Normal Flora
A) What is Normal Flora?

These are mixture of microorganisms regularly found at any anatomical site on /within the body of a healthy person. Some of these microorganisms are found in association with humans / animals only. Others are found in the environment as well.
Normal flora types

- Resident vs. Transient
- Resident populations
  (normal flora, microbiota, indigenous microbial population, microflora, microbial flora)

Vast majority of normal flora are bacteria.

Internal tissues normally sterile
Resident flora

- Resident flora: If disturbed, it promptly reestablishes itself/ microorganisms may colonize, proliferate and produce disease

- More important
TRANSIENT FLORA

- Non-pathogenic or potentially pathogenic microorganisms that inhabit the skin or mucous membranes for hours, days, or weeks
- Derived from the environment, does not produce disease
- Does not establish itself permanently on the surface
- Little significance
Relationship between normal flora and host

- **Commensalism**: One organism benefits, and the other is unaffected.
- **Mutualism**: Both organisms benefit.
- **Parasitism**: One organism benefits at the expense of the other.

SYMBIOSIS

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Normal flora

- Human body
  - $10^{13}$ cells
  - $10^{14}$ bacteria
Normal flora

- Some bacteria occupy more than one niche
- Some bacteria occupy only one niche: tissue tropism
- Tropism determined by bacterial ligand-host receptor interactions
- Variation in microflora at one site
- Combinations of microflora at same site
Where the Normal Flora Are Found

- Skin
- Conjunctiva
- Nasopharynx
- Oral cavity
- Gastrointestinal tract and rectum
- Urogenital tract
# NORMAL FLORA - Skin

<table>
<thead>
<tr>
<th>SITE</th>
<th>COMMON/ MEDICALLY IMPORTANT ORGANISMS</th>
<th>LESS COMMON BUT NOTABLE ORGANISMS</th>
</tr>
</thead>
</table>
| Cutaneous surfaces including urethra and outer ear | *Staphylococcus epidermidis* | *Staphylococcus aureus, Corynebacteria (diphtheroids)*  
*Streptococci, Anaerobes e.g.*  
*Peptostreptococci, Yeast (Candida sp.)* |

*Staphylococcus epidermidis*, invariably found on skin and nasal membranes.
Normal flora - Skin

- Human adult has 2 square meters of skin
  - Overall, a hostile environment toward bacteria
  - Periodic drying

  - Eccrine (simple sweat) glands
  - Apocrine glands: sweat and nutrients
  - Sebaceous glands: associated with hair follicles
Normal flora - Skin

- S. epidermidis: Major inhabitant making up more than 90% of the flora

- S. aureus: Nose, perineum, vulvar skin
  - Occurrence in nasal passages varies with age being greatest in newborns, less in adults

- Micrococci, Diphtheroids, Propionibacterium
  - Eg. P. acnes = children younger than 10 years are rarely colonized with it
Skin: 3 main microenvironments

- Axilla, perineum, toe webs
- Hands, face and trunk
- Upper arms and legs
Factors that are Important in Eliminating Non-resident microorganism from the Skin

1. Low pH
2. Fatty acids (sebaceous secretions)
3. Lysozyme

Neither profuse sweating nor washing and bathing can eliminate or significantly modify the normal resident flora.
Normal flora of the skin:

**Benefit**
- Inhibit fungal growth (athlete’s foot)

**Harm**
- Body odor
- Acne
- Opportunistic infections
Normal flora - Conjunctiva

- Variety of bacteria: low numbers present
  - High moisture
  - Blinking mechanically removes bacteria
  - Lachrymal secretions include lysozyme
# Normal flora – UPPER RESPIRATORY TRACT

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</tr>
</thead>
<tbody>
<tr>
<td>NOSE</td>
<td>Staphylococcus aureus</td>
<td>Staphylococcus epidermidis, Corynebacteria (diphteroids) Assorted Streptococci,</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>Viridans streptococci including Streptococcus mutans</td>
<td>Assorted streptococci, nonpathogenic Neisseria, nontypeable Haemophilus influenzae</td>
</tr>
</tbody>
</table>
Normal flora - Oral cavity

