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Microbiology
An Evolving Science

Chapter 23
Human Microflora and Nonspecific Host Defenses

Human Microflora

- Humans colonized by many microbes
- Normal flora
  - "Commensal" (mutualistic) organisms
- Microbe populations change constantly
  - Vary with type of tissue, condition
    - pH, moisture, other microbes present
    - Intestinal flora varies with food eaten
  - Can cause disease if reach abnormal location

Table 23.1 The prominent bacterial ecosystems of humans.

Microbial reservoirs	Total "bioburden" or colony-forming units	Aerobe-to-anaerobe ratio	How acquired
Skin	10^{4-6}/sweat gland	1:10	Birth canal Oral environments
Mouth	10^{6-8}	1:10	Birth canal Caregiver
Genitourinary tract	10^{4-5}/vagina/ureter	1:100	Surrounding external environment
Intestine	10^{11}/cm^3	1:1,000	Baby formula Mother Caregiver

Table 23.1 Microbiology: An Evolving Science
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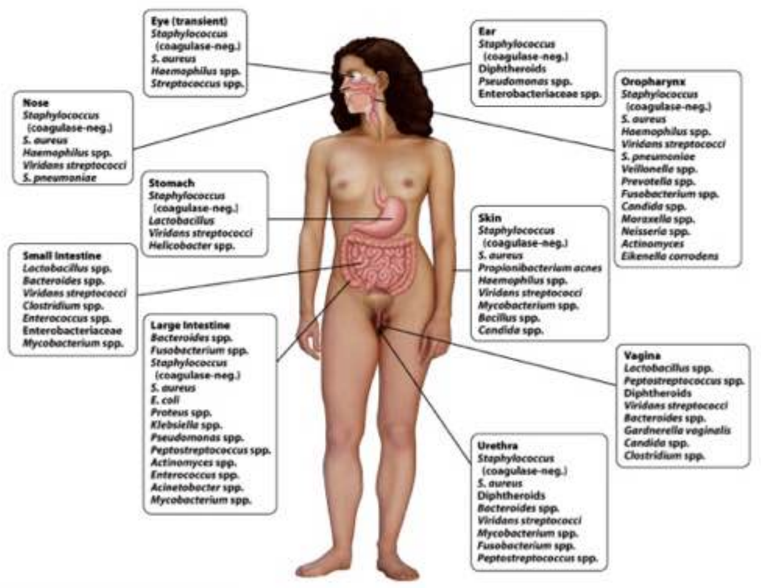

Figure 23.1 Microbiology: An Evolving Science
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Human Microflora: Skin

- Skin is difficult to colonize
  - Dry, salty, acidic, protective oils
- 10^{12} microbes in moist areas
  - Scalp, ears, armpits, genital and anal areas
- Mostly anaerobes
  - Gram$^+$ tolerate salt well
    - *Staphylococcus epidermidis*
    - *Propionibacterium* degrades skin oil
      - Inflames sebaceous glands
      - Causes acne

Propionibacterium acnes

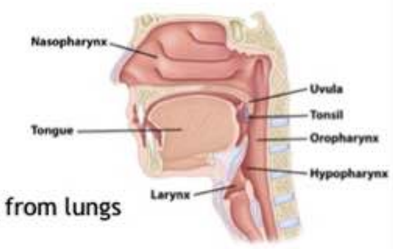
·Gram-positive, lipophilic rod
·Causes acne
·Oil glands secrete lipids, which this bacterium uses for food
·Secretes enzymes that convert triacylglycerides to free fatty acids

·Free fatty acids
  (A) smell
  (B) trigger inflammation
  (C) Inhibit the growth of Gram-negative bacteria

·Deodorants contain substances to inhibit the growth of Gram-positive bacteria

Human Microflora: Nose, Mouth

- Nasopharynx and Oropharynx
  - Many Gram+ anaerobes
    - *Staphylococcus* species
    - *Streptococcus* species
  - Nose cilia trap microbes
  - Mucous in mouth/throat carries bacteria to acidic stomach
  - Trachea cilia carry microbes away from lungs



