Microbial metabolism

• Definitions
  – Metabolism: The processes of catabolism and anabolism
  – Catabolism: The processes by which a living organism obtains its energy and raw materials from nutrients
  – Anabolism: The processes by which energy and raw materials are used to build macromolecules and cellular structures (biosynthesis)
Infection & Disease

• Relationship between microbe and host:
  - mutualism
  - commensalism
  - Parasitism

• Microbes live in human body as:
  - Colonists (normal flora)
  - Transient
  - Pathogen
Micrococci as found on human skin and nasal membranes
Definition of Normal Flora

• Refers to the microbes that normally live on the surfaces of an animal

• Also referred to as indigenous species or indigenous microbiota

*Actinomyces israelii*, part of the normal flora of the oral cavity.
### BACTIERIA COMMONLY FOUND ON THE SURFACES OF THE HUMAN BODY

<table>
<thead>
<tr>
<th>BACTERIUM</th>
<th>Skin</th>
<th>Conjunctiva</th>
<th>Nose</th>
<th>Pharynx</th>
<th>Mouth</th>
<th>Lower Intestine</th>
<th>Anterior urethra</th>
<th>Vagina</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus epidermidis</em> (1)</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (2)</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus mitis</em></td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus salivarius</em></td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus mutans</em> (3)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em> (4)</td>
<td>+/-</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> (5)</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em> (6)</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Neisseria sp. (7)</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Neisseria meningitidis* (8)</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Veillonellae sp.</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Enterobacteriaceae* (Escherichia coli) (9)</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Proteus sp.</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
BACTERIA COMMONLY FOUND ON THE SURFACES OF THE HUMAN BODY

<table>
<thead>
<tr>
<th>BACTERIUM</th>
<th>Skin</th>
<th>Conjunctiva</th>
<th>Nose</th>
<th>Pharynx</th>
<th>Mouth</th>
<th>Lower Intestine</th>
<th>Anterior urethra</th>
<th>Vagina</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-.</td>
<td>+/-</td>
</tr>
<tr>
<td><em>(Haemophilus influenzae)</em></td>
<td>+/-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-.</td>
<td>+/-.</td>
<td>+</td>
</tr>
<tr>
<td><em>Bacteroides sp.</em></td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-.</td>
<td>+/-.</td>
<td>+/-</td>
</tr>
<tr>
<td><em>Bifidobacterium bifidum</em></td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus sp.</em></td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><em>Clostridium sp.</em></td>
<td>+/-</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td><em>Clostridium tetani</em></td>
<td>+/-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corynebacteria</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+/-.</td>
<td>+/-.</td>
<td>+</td>
</tr>
<tr>
<td><em>Mycobacteria</em></td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Actinomycetes</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Spirochetes</em></td>
<td>+</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mycoplasmas</em></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-.</td>
<td>+</td>
</tr>
</tbody>
</table>
Where the Normal Flora Are Found

- Skin
- Conjunctiva
- Oral cavity
- Intestinal tract
- Upper respiratory tract
- Urogenital tract

Dental plaque consists of a biofilm of bacteria 300-500 cells in thickness.
Guide to the Normal Bacterial Flora of Humans

Staphylococci

- Includes *Staphylococcus epidermidis* and *Staphylococcus aureus*

- Located on skin and most mucous membranes
Corynebacteria

- Includes *Corynebacterium* and *Propionibacterium* species

- Located primarily on skin and upper respiratory tract

*Propionibacterium acnes* colonies. The bacterium is found on skin, nasal membranes and the conjunctiva of the eye.
Guide to the Normal Bacterial Flora of Humans

Streptococci

• Includes *Streptococcus salivarius*, *S. mitis* and *S. mutans*

• Located in oral cavity

*Streptococcus mutans*, the main bacterium implicated in dental caries.
Lactic acid bacteria

- Includes *Streptococcus* and *Lactobacillus* species
- Located in oral cavity, intestinal tract and vagina

*Lactobacillus acidophilus* and a vaginal squamous epithelial cell.
Guide to the Normal Bacterial Flora of Humans

Bifidobacteria

• Members of the genus *Bifidobacterium*

• Found in the intestinal tract

*Bifidobacterium bifidus*. Bifidobacteria make up over 90 percent of the bacteria in the intestine of breast-fed infants.
Enterococci

