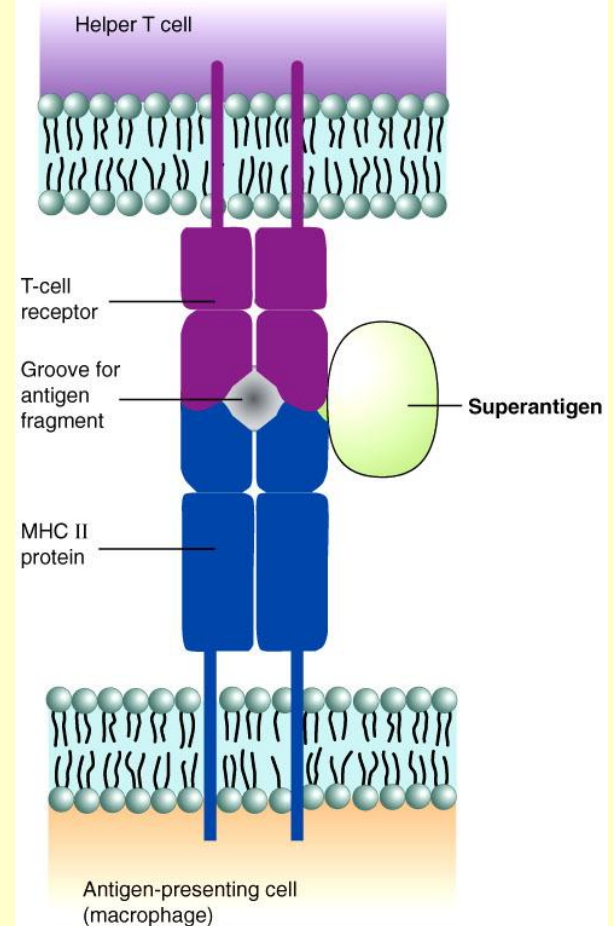


Damage to the Host

■ Superantigens

- **Override specificity of T cell response**
 - Causes toxic effects due to massive release of cytokines by large number of helper T cells
- **Superantigens short-circuit normal control mechanisms of antigen process and presentation**
 - Binds MHC class II and T cell receptor
 - Causes activation of 1 in 5 T cells
- **Superantigens also suspected in contributing to autoimmune disease**

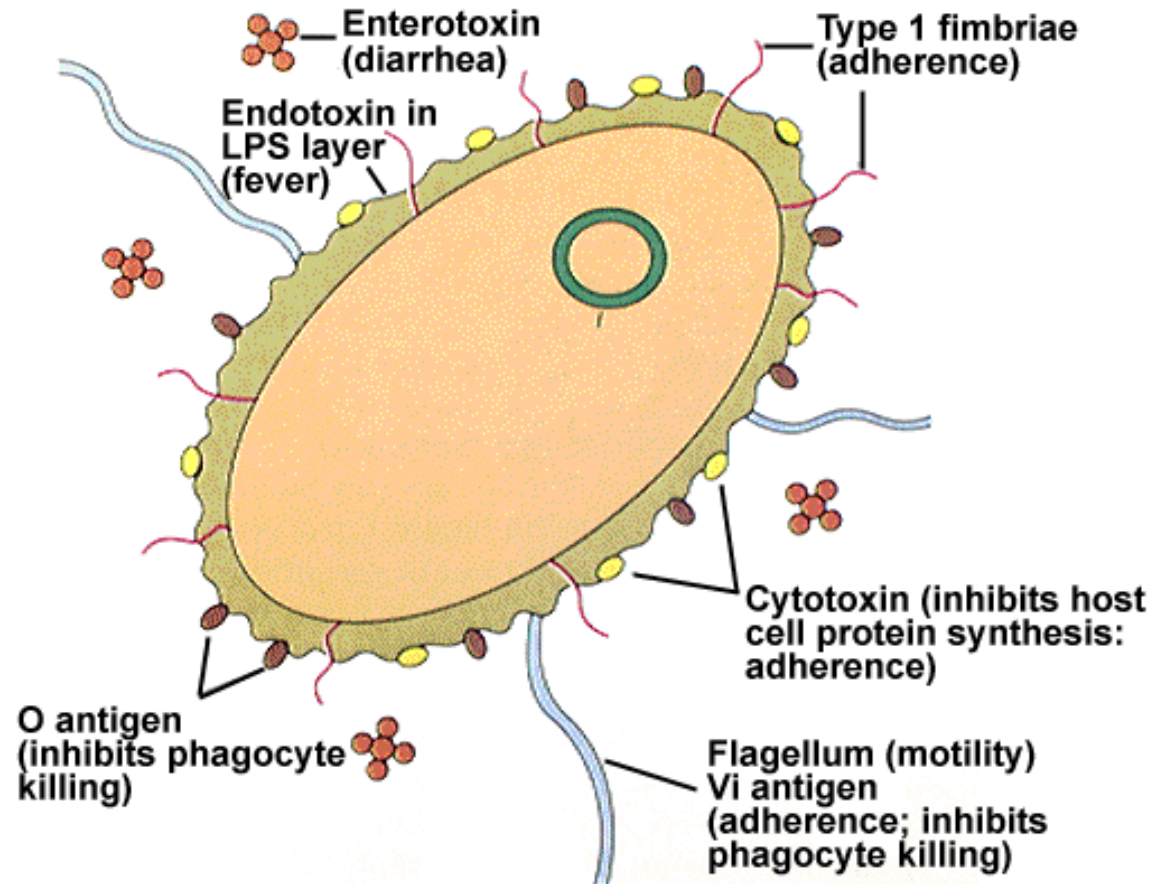
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Damage to the Host