- Dangerous if enter bloodstream
- Can form biofilm around teeth
  - Plaque
  - Cause of gum disease
  - *Streptococcus mutans*

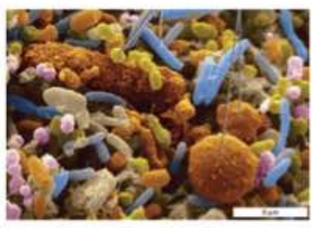
Human Microflora: Stomach

- Very high acidity
  - Few microbes survive
    - *Helicobacter pylori*
      - Survive at pH 1
      - Burrow into protective mucous
      - Cause of ulcers

- Loss of acidity
  - Caused by malnourishment
  - Allows pathogen growth
  - *Vibrio cholerae* survive
    - Pass through stomach

Human Microflora: Intestine

- Vast majority of human microflora
  - 10^{9-11} cells/ cm^3
- Bacteria ferment ingested food
  - Also intestinal mucous—*Escherichia coli*
- Provide nutrients, inhibit pathogens



- *Bacteroides thetaiotaomicron*
- Probiotics supply bacteria
  - *Lactobacillus, Bifidobacterium*

Human Genitourinary Microflora

- Cannot culture bacteria from kidney and bladder
- Urethra and vagina contain bacteria
  - Gram+ cells
  - Gram- Enterobacteriaceae
    - Flora changes with monthly cycles
  - Acidic secretions prevent pathogens
    - *Lactobacillus acidophilus* in vagina
      - Probiotic treatment

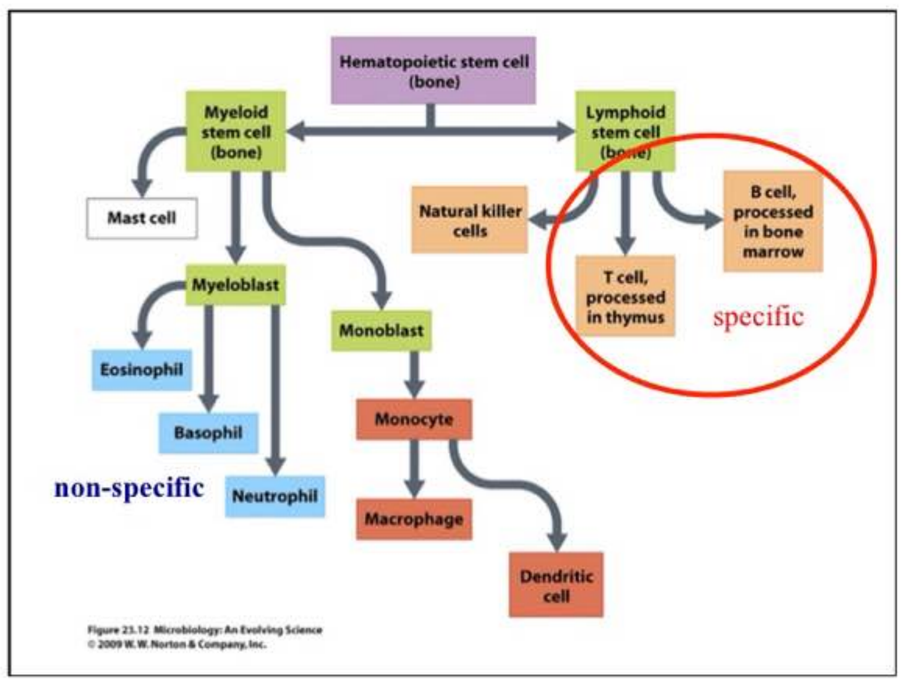
Risks, Benefits of Microflora

- Commensal flora benefits human host
  - Makes vitamins
  - Digests food
  - Prevents colonization by pathogens
  - Make immunomodulins