- Includes *Enterococcus faecalis* and *Enterococcus faecium*

- Located in the intestinal tract

*Enterococcus faecalis* - so regularly found in the intestine that some countries use the bacterium as their indicator of fecal pollution of water.
Guide to the Normal Bacterial Flora of Humans

Clostridia

- Members of the genus *Clostridium*

- Found in the intestinal tract

*Clostridium difficile*. Clostridia are anaerobic endospore-forming bacteria, found mainly in the large intestine.
Gram-negative cocci

- Includes *Neisseria*, *Moraxella* and *Veillonella* species

- Located in the nasopharynx

*Neisseria* species are found commonly in the throat.
Enteric bacteria

- Gram-negative rod-shaped bacteria including *E. coli* and its relatives
- Located in the intestinal tract

*Escherichia coli* Gram stain and colonies on EMB agar.
Bacteroides

- Members of the genus *Bacteroides*

- Found in the oral cavity and the intestinal tract

*Bacteroides fragilis* is the most common bacterium in the colon, outnumbering *E. coli* by 1000:1
Guide to the Normal Bacterial Flora of Humans

Potential pathogens in the upper respiratory tract

- *Staphylococcus aureus*
- *Streptococcus pyogenes*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

*Streptococcus pneumoniae*, the leading cause of bacterial pneumonia in humans is normal flora in up to 70 percent of individuals.
Basis for associations between humans and normal flora

- Tissue tropism
- Specific adherence
- Microbial construction of biofilms
Basis for associations between humans and normal flora

Tissue tropism is the predilection or preference of a microbe for a specific tissue.

Lactobacilli colonize the vaginal epithelium because glycogen is produced there which provides the carbon source (sugar) for their growth.
EXAMPLES OF TISSUE TROPISM OF SOME BACTERIA ASSOCIATED WITH HUMANS

<table>
<thead>
<tr>
<th>BACTERIUM</th>
<th>TISSUE</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Corynebacterium diphtheriae</em></td>
<td>Throat</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>Urogenital epithelium</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em></td>
<td>Tooth surfaces</td>
</tr>
<tr>
<td><em>Streptococcus salivarius</em></td>
<td>Tongue surfaces</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td>Small intestine epithelium</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>Small intestine epithelium</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Nasal membranes</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>Skin</td>
</tr>
</tbody>
</table>
Specific adherence is the ability of microbe to attach or adhere to a specific tissue due to receptor-ligand (adhesin) interactions.
<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Bacterial ligand for attachment</th>
<th>Host cell or tissue receptor</th>
<th>Attachment site</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>Protein F</td>
<td>Amino terminus of fibronectin</td>
<td>Pharyngeal epithelium</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em></td>
<td>Glycosyl transferase</td>
<td>Salivary glycoprotein</td>
<td>Pellicle of tooth</td>
</tr>
<tr>
<td><em>Streptococcus salivarius</em></td>
<td>Lipoteichoic acid</td>
<td>unknown</td>
<td>Buccal epithelium of tongue</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Cell-bound protein</td>
<td>N-acetylhexosamine-galactose disaccharide</td>
<td>Mucosal epithelium</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Cell-bound protein</td>
<td>Amino terminus of fibronectin</td>
<td>Mucosal epithelium</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>N-methylphenylalanine pili</td>
<td>Glucosamine-galactose carbohydrate</td>
<td>Urethral/cervical epithelium</td>
</tr>
<tr>
<td><em>Enterotoxigenic E. coli</em></td>
<td>Type-1 fimbriae</td>
<td>Species-specific carbohydrate(s) (e.g. mannose)</td>
<td>Intestinal epithelium</td>
</tr>
<tr>
<td><em>Uropathogenic E. coli</em></td>
<td>Type 1 fimbriae</td>
<td>Complex carbohydrate</td>
<td>Urethral epithelium</td>
</tr>
<tr>
<td><em>Uropathogenic E. coli</em></td>
<td>P-pili (pap)</td>
<td>Globobiose linked to ceramide lipid</td>
<td>Upper urinary tract</td>
</tr>
<tr>
<td><em>Bordetella pertussis</em></td>
<td>Fimbriae (“filamentous hemagglutinin”)</td>
<td>Galactose on sulfated glycolipids</td>
<td>Respiratory epithelium</td>
</tr>
<tr>
<td><em>Vibrio cholerae</em></td>
<td>N-methylphenylalanine pili</td>
<td>Fucose and mannose carbohydrate</td>
<td>Intestinal epithelium</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>Peptide in outer membrane</td>
<td>Surface protein (fibronectin)</td>
<td>Mucosal epithelium</td>
</tr>
</tbody>
</table>
Basis for associations between humans and normal flora

Biofilms are constructed by some normal flora in order to colonize tissues.

