SENGAMALA THAYAAR EDUCATIONAL TRUST WOMEN'S COLLEGE
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Sundarakkottai, Mannargudi-614 016. Thiruvarur (Dt.),
Tamil Nadu, India.

MEDICAL MICROBIOLOGY
SEMESTER – IV
NORMAL FLORA
SUBJECT CODE: P16MB41

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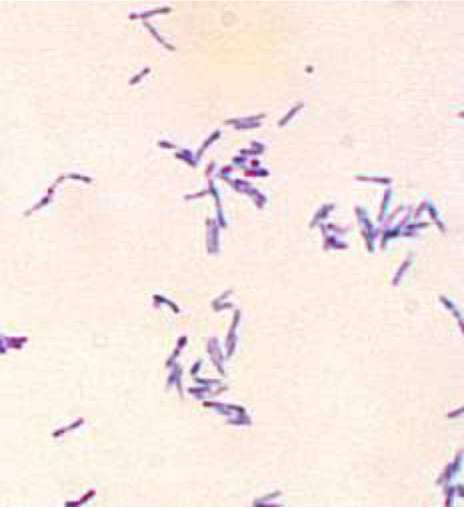


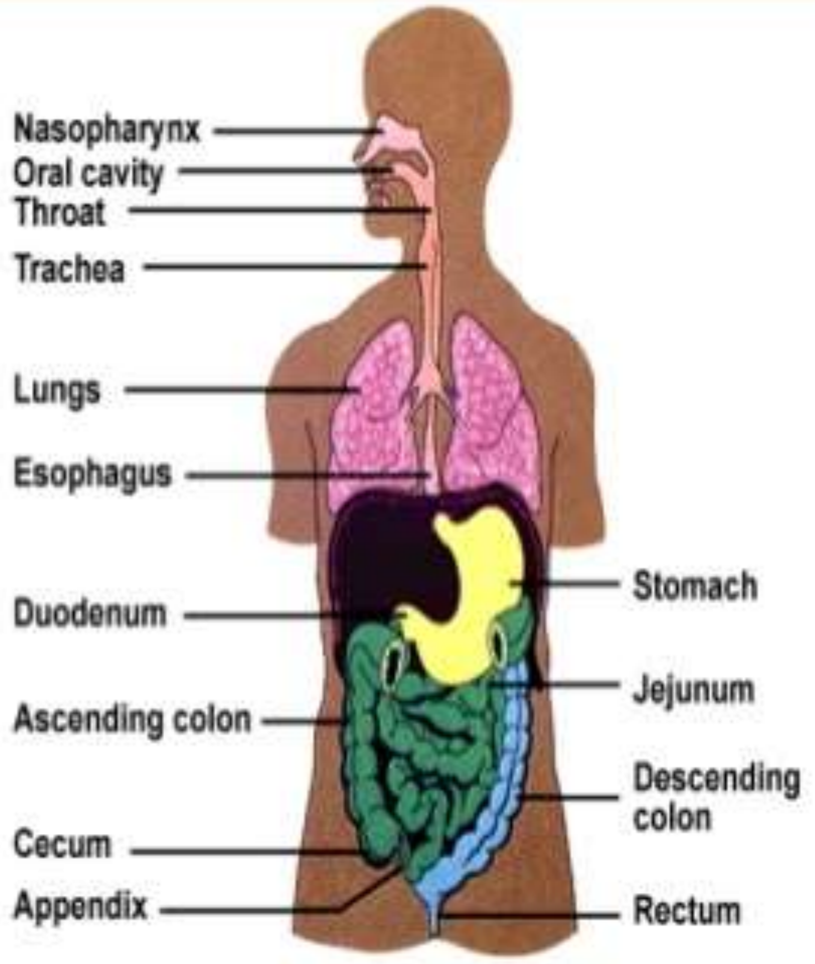
Normal Flora

- More bacterial than human cells in the body
  - provide some nutrients (vitamin K)
  - stimulate immune system, immunity can be cross-reactive against certain pathogens
  - Prevent colonization by potential pathogens (antibiotic-associated colitis, *Clostridium difficile*)

NORMAL FLORA

LOCATION SITE OF NORMAL FLORA ON HEALTHY PERSON

- Skin
- Eyes (i.e.Cunjunctiva)
- Nose (i.e. Respiratory tract)
- Mouth (i.e Human Oral Cavity)
- Ears
- Urogenetal tract
- Gastrointestinal tract



