Course: B.Sc. Microbiology

Semester IV.

MBIO CC409. Environmental Microbiology

Human Microbiota

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Microbiome

Micro – small; Biome -a large naturally occurring community of flora and fauna occupying a major habitat

- **Microbiome:** Microbial residents including bacteria, fungi, protozoa, and viruses colonizing the epithelial surfaces of humans (and other multicellular eukaryotes), such as the gut, oral cavity, skin, and hair, etc., including the number, their genetic material and environment is called microbiome.
- This term was term coined by **Joshua Lederberg**, a Nobel Prize laureate, "to signify the ecological community of **commensal, symbiotic, and pathogenic microorganisms** that literally share our body space.
- **Microbiomics:** It is the study of microbiome.
- **Microbiota:** The living microbes that constitute the microbiome are called microbiota.
- **Human microbiota:** It is the collection of microorganisms living **inside and on the surface** of human body.
- In December 2007, the National Institutes of Health launched the **Human Microbiome Project (HMP)** with the goal to allow better understanding of the importance and roles of the human microbiome in human health and disease.
- An understanding of the human microbiota and their microbiome provides:
- understanding about causes and consequences of microbial colonization in their respective microbiome.
- a greater insight into the possible infections that might result from injury to these body sites.
- an increased awareness of the role of normal micro biota in stimulating the host immune response can be gained.

Human microbiome

- With no exception, humans too are an important ecosystem for a wide variety of microorganisms.
- Average adult carries 10 times more microbial cells (10^{14}) than human cells (average about 10^{13}).
- The microbial colonization process begins on exposure to the vaginal microbiota shortly after birth and introduction to new microorganisms continues throughout infancy.
- Interaction between host and microbes are dynamic, such that microorganisms colonize a specific site on the host that meets its physiological needs.
- In some instances, after a microorganism contacts or enters a host, a positive mutually beneficial relationship occurs and becomes integral to the health of the host offering some protection from invading microorganisms.
- However, its members may themselves become pathogenic and produce disease under certain circumstances; they then are termed opportunistic microorganisms or pathogens.
- Opportunistic microorganisms often cause disease in compromised hosts. A compromised host is seriously debilitated and has a lowered resistance to infection. There are many causes of this condition, including malnutrition, alcoholism, cancer, diabetes, leukemia, another infectious disease, trauma from surgery or an injury, an altered normal microbiota from the prolonged use of antibiotics, and immunosuppression by various factors (e.g., drugs, viruses (HIV), hormones, and genetic deficiencies).

Human microbiota

- Unlike the host genome, which is relatively constant, the microbiome is dynamic and changes with early development, environmental factors such as diet and use of antibiotics and especially in response to disease.
- The most dramatic changes in composition occur in infancy and early childhood, while an adult's microbiota is relatively stable over time.
- Regardless of age, internal tisssues (eg., brain, blood, cerebrospinal fluid, muscle) of a healthy human are normally free of microorganisms.
- The intestinal microbiome of an infant is affected by gestational age (full term or premature), mode of delivery (vaginal birth or caesarean section), type of feed (breast milk or formula feeds), maternal nutritional status (overweight or undernourished) and use of antibiotics.
- For eg, babies born vaginally acquire most of the microorganism from their mother, whereas babies born by cesarean delivery acquire the microorganisms of their caretakers (nurses, doctors, midwives, parents, etc.)
- The complexity and plasticity of the infant microbiota during this early-life development is believed to be important in maintaining homeostasis with the host's immune system and has an impact on health later in life.
- Bacteria and archaeal species makes most of the normal microbiota, while others includes fungi (mostly yeasts), and protists are comparatively less.
- Bacteria common to human skin and mucosal surfaces of oral and gastrointestinal tract are represented by 5 phyla namely, actinobacteria, bacteroidetes, firmicutes, fusobacteria and proteobacteria.

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- In breast-fed infants, members of actinobacterial genus ***Bifidobacteria*** represents more than 90% of the culturable intestinal bacteria, while that of enterobacteriaceae and enterococci (members of phyla proteobacteria and firmicutes, respectively) in smaller proportions.
- Switching to cow's milk or solid food, results in loss of ***Bifidobacteria*** predominance, while members of firmicutes, proteobacteria and bacteroidetes (specially enterobacteria, enterococci, lactobacilli, clostridia, and ***Bacteroides*** species) increases and outcompete actinobacteria in a polysaccharide rich environment.
- **SKIN**
- They can be residents (normal) or transient. Residents normally grow on skin, becomes fixed in well defied distribution pattern. While transient are temporarily present, don't get firmly entrenches and are typically unable to multiply.
- The skin surrounding can be divided into 3 niches: dry, moist and sebaceous.
- Bacterial diversity : Dry (actinobacteria , bacteroidetes, proteobacteria) and firmicutes > moist (mostly firmicutes and actinobacteria) > sebaceous skin (actinobacteria dominates).
- **STOMACH** contains very few microorganisms due to its acidic pH.
- They are ***Streptococcus, Staphylococcus, Lactobacillus***, ***Peptostreptococcus*** species and yeast viz. ***Candida s***pecies.