- Opportunistic pathogens
  - Surface breach allows bacterial entry
  - Immunocompromised hosts
    - E.g., *Bacteroides fragilis*
    - E.g., *Clostridium difficile*

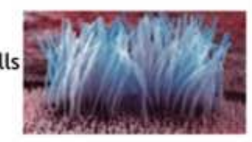
Overview of the Immune System

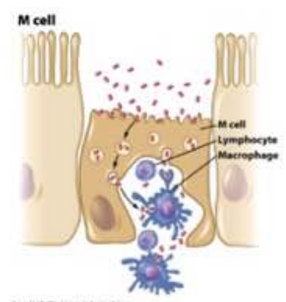
- Innate Immunity
  - Barriers to infection
  - Nonspecific reaction to destroy invading cells
    - Complement proteins
- Adaptive Immunity
  - Reaction to specific antigens
    - Parts of foreign proteins, sugars, chemicals
  - Body reacts to antigens when exposed
    - Retains "memory" of those antigens
    - Faster response if exposed a second time



Innate Host Defenses

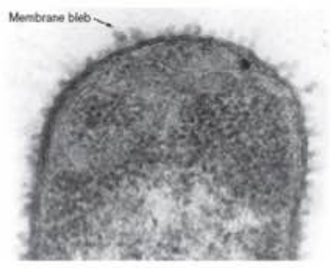
- Physical barriers to infection
  - Skin
    - Keratin, oil, cells that phagocytose microbes
    - Dead skin cells, washing, remove attached cells
  - Mucous
    - Trap, destroy pathogens
    - Mucous layers slough off, removed
  - Cilia remove microbes from lungs
  - Toll-like receptor proteins on tissues
    - Gut—M cells
    - Skin—Langerhans cells



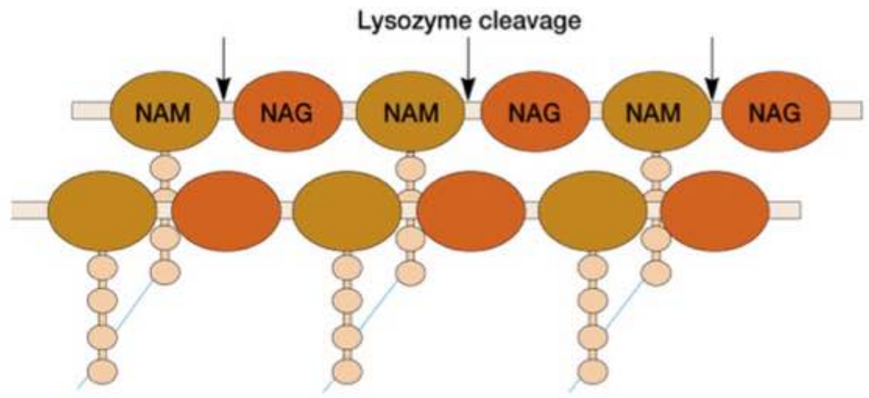


Innate Host Defenses

- Chemical barriers to infection
  - Acidic pH: stomach, skin, vagina
  - Lysozyme: tears, skin
    - Destroys peptidoglycan
  - Antimicrobial peptides
    - Destroy microbial plasma membrane



Lysozyme



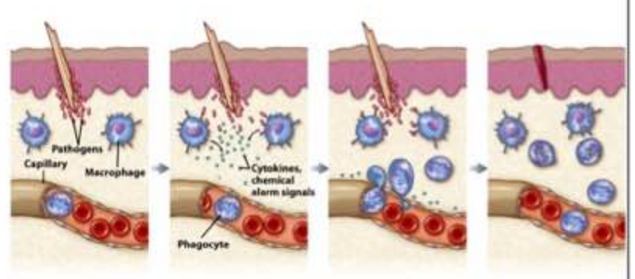
Petidoglycan is composed of alternating NAM and NAG sugars
NAM: N-acetylmuramic acid
NAG: N-acetylglucosamine