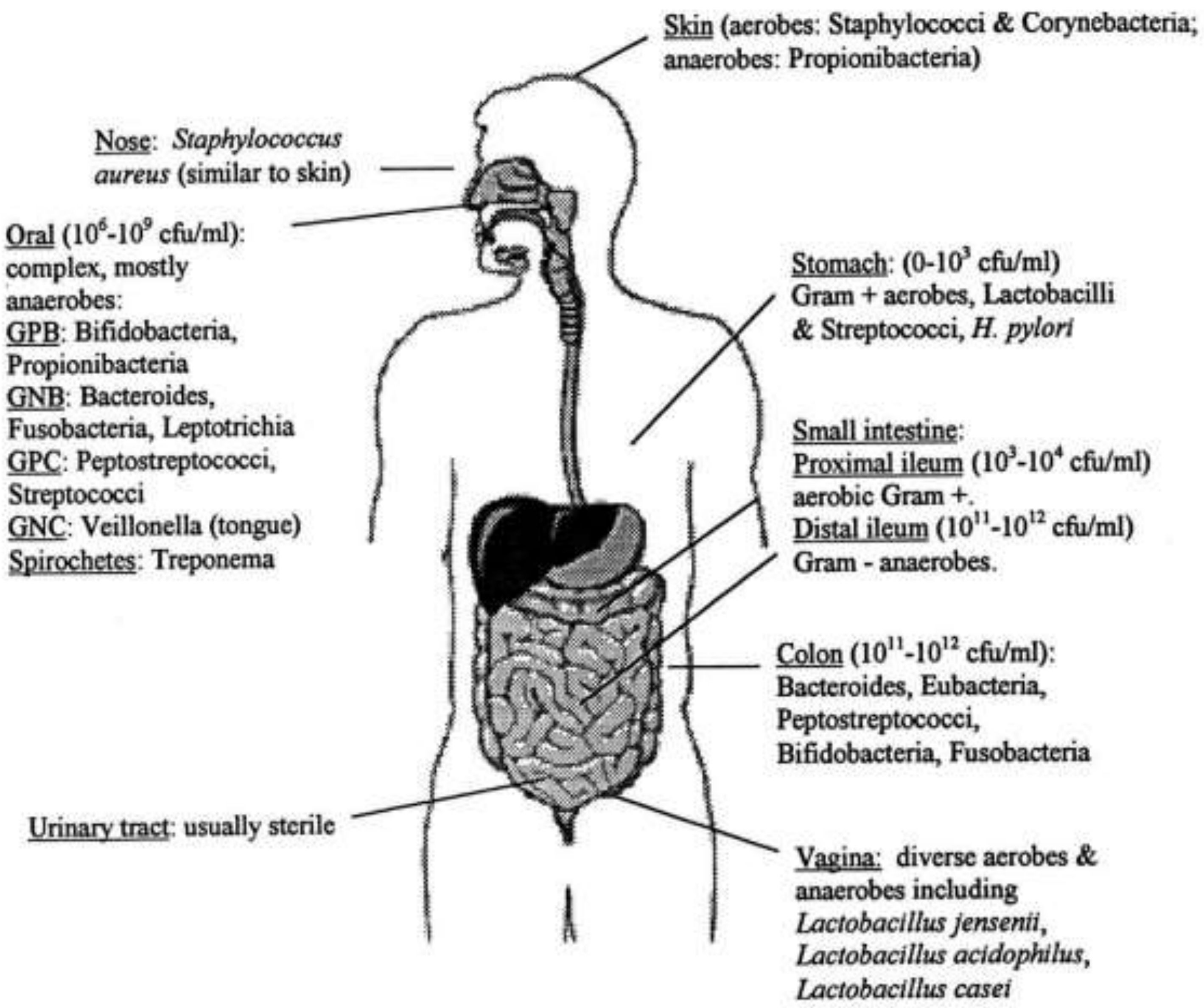


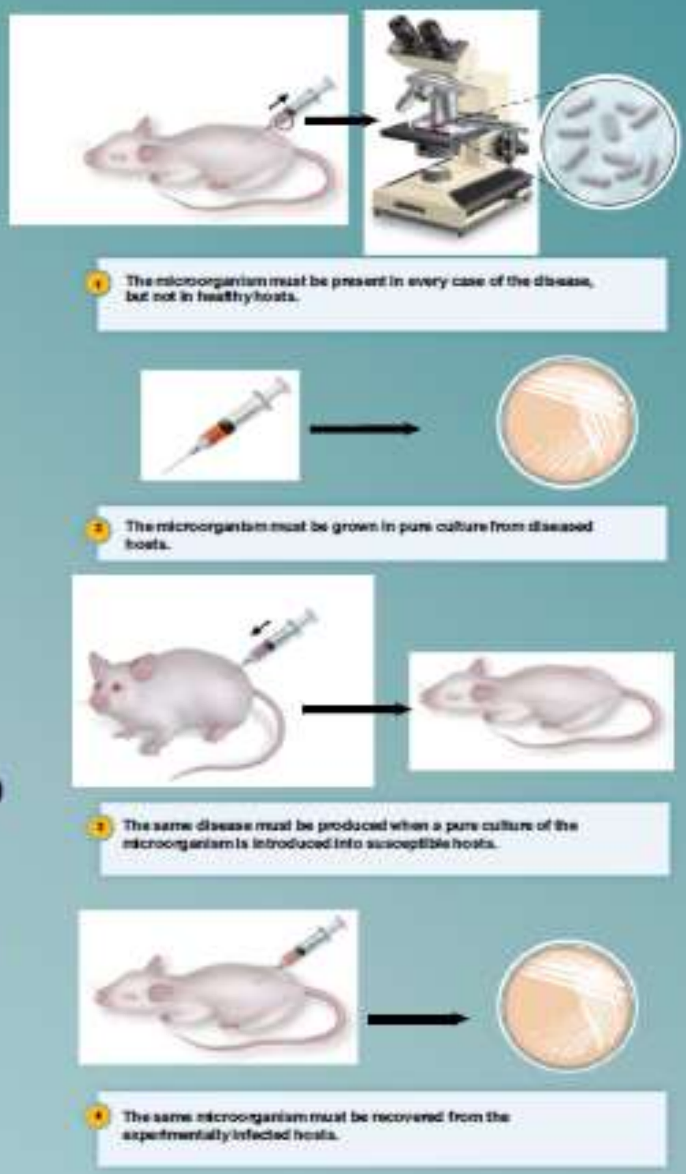
Fig. 1. Predominant flora in different niches of the human body. Compiled from references: (3), (9–13).