Endotoxins

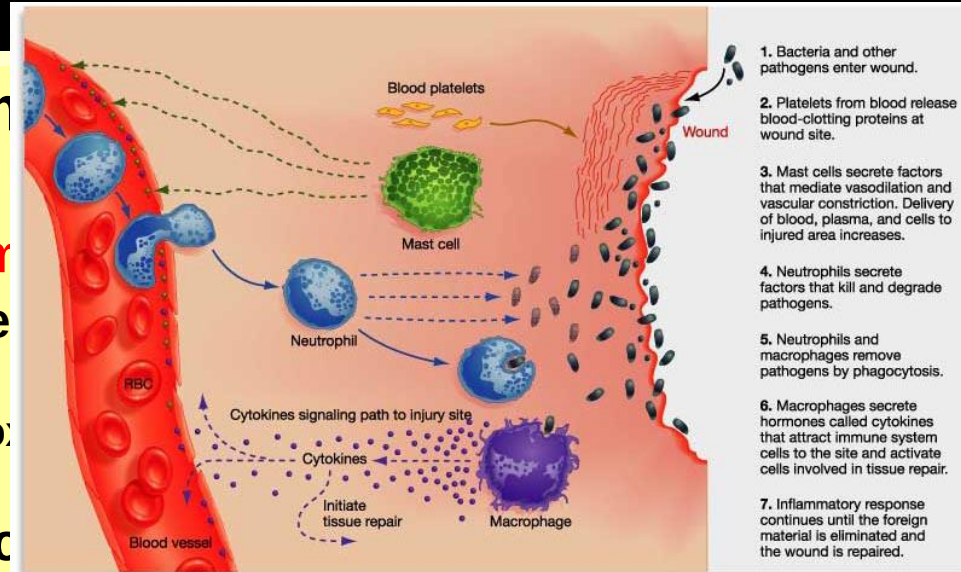
- Endotoxins are cell wall
 - Toxin fundamental to the organism
- Endotoxins are therefore not subunit vaccines
- Lipid A response
- Symptoms associated with immune response
- Toxin responsible for septic shock
 - a.k.a endotoxic shock



Damage to the Host

Damaging effects of the immune response

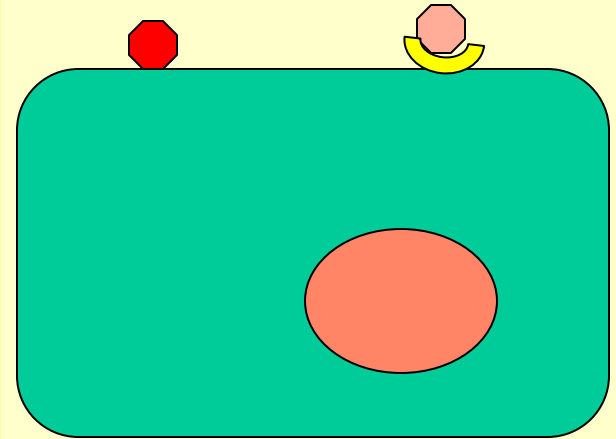
- Damage associated with **inflammation**
 - Inflammatory response can damage host tissue to phagocytic cells
 - Cells release enzymes and toxins to destroy tissue
- Life-threatening aspects of bacterial meningitis are due to inflammation
- Damage associated with **antibodies**
 - Antigen-antibody complexes
 - Complexes form and settle in joints and kidneys
 - » Causes destructive inflammation
- **Cross-reactive antibodies**
 - Some antibodies produced in response to infection bind to body's own tissues
 - Promotes **autoimmune response**