Acute Inflammatory Response

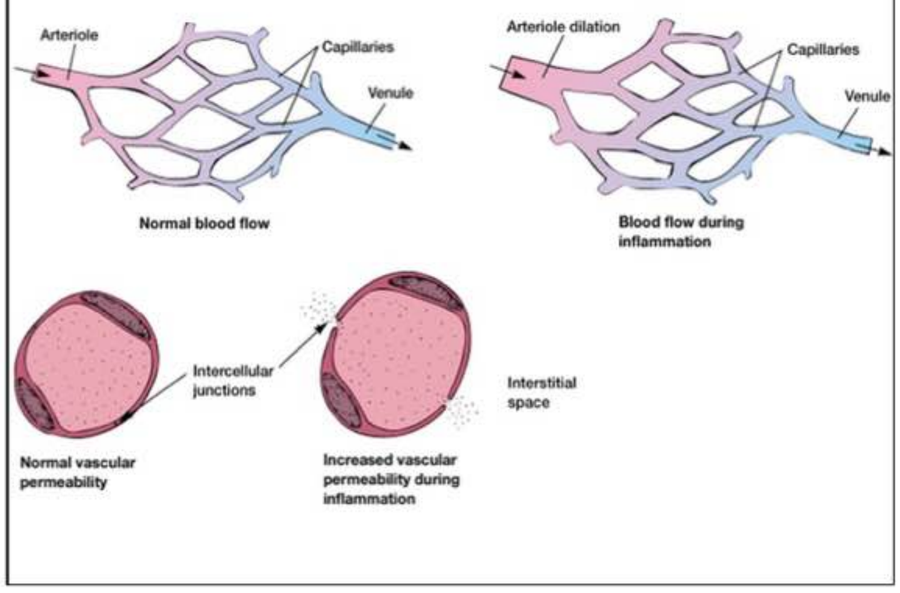
- Damaged tissue secretes bradykinin
  - Stimulates mast cells
- Mast cells degranulate
  - Release histamine, stimulates blood vessels
- Histamine stimulates vessels to open further
  - Blood plasma, platelets released into area
  - Prostaglandin released
- Prostaglandin stimulates nerve cells
  - Signal itching, pain

Acute Inflammatory Response

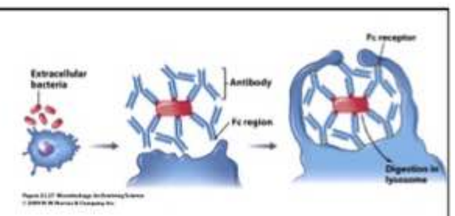
- Infection releases microbes to tissue
- Macrophages phagocytose bacteria
  - Release vasoactive factors
- Capillary cells express proteins that slow macrophage movement
- Macrophages extravasate
  - Squeeze between capillary cells
  - Leave capillary
  - Attack bacteria



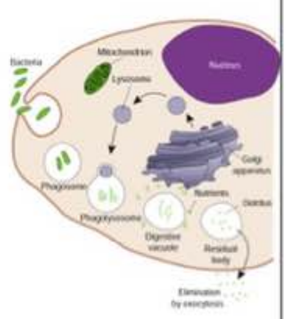
Cytokine-mediated inflammation



Phagocytosis

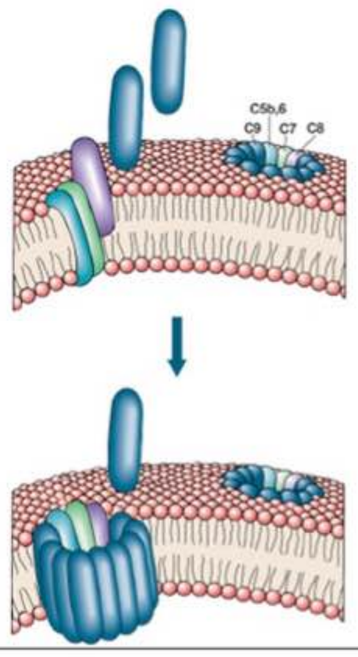


- Phagocytes must avoid attacking host cells
  - Host cell CD47 prevents attack
  - Phagocyte toll-like receptors bind bacteria
  - Phagocyte receptors bind opsonized bacteria
    - Cells coated with antibodies