SIGNIFICANCE OF NORMAL FLORA

- 1.The normal flora influences the anatomy, physiology, susceptibility to pathogens, and morbidity of the host.
- 2. The effect of the normal flora on the host was not well
- understood until germ-free animals became available.
- Cesarean Section => Germ-free animals => Isolators w/o detectable pathogens (viruses, bacteria & others)
- 3. Two interesting observations:
- a. the germ-free animals lived almost twice as long as their conventionally maintained counterparts.
- b. the major causes of death were different in the
- two groups.

16.4. Establishing the Cause of Infectious Disease

- Koch's Postulates
  - Criteria Robert Koch used to establish that *Bacillus anthracis* causes anthrax
    - Microorganism must be present in every case of disease
    - Organism must be grown in pure culture from diseased host
    - Same disease must be produced when pure culture is introduced into susceptible hosts
    - Organisms must be recovered from experimentally infected hosts

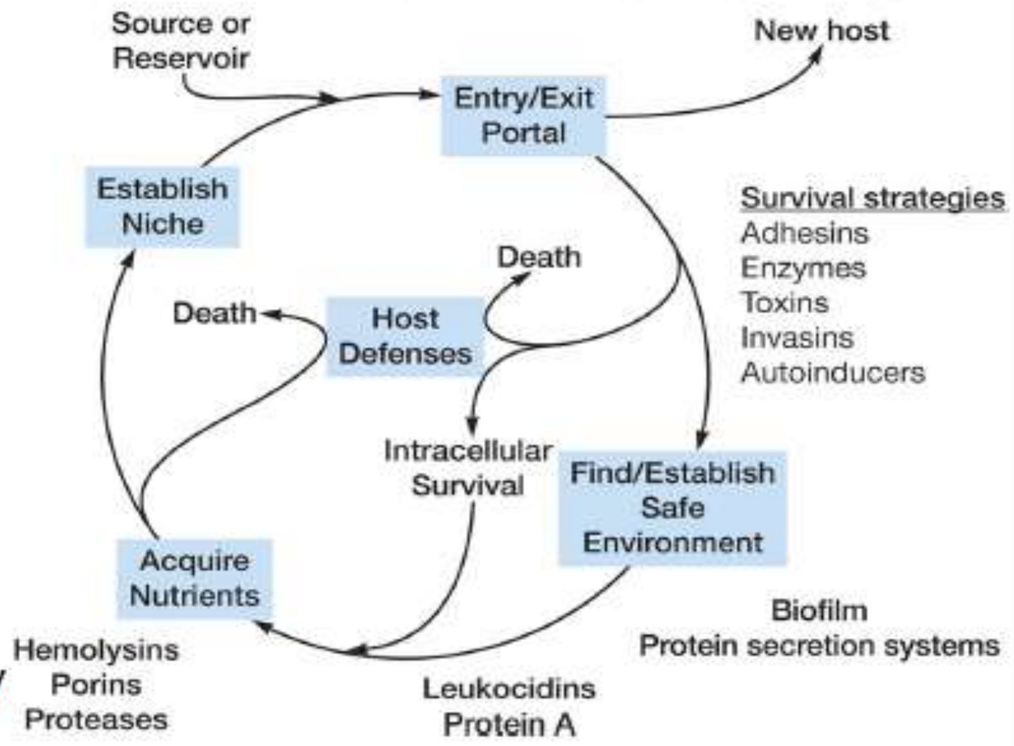


Types of Pathogens

- Primary Pathogens
  - Cause disease upon infection, not normally associated with host
    - Plague (*Yersinia pestis*), influenza virus
- Opportunistic Pathogens
  - Cause disease under some circumstances, sometime members of normal flora
    - Pseudomonas, *Candida albicans*

