Microbial Mechanisms of Pathogenicity
& Innate Immunity: Nonspecific Defenses of the Host

Microbial Mechanisms of Pathogenicity

- Pathogenicity:
- Virulence: The extent of pathogenicity.
  - - function of:
    - - infectivity = ability to overcome host resistance
    - - toxicity to host ( )
  - - high infectivity + high toxicity =
  - - exs. plague, smallpox, Ebola

Portals of Entry

- Mucous membranes
  - respiratory tract, GI tract, genitourinary tract, conjunctiva
- Skin
  - most often thru broken skin, sometimes hair follicles, sweat ducts
- Parenteral route
- - injections, bites, surgery, cuts, dry skin splitting

Virulence Factors: Adherence

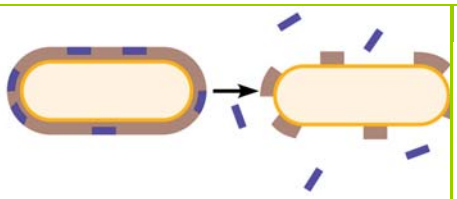
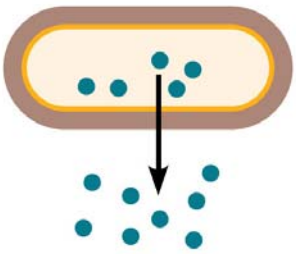
- Adhesins/ligands bind to receptors on host cells
  - favor establishment ( )
  - Glycocalyx: *Streptococcus mutans*
  - Fimbriae:

Virulence Factors: Enzymes

- promote pathogen survival, spreading, host injury
- Coagulase:
- Kinases: Digest fibrin clots
- Hyaluronidase: Hydrolyses hyaluronic acid
- Collagenase:
- IgA proteases: Destroy IgA antibodies
- Siderophores:
- Antigenic variation: Alter surface proteins

Toxins

- Toxin: Substances that contribute to pathogenicity.
- Toxigenicity:
- Toxemia: Presence of toxin in the host's blood.
- Toxoid:
- Antitoxin: Antibodies against a specific toxin.

	Endotoxins	Exotoxins
		
Source:	Gram	Mostly Gram
Relation to microbe:	Present in LPS of outer membrane	By-products of growing cell
Chemistry:		
Fever?		
Neutralized by antitoxin?	No	Yes
LD_{50}:	Relatively large	Small

Exotoxins

- Membrane-disrupting toxins
  - Lyse host's cells by
    - Making protein channels in the plasma membrane (e.g.).
    - Disrupting phospholipid bilayer.
  - Enterotoxins –
    - What is the purpose of diarrhea?

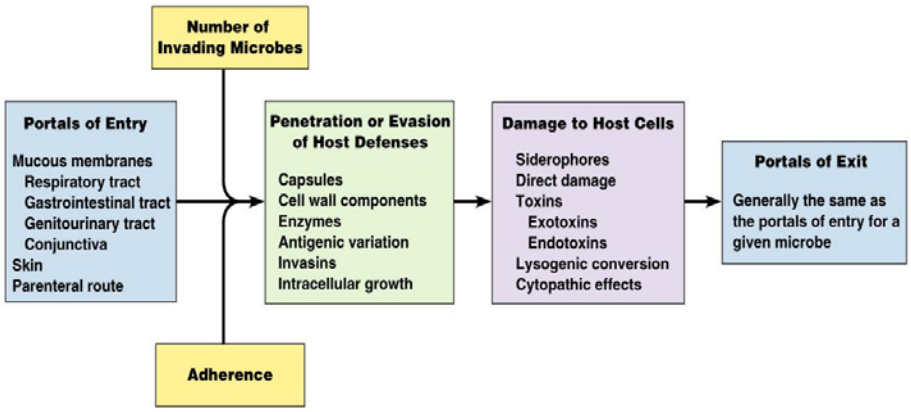
- Superantigens
  - Cause an intense immune response due to release of cytokines from host cells.
  - Fever, nausea, vomiting, diarrhea, shock, and death.
    - *Staphylococcus aureus* and *Streptococcus pyogenes* (best studied)
    - Examples: food poisoning, toxic shock syndrome, scarlet and rheumatic fever, arthritis, multiple sclerosis, diabetes

Portals of Exit

- Respiratory tract
  -
- Gastrointestinal tract
  - Feces and saliva
- Genitourinary tract