Example of a biofilm formed by bacteria in the small intestine
BACTERIA FOUND IN THE LARGE INTESTINE OF HUMANS

<table>
<thead>
<tr>
<th>BACTERIUM</th>
<th>Range of Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroides fragilis</td>
<td>100</td>
</tr>
<tr>
<td>Bacteroides melaninogenicus</td>
<td>100</td>
</tr>
<tr>
<td>Bacteroides oralis</td>
<td>100</td>
</tr>
<tr>
<td>Lactobacillus</td>
<td>20-60</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>25-35</td>
</tr>
<tr>
<td>Clostridium septicum</td>
<td>5-25</td>
</tr>
<tr>
<td>Clostridium tetani</td>
<td>1-35</td>
</tr>
<tr>
<td>Bifidobacterium bifidum</td>
<td>30-70</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>30-50</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>100</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>100</td>
</tr>
<tr>
<td>Salmonella enteritidis</td>
<td>3-7</td>
</tr>
<tr>
<td>Salmonella typhi</td>
<td>0.00001</td>
</tr>
<tr>
<td>Klebsiella sp.</td>
<td>40-80</td>
</tr>
<tr>
<td>Enterobacter sp.</td>
<td>40-80</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>5-55</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3-11</td>
</tr>
<tr>
<td>Peptostreptococcus sp.</td>
<td>common</td>
</tr>
<tr>
<td>Peptococcus sp.</td>
<td>moderate</td>
</tr>
<tr>
<td>Methanogens (Archaea)</td>
<td>common</td>
</tr>
</tbody>
</table>
Overall benefits of the normal flora

- Synthesis and excretion of vitamins used by the host
- Competition with pathogens for nutrients and colonization sites
- Direct antagonism against pathogens
- Stimulate the development of immunological tissues
- Stimulate the activity of the immune system by production of natural antibodies
Overall harmful effects of the normal flora

• Competition with host for nutrients
• Transition to an abnormal region
• Bacterial synergism between normal flora and potential pathogens
• Carrier state
• Transformation of food to carcinogens

• Endogenous disease and opportunistic infection (immunocompromised)
Development of infection

- Attachment of pathogens and hosts
- Pathogenicity and
- Host condition

Pathogen Microorganisms

- True pathogens
- Opportunistic Pathogens
True pathogens

• Pathogens which produce infections and cause disease in healthy people with complete immunity system. Plague (Yersinia), influenza, Rabies virus, malaria
Opportunistic Pathogens

- Immunodeficiency
- Abnormal region
Factors important for getting infections

- Infancy, prematurity
- Malnutrition
- Genetic defects in immunity
- Acquired immune deficiency syndrome (AIDS)
- Physical and mental stress
- Organ transplant
- Cancer
- Chemotherapy/Immunosuppressive drugs
- Anatomical defects
- Diabetes
- Liver disease
- Surgery
Portal of infections entrance

• Exogenous source
• Endogenous source
• Infectious dose (inoculum size)
Mechanisms of invasion and establishment of the Pathogens

- Following entry of Pathogen, next stage in infection requires:
  - Binding to the host
  - Penetration of barriers
  - Establishment in the tissues
  - Achievement of pathogens depends upon its biochemical and structural characteristics
Mechanisms of invasion and establishment of the Pathogens

- Adhesion: A process by which microbes gain a more stable foothold at the portal of entry.
- Bacterial pathogens mostly attach by: fimbriae(pili), flagella, Adhesive slimes or capsules
- Viruses attach by specialized receptors
- Protozoa can infiltrate by locomotion of organelles
Mechanisms of adhesion by Pathogens