- Ecology and developmental stages
  - Birth: sterile mouth within 4-12 hours (lactobacilli, streptococci)
  - Neonate (Streptococcus salivarius, staphylococci, Neisseriae, Moraxella catarrhalis)
  - Teeth appear (Streptococcus mutans, Streptococcus parasanguis)
  - Gingival crevice area (Anaerobic species, yeasts)
  - Puberty (Bacteroides, spirochetes)
- $10^8$ bacteria/mL of saliva; potentially >700 species
Normal flora of the oral cavity

**Benefit**
- Compete with pathogens for colonization sites
- Produce substances that inhibit pathogens
- Stimulate local immunity

**Harm**
- Plaque formation and dental disease
Normal flora- Oropharynx

- If large numbers are introduced into the bloodstream (following tooth extraction or tonsillectomy) they may settle on deformed/prosthetic heart valves and produce endocarditis.

- Aspiration of saliva (containing $10^{12}$ of these organism and aerobes) ma result in necrotizing pneumonia, lung abscess, and empyema.
Normal flora - Respiratory tract

- Lower respiratory tract
  (trachea, bronchi, pulmonary tissues)
  - Usually sterile
  - Ciliated epithelium
  - Mucus blanket: entrapment
  - Alveolar macrophages
  - If breached: opportunistic infections
Normal flora - Gastrointestinal tract

- GI ecology varies
- Esophagus saliva, food
- Stomach harsh $10^2$
- Small intestine ($10^3$ - $10^8$)
  - Proximal small intestine (duodenum and jejunum)
  - Distal small intestine (ileum)
- Large intestine
  - $10^9$-$10^{11}$/ml
  - $>350$ species
    - *E. coli* = 0.1% of total population
  - Primarily anaerobic
    - Facultative aerobes deplete oxygen
  - Adult excretes $3 \times 10^{13}$ bacteria/day
    - 25%-35% of fecal mass = bacteria
## Normal flora - Gastrointestinal tract

<table>
<thead>
<tr>
<th>Location (adult)</th>
<th>Bacteria/gram contents</th>
</tr>
</thead>
<tbody>
<tr>
<td>duodenum</td>
<td>$10^3$-$10^6$</td>
</tr>
<tr>
<td>jejunum and ileum</td>
<td>$10^5$-$10^8$</td>
</tr>
<tr>
<td>cecum and transverse colon</td>
<td>$10^8$-$10^{10}$</td>
</tr>
<tr>
<td>sigmoid colon and rectum</td>
<td>$10^{11}$</td>
</tr>
<tr>
<td>SITE</td>
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</tr>
<tr>
<td>-------------------</td>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>Gingival crevices</td>
<td>Anaerobes, Prevotella, Fusobacterium, Streptococcus, Actinomyces</td>
</tr>
<tr>
<td>Stomach</td>
<td>NONE</td>
</tr>
</tbody>
</table>
Normal flora of GI tract – stomach

*Helicobacter pylori*

**Harm**
- Causes gastric ulcers
- Probable association with duodenal ulcers
Normal flora of GI tract: SMALL INTESTINE
streptococci, lactobacilli, enterococci, enterics, anaerobic
rods and cocci

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Production of vitamins and nutrients</td>
<td>• Possible relationship with inflammatory conditions</td>
</tr>
<tr>
<td>• Competition with pathogens for colonization sites</td>
<td>• Transfer antibiotic resistance to pathogens</td>
</tr>
<tr>
<td>• Production of substances that inhibit pathogens</td>
<td></td>
</tr>
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<tr>
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</tr>
<tr>
<td>Colon (microaerophilic/anaerobic)</td>
<td>INFANTS Breast-fed: Bifidobacterium Bottle-fed: mixed flora, less lactobacilli ADULTS Bacteroides (predominant) Escherichia Bifidobacterium</td>
</tr>
<tr>
<td><strong>sterile at birth, but organisms are soon introduced with food</strong></td>
<td></td>
</tr>
</tbody>
</table>
Normal flora of GI tract: LARGE INTESTINE
Bacteroids, clostridia, bifidobacteria, lactic acid bacteria, enterococci, enterics