- Skin - lesions
- Blood
  - Biting arthropods and needles or syringes

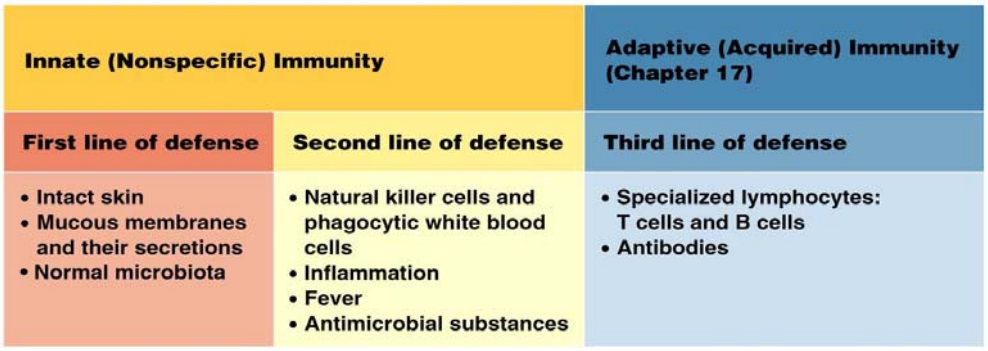
Mechanisms of Pathogenicity



Nonspecific Defenses of the Host

- Susceptibility:
- Immunity: Ability to ward off disease.
- Innate immunity:
- Adaptive ( ) immunity: Immunity, resistance to a specific pathogen.

Host Defenses



Physical Factors ( )

-
- Epidermis consists of tightly packed cells with Keratin, a protective protein

- Mucous membranes
- Ciliary escalator: Microbes trapped in mucus are transported away from the lungs.
- Lacrimal apparatus:
- Saliva: Washes microbes off.
- Urine:
- Vaginal secretions:

Chemical Factors ( )

- Fungistatic fatty acid in sebum.
-
- Lysozyme in perspiration, tears, saliva, and tissue fluids.
- Low pH (1.2-3.0) of gastric juice.
- Transferrins in blood find iron.
- NO ( ) inhibits ATP production.

Normal Microbiota ( )

- Microbial antagonism/competitive exclusion: Normal microbiota compete with pathogens.

White Blood Cells ( )

- Neutrophils:
- Basophils:
- Eosinophils: Toxic to parasites and some phagocytic
- Dendritic cells: Initiate adaptive immune response
- Monocytes: Phagocytic as mature macrophages
  - Fixed macrophages in lungs, liver, and bronchi
  - Wandering macrophages roam tissues.
- Lymphocytes:

Phagocytosis

- *Phago:* from Greek, meaning _____
- *Cyte*: from Greek, meaning _____
- Ingestion of microbes or particles by a cell, performed by phagocytes.

Inflammation ( )

- Redness ( )
- Pain
- Heat
- Swelling ( )
- Acute-phase proteins activated (complement, cytokine, and kinins)
- Vasodilation (histamine, kinins, prostaglandins, and leukotrienes)
- Margination and emigration of WBCs
-

Chemicals Released by Damaged Cells

Histamine	Vasodilation, increased permeability of blood vessels
Kinins	Vasodilation, increased permeability of blood vessels
Prostaglandins	Intensify histamine and kinin effect
Leukotrienes	Increased permeability of blood vessels, phagocytic attachment

Fever: Abnormally High Body Temperature (Second line defense)

- Hypothalamus normally set at _____
- Gram-negative endotoxin cause phagocytes to release interleukin–1 (IL–1).
- Hypothalamus releases prostaglandins that reset the hypothalamus to a high temperature.
- Body increases rate of metabolism and shivering which raise temperature.
- When IL–1 is eliminated, body temperature falls (

- Advantages
  - Increase transferrins
  - Increase IL–1 activity
  - Overall enhancement of immune function
  -
- Disadvantages
  - Tachycardia ( )
  - Acidosis
  -

The Complement System ( )

- Serum proteins activated in a cascade.
- Function:
- Three pathways to activate complement:
  - Classical
  - Alternative
  - Lectin

Interferons (IFNs) ( )

- Alpha IFN and Beta IFN: Cause cells to produce antiviral proteins that inhibit viral replication.
- Gamma IFN: Causes neutrophils and macrophages to phagocytize bacteria.

Innate Immunity ( )

- Transferrins
  -
- Antimicrobial peptides
  -

Study Objectives

1. Define: pathogenicity, virulence, infectivity, and toxicity.

2. Describe the three main portals of entry and give examples. Relate portals of entry with portals of exit.

3. Describe virulence factors and how they enhance infection. Give examples.

4. Define: toxin, toxigenicity, toxemia, toxoid, and antitoxin.

5. Compare and contrast exotoxins with endotoxins.

6. What is an enterotoxin?

7. What are superantigens?

8. Define: susceptibility, immunity, innate immunity, and adaptive (acquired) immunity.

9. Describe the first line physical defenses and how they protect us from pathogens.

10. Describe the first line chemical defenses and how they protect us from pathogens.

11. Explain how our normal microbiota protects us from pathogens.

12. Explain the process of phagocytosis and describe the WBC's involved in the process.

13. Describe the second line defense of inflammation and how it protects us from pathogens. How can inflammation harm us?

14. Describe the second line defense of fever and how it protects us from pathogens. How can fever harm us?

15. In general terms, describe how complement protects us from pathogens. Compare and contrast the classical pathway with the alternative pathway of complement activation.

16. How do interferons protect us against pathogens?

17. How do transferrins protect us against pathogens?