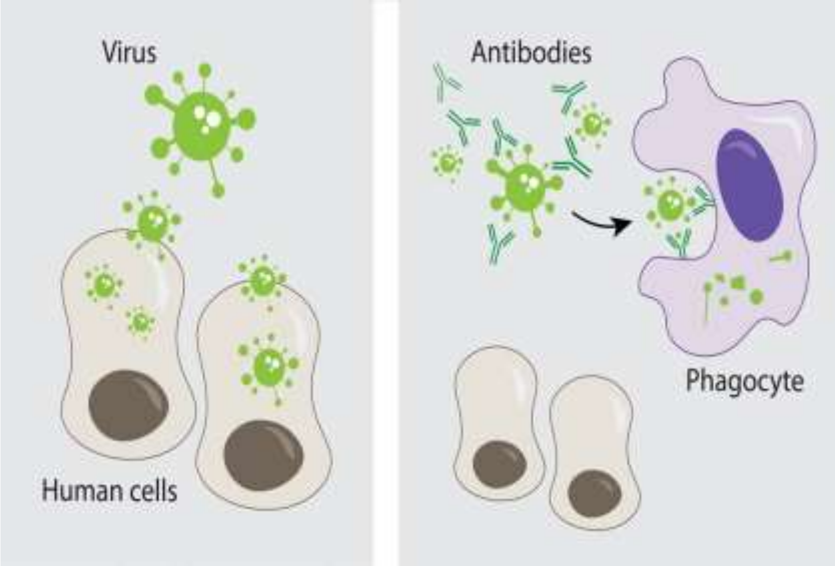
Infectious Process

- A pathogen must contact a host AND survive within it to cause a disease. To survive, it needs
  - a suitable environment
  - a source of nutrients
    - in competition with eukaryotic host cells
  - Protection from harmful elements
    - ***virulence factors*** allow a pathogen to outcompete host cells and resist their defenses