**Benefit**
- Competition with pathogens for colonization sites
- Production of substances that inhibit pathogens
- Stimulate development and activity of immune system

**Harm**
- Relationship with inflammatory bowel diseases
- Production of carcinogens and relationship with colon cancer
- Methanogenesis
Normal flora - Urogenital tract

- Upper urinary tract (kidneys, ureters, bladder) usually sterile
- Male anterior urethra Same as skin: enteric and enterococcus
- Vagina: complex microbiota
  - At birth Same as mother (PH 5)
  - Neonate Same as skin+enteric+ strept (PH 7)
  - At puberty Lactobacillus+same as skin+anaerobes+strep (PH 5)
  - At menopause: return to prepuberty flora
Normal flora of the VAGINA - during child-bearing age lactobacilli and other lactic acid bacteria

Benefit
- Competition with pathogens for colonization sites
- Production of lactic acid that inhibits pathogenic bacteria and yeasts

Harm
- none
What are the roles of Normal Flora:

1. **May be source of opportunistic infections**
   e.g. In-patients with impaired defense Mechanisms.

2. **Immunostimulation**
   a) They produce antibodies which may contribute to host defenses.
   b) Some of these antibodies may cross react with normal tissue components.
3) **Protection from External Invaders**

Because of the normal flora occupy body’s epithelial surfaces, they are able to prevent other bacteria from establishing themselves by blocking receptors (attachment), competing for essential nutrients or producing anti-bacteria substances.

*E.g.* Fatty acids, peroxides, Bacteriocins.
4) **Production of Carcinogens:** Some normal flora may modify, through their enzymes, some chemicals in our diets into carcinogens.

   e.g. Artificial sweeteners may be enzymatically modified into bladder carcinogens.

   Predominant and important flora of various body sites in normal health.
5) Nutrition
Some of the normal intestinal flora e.g. *E. coli* & *Bacteroids* produce Vitamin K in the gut which is available for use by host.

6) Stimulate development of certain tissues: Caecum and lymphatic tissues (Peyer’s patches) in GI tract and influence immunology of gut-associated lymphatics
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
- Bacterial synergism between normal flora and potential pathogens
- Low grade toxemia produced in host
- Endogenous disease and opportunistic infection
Opportunistic flora

- Some normal flora become opportunistic pathogens
  - *(Staphylococcus aureus, Streptococcus mutans, Enterococcus faecalis, Streptococcus pneumoniae, Pseudomonas aeruginosa, etc.)*

- Breach of skin/mucosal barrier: trauma, surgery, burns

- Bacterium at one site may be commensal, but might be pathogenic at another site
Opportunistic flora

- Growth of commensals may put patient at risk: Broad-spectrum antibiotic therapy decreases total number of bacterial in gut
- During repopulation, faster-growing aerobic Enterobacteriaceae over slower-replicating anaerobes increases probability of gram-negative bacteremia
- Cross-reactive responses to host tissue: Superantigen
- Chronic, low-grade inflammation
- Perturbation of cytokine network
Gastrointestinal flora

- Antibiotics overuse
- Antibiotic associated diarrhoea
- *C. difficile* -associated diarrhea (CDAD)
- Pseudomembranous colitis
  - toxic megacolon
Normal flora - Risks and Opportunistic
Probiotics/Prebiotics

- **Probiotic**
  - Oral administration of living organisms to promote health
  - Mechanism speculative: competition with other bacteria; stimulation of nonspecific immunity
  - Species specific: adherence and growth (tropism)

- **Prebiotic**
  - Non-digestible food that stimulates growth or activity of GI microbiota, especially bifidobacteria and lactobacillus bacteria (both of which are noninflammatory)
  - Typically a carbohydrate: soluble fiber
Guide to the Normal Bacterial Flora of Humans

**Staphylococci**

- Includes *Staphylococcus epidermidis* and *Staphylococcus aureus*

- Located on skin and most mucous membranes

*Staphylococcus epidermidis*, invariably found on skin and nasal membranes.
Corynebacteria

- Includes *Corynebacterium* and *Probionibacterium* 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
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 *Veilonella* 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.