(a) Fimbriae

(b) Capsules

(c) Spikes

(d) Hooks or filaments
Virulence factors

- Exoenzymes
- Toxins
- Antiphagocytic factors
- Many substances called toxins function as enzyme
Exoenzymes

• Extracellular enzymes:
  Secreted by many bacteria, fungi, protozoa and worms
  Break down & inflict damage on tissues
  Enzymes dissolve host defense barriers
  Mucinase: digests protective coating on mucous membranes & is a factor of amebic dysentery
Keratinase: principle components of skin and hair secreted by fungi and causes ringworm

Collagenase: Principle fiber of connective tissue an invasive factor of Clostridia

Hyaluronidase: hyaluronic acid which cements animal tissues staphylococci, streptococci, clostridia & pneumococci
Extracellular enzymes

• Some enzymes react with blood components coagulase produced by Staphylococci, clotting of blood plasma
• kinases (Staphylokinase, Streptokinase): dissolving of fibrin clots
• Streptase (kind of streptokinase) for therapy of thrombi
Bacterial toxins

• Potent source of cellular damage
• Toxin: Specific chemical product of microbes, animals and plants that is poisonous to other organisms
• Toxigenicity* is a genetically controlled characteristic and is responsible of Toxinoses
• Toxemia: toxin is spread by blood from site of infection (Tetanus and Diphtheria)
• Intoxication: ingestion of Toxins (botulism)
Classification of Toxins

- Toxins named according to target:
  - Neurotoxin
  - Enterotoxin
  - Hemotoxin
  - Nephrotoxin
Tradition classification of toxins

• According to their origins:
  ❖ Exotoxin: an unbound toxin molecule secreted by a living bacterial cell into the infected tissue called Exotoxin
  ❖ Strong specificity to target cell
  ❖ Dangerous and deadly
  ❖ Affect cell by damaging cell membrane
• Hemolysin: CM of RBC & release Hb
• When cultivate on Blood Agar colonies are different
  - Streptolysins of St. pyogenes
  - alpha and beta toxins of S. aureus
  - Pattern of hemolysis identify bacteria and degree of Pathogenicity
Figure 13.13
The origins and effects of circulating exotoxins and endotoxins. (a) Exotoxins, given off by live cells, have highly specific targets and physiological effects. (b) Endotoxins, given off when the cell wall of gram-negative bacteria disintegrates, have more generalized physiological effects.
Toxin of Cl. tetani blocks the action of spinal neurons
Toxin of Cl. botulinum Prevents transmission of nerve-muscle stimuli
Pertussis toxin inactivates the respiratory cilia
Cholera toxin provokes profuse salt and water loss from intestinal cell
Endotoxine: released after lyses of cell
- Lipopolysaccharides part of OM of gram negative
- Systemic effects on tissues and organs
- Depending to present amount of Endotoxin it causes fever, inflammation, hemorrhage and diarrhea
- Blood infections with G negatives like Salmonella, Shigella, Niesseria meningitidis And E.coli are dangerous
Antiphagocytic factors

- Phagocytes: specific type of WBC which engulf and destroy pathogen bacteria by enzymes and other antibacterial chemicals
- Killing Phagocytes by specific substances
- Leukocidins of Staphylococci and Streptococci are toxic to WBC
• Some Microorganisms secret slime layer and capsules that make them Physically resistant to phagocytosis St. pneumoniae, Sal.typhi, Neisseria meningitidis & cyptococcus neoformans

• Some bacteria are adapted to survival inside Phagocytes after ingestion Legionella, Mycobacterium, rickettsia
Patterns of Infection

• Localized infection (boil, warts, fungal skin infection)
• Systemic infection: spread from initial site to other tissues
• Viral: measles, rubella, and chicken pox
• Bacterial: brucellosis, typhoid fever … Rabies: from bite wound along nerve tract to brain
• Focal infection: TB
• Toxemia (local infection and general effect), tetanus
• Mixed infection: several agents simultaneously (synergetic infections)
• Cooperate in breaking down a tissue
• Gas gangrene, dental caries are mixed infections
Signs and symptoms

- Pathologic changes cause signs and symptoms
- Signs (noted by observers)
- Subjective evidence sensed by patients
- Complex of signs and symptoms called Syndrome