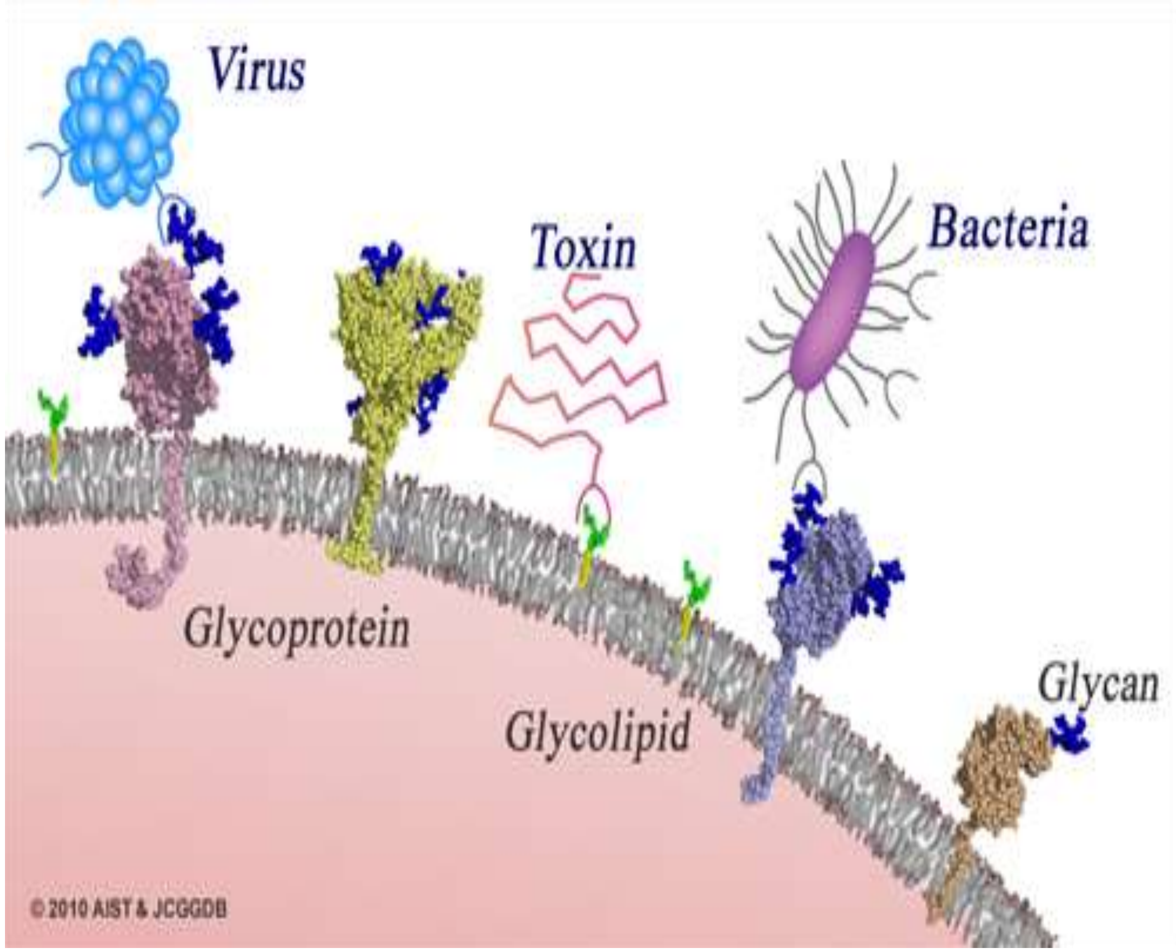
Establishing an Infection

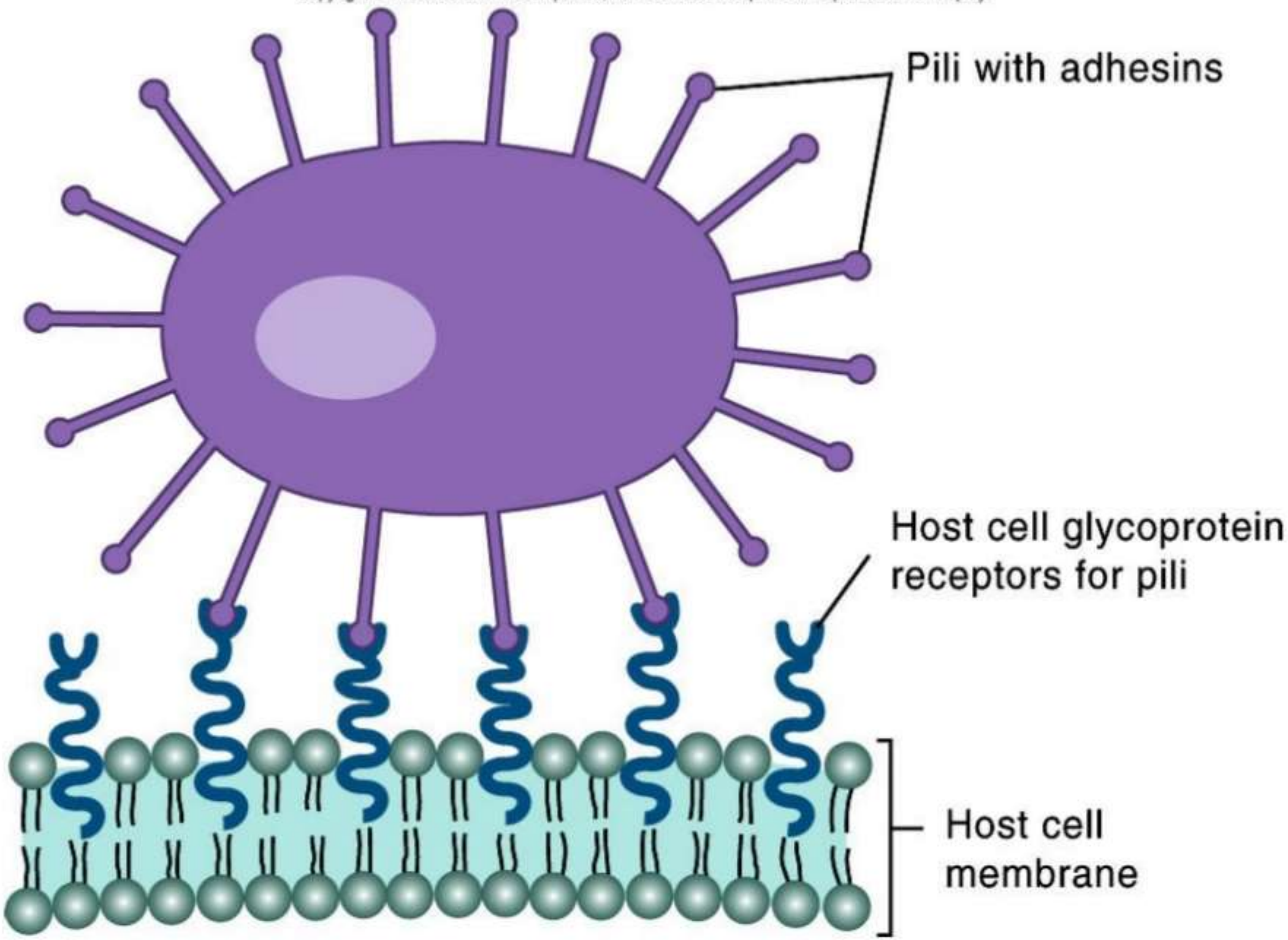
- 1. Encounter:
  - fecal-oral (cholera)
  - human-human (tuberculosis)
  - animal-human (rabies)
  - vector-borne (plague, lyme disease)
  - environmental contact (anthrax)



Establishing an Infection

- 2. Adherence
  - Prevents early clearance
  - Often bind host tissues via pili
  - Specificity can determine host range of pathogen