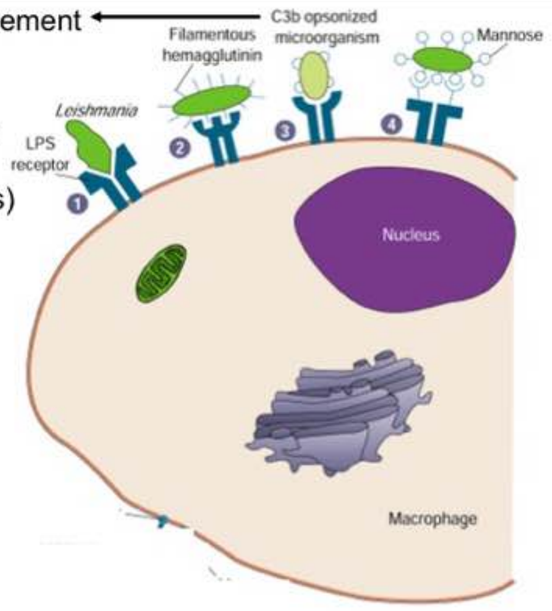


- Phagocytes kill, digest engulfed bacteria
  - Produce peptides to kill bacteria
  - Kill with reactive oxidative burst
    - O_2^-, HOOH, $^{\cdot}OH$, NO, NO_2^-, NO_3^- in phagosome

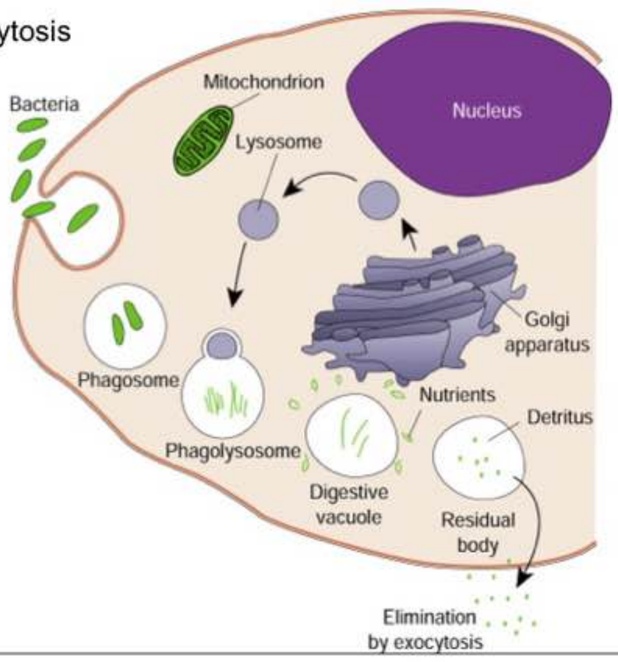
Complement Membrane Attack Complex (MAC)



C3b = complement protein that triggers opsonization (which is phagocytosis)