Mechanisms of Viral Pathogenesis

■ Binding to host cells and invasion

- All viruses have surface proteins to interact with specific host cell receptors
- Once attached, viruses are taken up through receptor mediated endocytosis or membrane fusion
 - Membrane fusion occurs in enveloped viruses
- Viruses released from infected cell may infect new cell or disseminate into bloodstream



Mechanisms of Viral Pathogenesis

■ Avoiding immune responses

– Avoiding antiviral effects of interferon

- Interferons alter regulatory responses of cell in event of viral infection

– Helps limit viral replication

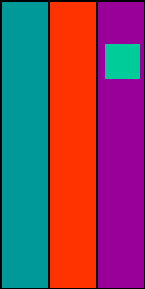
- » Some viruses encode specific proteins to interrupt inhibition of viral replication

– Regulation of host cell death by viruses

- Conversion of host cell mass to viral components
 - Causes loss of cell structure and integrity
- Kill host after production of large numbers of viral copies
 - Allows spread to other cells
- Viruses induce apoptosis
 - Limits inflammatory response and stimulation of immunity
- Block antigen presentation of MHC class I



Mechanisms of Eukaryotic Pathogenesis



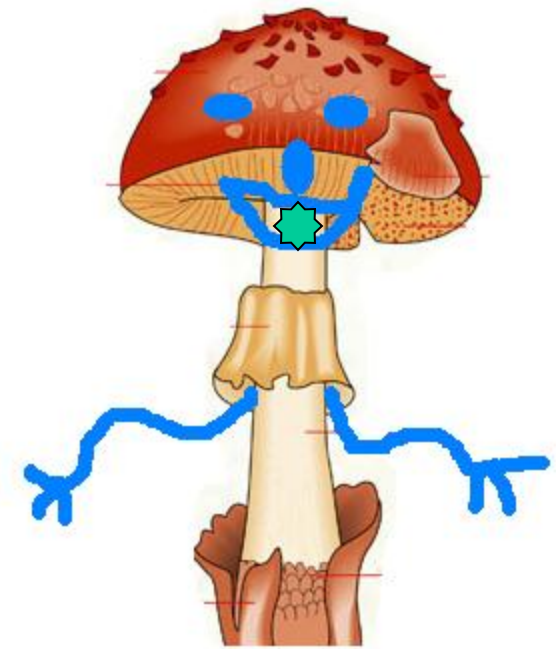
Fungi

- Most fungi are saprophytes
 - Feed off decaying matter
- Those that cause disease are generally opportunistic
 - *Candida albicans*
- Most serious fungal infections caused by dimorphic fungi
 - Occur as molds in environment but assume other forms in tissues
 - Usually yeasts

Mechanisms of Eukaryotic Pathogenesis

Fungi

- Infection begins with inhalation of airborne spores
- Spores lodge in lung tissues
- Undergo morphological change
 - Live inside macrophages
- Infection generally controlled by immunity
 - Unless overwhelming infection occurs or individual is immunocompromised
- Some fungi produce toxins called mycotoxins
 - Can cause disease that damages liver



I think I got fugus infection.

Mechanisms of Eukaryotic Pathogenesis

Eukaryotic parasites

- Most live within intestinal tract or bite of an arthropod
 - *Schistosoma* species can enter
- Parasites attach to host via
- Use a variety of mechanisms
 - Some hide within cells
- Extent of damage varies
 - Some organisms compete for malnutrition
 - Some accumulate enough org of intestines and other organs
 - Some produce enzymes that damage directly

Parasite

*An animal that lives on or in another animal and eats that animal to live. The parasite usually doesn't kill the host animal.



Leech

Parasite

*An animal that lives on or in another animal and eats that animal to live. The parasite usually doesn't kill the host animal.



Flea

Parasite

*An animal that lives on or in another animal and eats that animal to live. The parasite usually doesn't kill the host animal.



Tick

Parasite

*An animal that lives on or in another animal and eats that animal to live. The parasite usually doesn't kill the host animal.



Louse