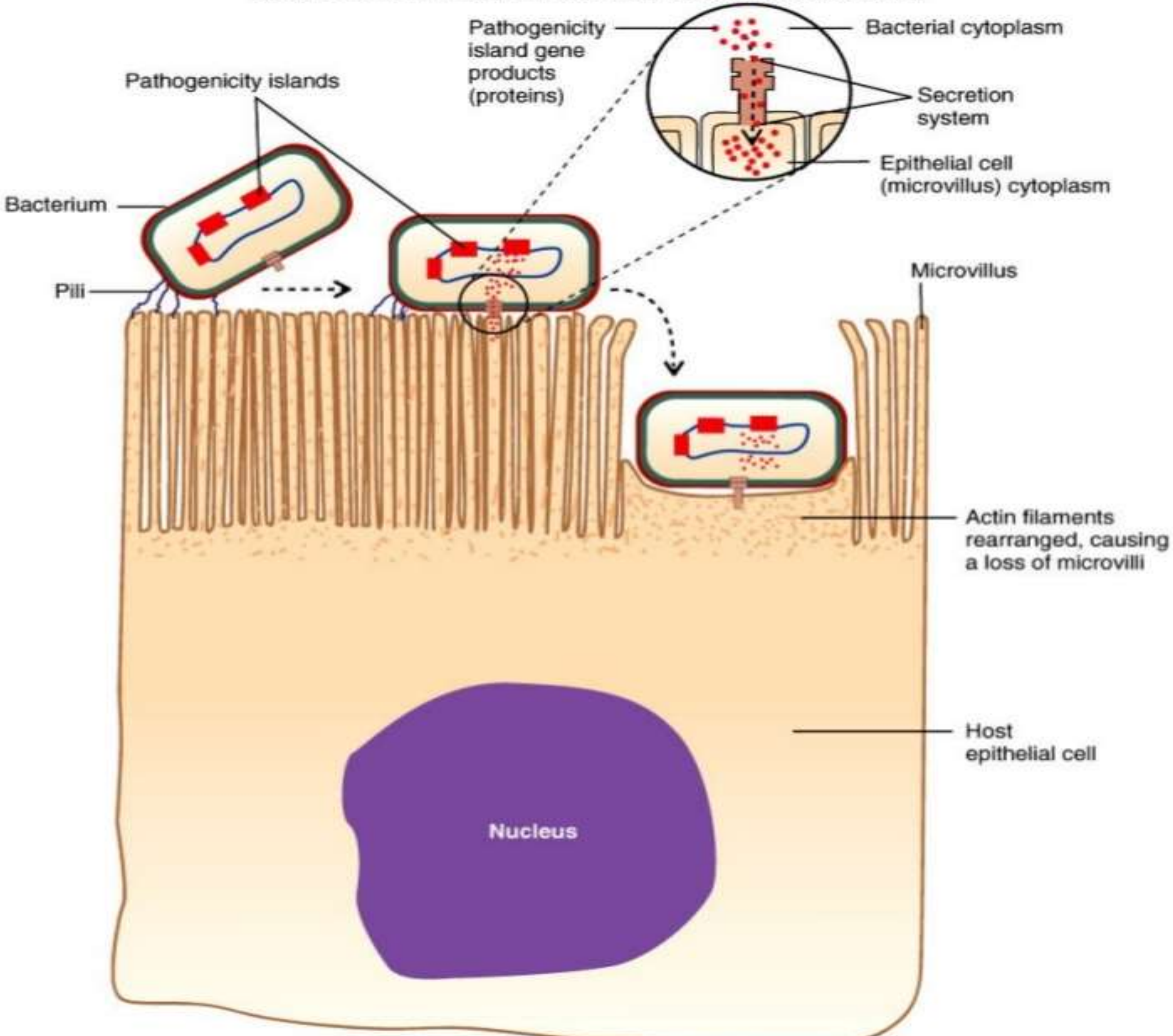

Pili with adhesins
Host cell glycoprotein
receptors for pili
Host cell
membrane

Establishing an Infection

- 3. Colonization: multiplication and maintainance
  - Competition with normal flora
  - Resist:
    - bile
    - stomach acid
    - peristalsis
    - skin secretions
    - IgA (mucosal antibodies)
    - compete with host for iron

Establishing an Infection

- 4. Molecule Delivery
  - Affects target cell structure and host response



Pathogenicity island gene products (proteins)
Bacterial cytoplasm
Pathogenicity islands
Secretion system
Epithelial cell (microvillus) cytoplasm
Bacterium
Pili
Microvillus
Actin filaments rearranged, causing a loss of microvilli
Host epithelial cell
Nucleus

Invasion:Breaching Anatomical Barriers

- Find new niche with few competitors
- Gain access to rich nutrient supply
- 1. Skin: tough barrier, rely on wounds or insect vectors
- 2. Crossing mucous membrane (e.g. intestinal epithelial cells)