Phagocytosis

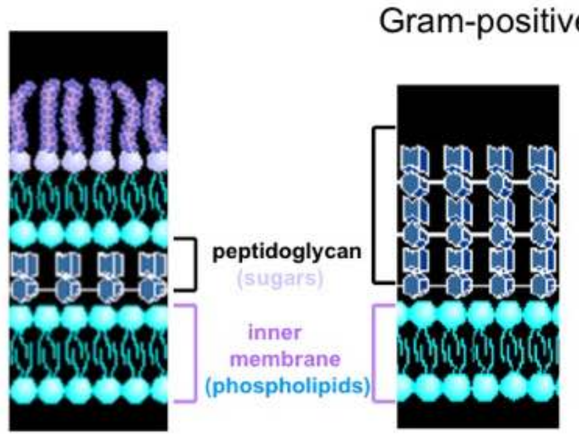


Bacterial cell envelopes

endotoxin
=
lipids with chain of sugars attached

Gram-negative

Gram-positive

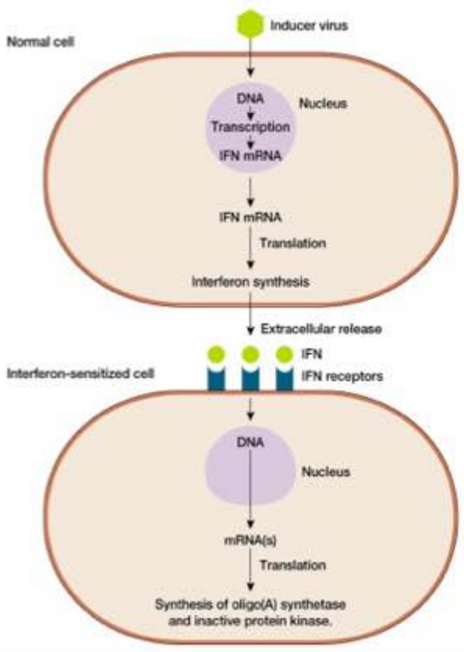


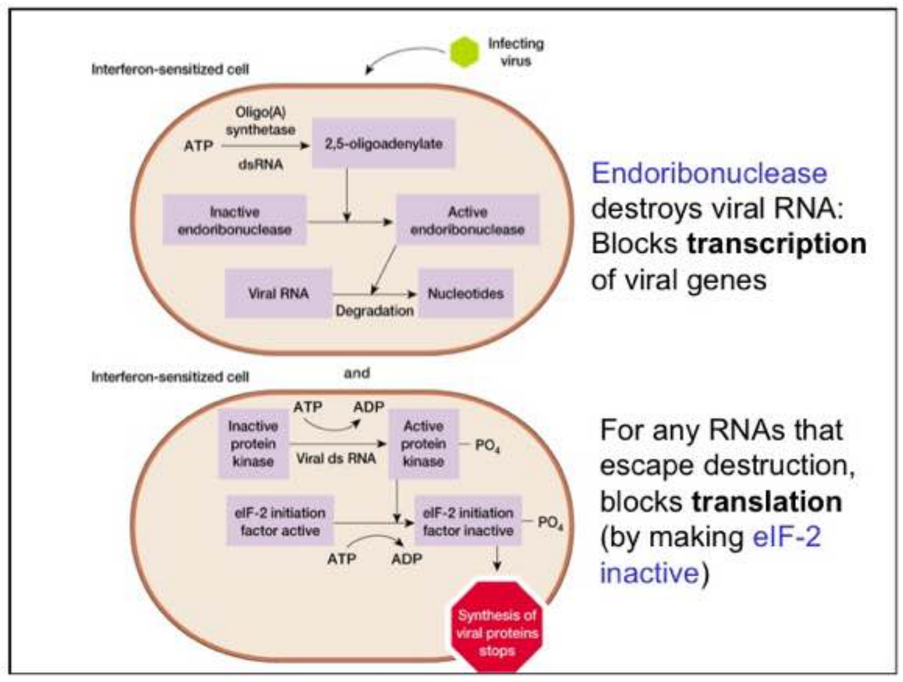
lipopolysaccharide asymmetric outer membrane phospholipids

peptidoglycan (sugars)

inner membrane (phospholipids)

Interferon: protection against viruses





Fever

- Vasoconstriction accumulates heat
- Pyrogens induce temperature rise
  - Exogenous pyrogens
    - LPS
    - Cause release of endogenous pyrogens
  - Endogenous pyrogens
    - Interferon, TNF, IL-6
    - Signal brain to raise temperature
    - Reduce iron availability to bacteria
- High temperature stresses invading microbes