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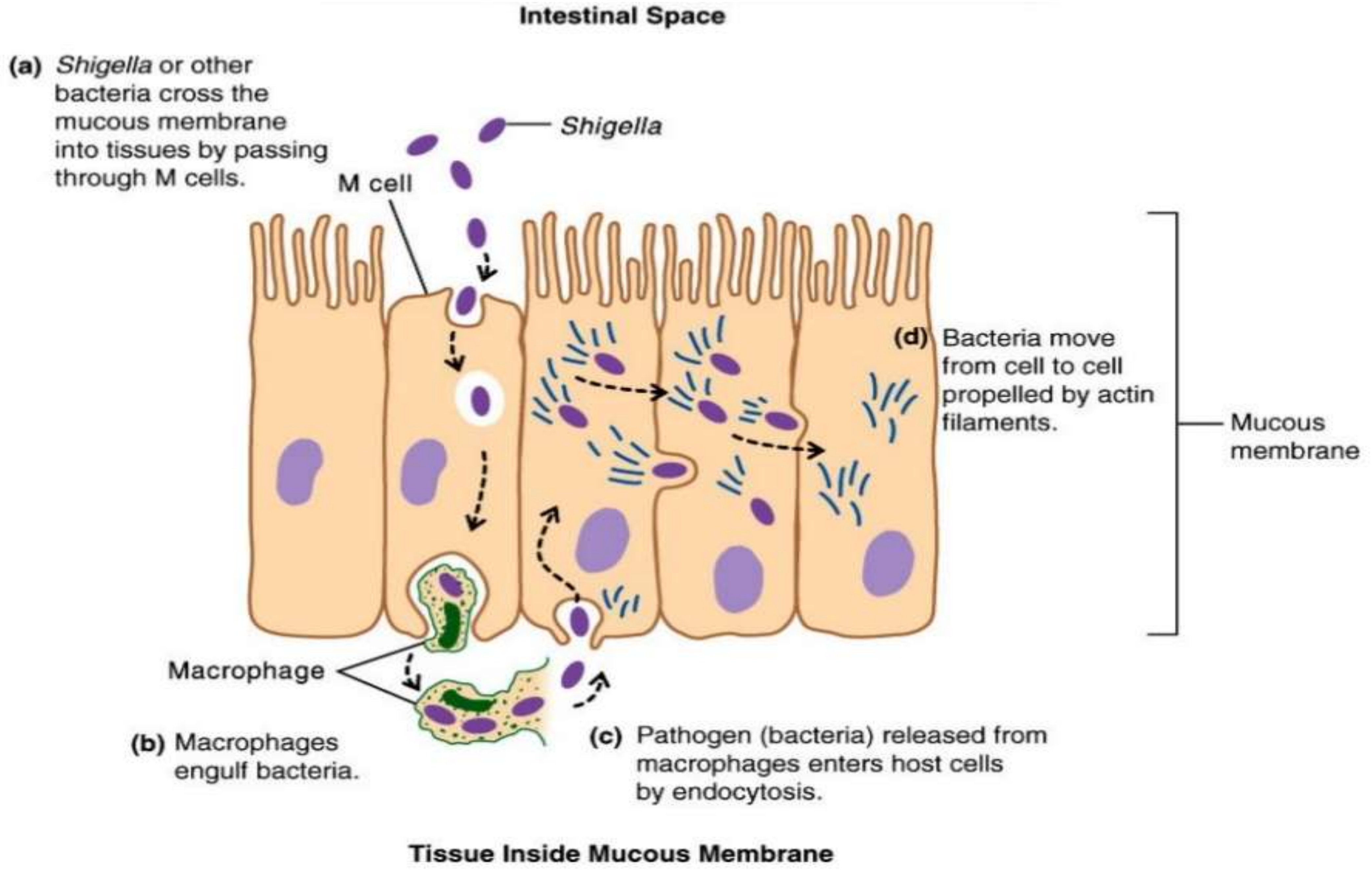
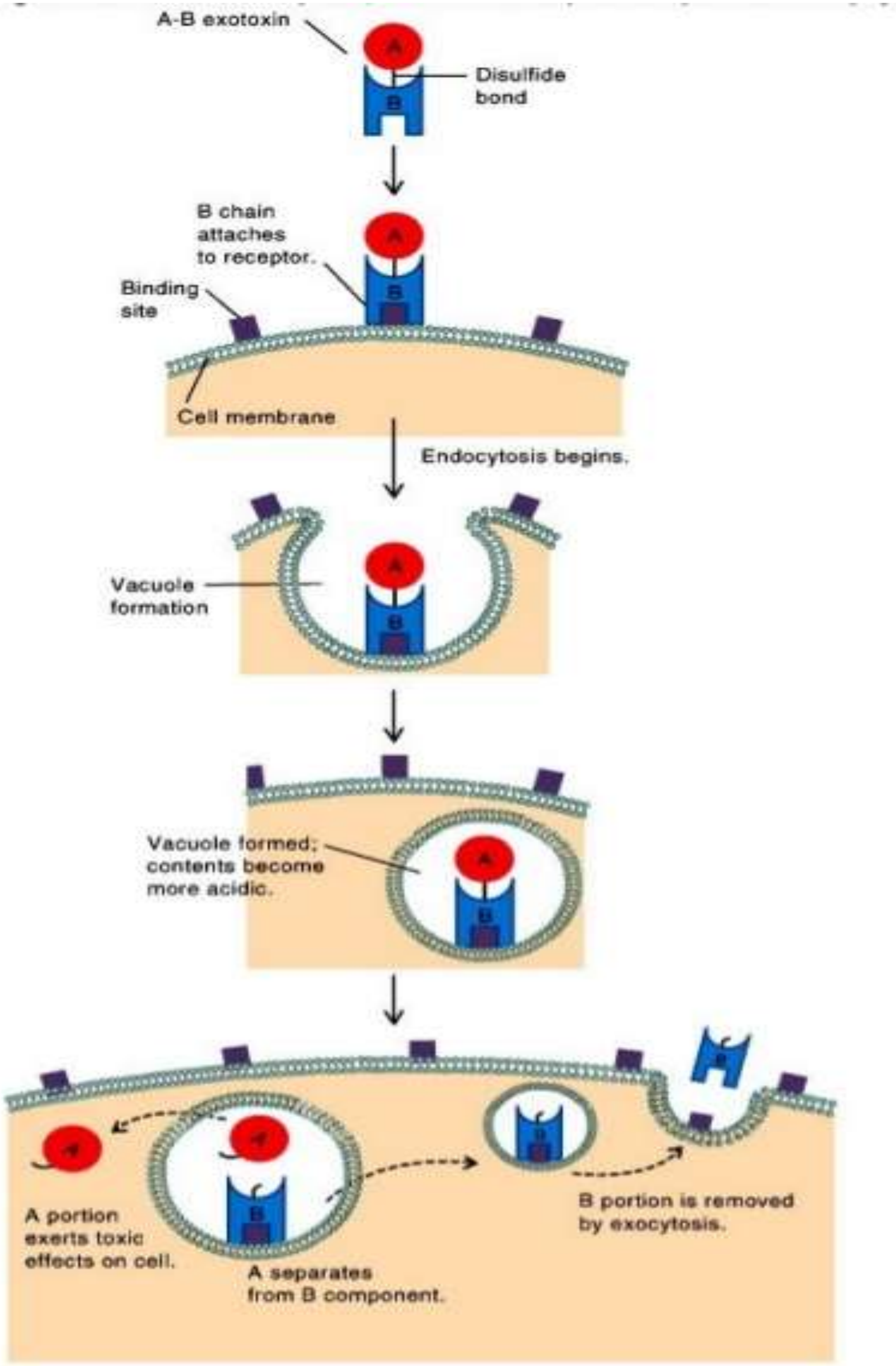

Intestinal Space
(a) Shigella or other bacteria cross the mucous membrane into tissues by passing through M cells.
Shigella
M cell
(d) Bacteria move from cell to cell propelled by actin filaments.
Mucous membrane
Macrophage
(b) Macrophages engulf bacteria.
(c) Pathogen (bacteria) released from macrophages enters host cells by endocytosis.
Tissue Inside Mucous Membrane

16.7. Avoiding the Host Defenses

- Avoiding Destruction by Phagocytes
  - Preventing Encounters with Phagocytes
    - C5a peptidase: degrades chemoattractant C5a
      - E.g., *Streptococcus pyogenes*
    - Membrane-damaging toxins: kill phagocytes, other cells
      - E.g., *S. pyogenes* makes streptolysin O

Damage to Host (Disease)

- 1. Exotoxins
  - May require prior colonization (cholera)
  - May cause food poisoning even in absence of organism
    - Botulism or *Staphylococcus aureus* toxin
  - Immune system often target toxin for neutralizing Ab's
    - Vaccine against toxin
  - A-B toxins: A is catalytic subunit, B binds host cells


A-B exotoxin
A
B
Disulfide bond
B chain attaches to receptor.
Binding site
Cell membrane
Endocytosis begins.
Vacuole formation
Vacuole formed; contents become more acidic.
A portion exerts toxic effects on cell.
A separates from B component.
B portion is removed by exocytosis.

Example	Name of Disease; Name of Toxin	Characteristics of the Disease	Mechanism	Page Reference
A-B TOXINS—Composed of two subunits, A and B. The A subunit is the toxic, or active, part; the B subunit binds to the target cell.				
Neurotoxins				
Clostridium botulinum	Botulism; botulinum toxin	Flaccid paralysis	Blocks transmission of nerve signals to the muscles by preventing the release of acetylcholine.	p. 652
Clostridium tetani	Tetanus; tetanospasmin	Spastic paralysis	Blocks the action of inhibitory neurons by preventing the release of neurotransmitters.	p. 555
Enterotoxins				
Enterotoxigenic *E. coli*	Traveler's diarrhea; heat-labile enterotoxin (cholera-like toxin)	Severe watery diarrhea	Modifies a regulatory protein in intestinal cells, causing those cells to continuously secrete electrolytes and water.	p. 590
Vibrio cholerae	Cholera; cholera toxin	Severe watery diarrhea	Modifies a regulatory protein in intestinal cells, causing those cells to continuously secrete electrolytes and water.	p. 586
Cytotoxins				
Bacillus anthracis	Anthrax; edema factor, lethal factor	Inhaled form—septic shock; cutaneous form—skin lesions	Edema factor modifies a regulatory protein in cells, causing accumulation of fluids. Lethal factor inactivates proteins involved in cell signaling functions.	p. 497
Bordetella pertussis	Pertussis (whooping cough); pertussis toxin	Sudden bouts of violent coughing	Modifies a regulatory protein in respiratory cells, causing accumulation of respiratory secretions and mucus. Other factors also contribute to the symptoms.	p. 501
Corynebacterium diphtheriae	Diphtheria; diphtheria toxin	Pseudomembrane in the throat; heart, nervous system, kidney damage	Inhibits protein synthesis by inactivating an elongation factor of eukaryotic cells. Kills local cells (in the throat) and is carried in the bloodstream to various organs.	p. 490
E. coli O157:H7	Bloody diarrhea, hemolytic uremic syndrome; shiga toxin	Diarrhea that may be bloody; kidney damage	Inactivates the 60S subunit of eukaryotic ribosomes, halting protein synthesis.	p. 590
Shigella dysenteriae	Dysentery, hemolytic uremic syndrome; shiga toxin	Diarrhea that contains blood, pus, and mucus; kidney damage	Inactivates the 60S subunit of eukaryotic ribosomes, halting protein synthesis.	p. 588

Damage to Host (Disease)

- 2. Membrane-damaging toxins
  - Hemolysins
    - Cause cell-lysis: Streptolysin O
  - Phospholipases
    - Cleave lipids in membranes: *Clostridium perfringens*
      - Gas gangrene

THANK YOU