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- **INTESTINE-**
- The distal portion of the small intestine and the entire large intestine have the largest microbial community in the body.
- These primarily consist of anaerobic, Gram-negative bacteria and Gram-positive rods. The metagenomic profile of colonic bacteria in adults includes 60-80% firmicutes, 20-40% bacteriodetes, and proteobacteria.
- Individuals whose microflora are dominated by *Bacteroides* or *Ruminococcus* spp. tend to have a diet rich in animal protein and saturated fats, while those who consume a largely plant-based diet host a large population of *Prevotella* spp.
- **GENITOURINARY TRACT-**
- The upper urinary tract (kidneys, ureters, and urinary bladder) is usually free of microorganisms.
- In both males and females, a few common bacteria (*Staphylococcus epidermidis, Enterococcus faecalis, and Corynebacterium* spp.) usually are cultured from the distal portion of the urethra.
- In the male, metagenomic sequencing suggests several anaerobic Gram-negative bacteria.
- In contrast, the adult female genital tract has a more complex and constantly changing microbiota. The culturable microorganisms are the acid-tolerant lactobacilli, primarily *Lactobacillus acidophilus*, often called Doderlein's bacillus. They ferment glycogen produced by the vaginal epithelium, forming lactic acid, resulting in the pH of the vagina and cervix is maintained between 4.4 and 4.6, inhibiting other microorganisms.

Normal human microbiota cultured from various body sites

Body System	Body Site	Microorganisms	
Eye	Conjunctiva	Coagulase-negative staphylococci *Hemophilus* spp.	*Staphylococcus aureus* *Streptococcus* spp.
	Outer ear	Coagulase-negative staphylococci Diphtheroids	*Pseudomonas* spp. Enterobacteria (occasionally)
Skin	Nonmucous membrane surfaces	Coagulase-negative staphylococci Diphtheroids *Propionibacterium acnes* *Staphylococcus aureus* *Streptococcus* spp.	*Bacillus* spp. *Malassezia furfur* *Candida* spp. *Mycobacterium* spp. (occasionally)
Respiratory tract	Nose	Coagulase-negative staphylococci *Streptococcus* spp. (including *S. pneumoniae*) *Staphylococcus aureus*	*Neisseria* spp. *Haemophilus* spp.
Gastrointestinal tract	Mouth and oropharynx	*Streptococcus* spp. (including *S. pneumonia*) Coagulase-negative staphylococci *Veillonella* spp. *Fusobacterium* spp. *Treponema* spp. *Porphyromonas* spp. *Prevotella* spp. *Neisseria* spp.	*Branhamella* spp. *Hemophilus* spp. Diphtheroids *Candida* spp. *Actinomyces* spp. *Eikenella corrodens* *Staphylococcus aureus*

Normal human microbiota cultured from various body sites

	Stomach	*Streptococcus* spp. *Staphylococcus* spp.	*Lactobacillus* spp. *Peptostreptococcus* spp.
	Small intestine	*Lactobacillus* spp. *Bacteroides* spp. *Clostridium* spp.	*Mycobacterium* spp. *Enterococcus* spp. Enterobacteria
	Large intestine	*Bacteroides* spp. *Fusobacterium* spp. *Clostridium* spp. *Peptostreptococcus* spp. *Escherichia* coli *Klebsiella* spp. *Proteus* spp. *Lactobacillus* spp.	*Enterococcus* spp. *Streptococcus* spp. *Pseudomonas* spp. *Acinetobacter* spp. Coagulase-negative staphylococci *Staphylococcus aureus* *Mycobacterium* spp. *Actinomyces* spp.
Genitourinary tract	Distal urethra	Coagulase-negative staphylococci Diphtheroids *Streptococcus* spp. *Mycobacterium* spp.	*Bacteroides* spp. *Fusobacterium* spp. *Peptostreptococcus* spp.
	Vagina	*Lactobacillus* spp. *Peptostreptococcus* spp. Diphtheroids *Streptococcus* spp.	*Clostridium* spp. *Bacteroides* spp. *Gardnerella vaginalis* *Candida* spp.

Role of human microbiota

- HMP is evaluating the role of microbial genes and their products have in maintaining homeostasis in the host.
- The human microbiome has extensive functions making it an essential organ of the body without which we would not function correctly. Some of the important functions are as follow :
- Production of short-chain fatty acids (SCFAs) such as acetic acid, propionic acid and butyric acid and serves as an energy source to the host intestinal epithelium
- Digestion of dietary fibre that cannot be digested by the stomach and small intestine viz., such as xyloglucans, that digested by a specific species of *Bacteroides;* fructo-oligosaacharides and oligosaachahrides, by *Lactobacillus* and *Bifidobacterium.*
- microbial synthesis of vitamins (riboflavin, biotin, cobalamin, Vit K)
- Fat and protein homeostasis
- Stimulate the normal development of the humoral and cellular mucosal immune systems
- Defense against pathogens
- Stimulate the development of certain tissues i.e., intestines, certain lymphatic tissues, capillary density, etc.
- However, not all microbiota lead to health benefits. Some induce inflammation under certain conditions.

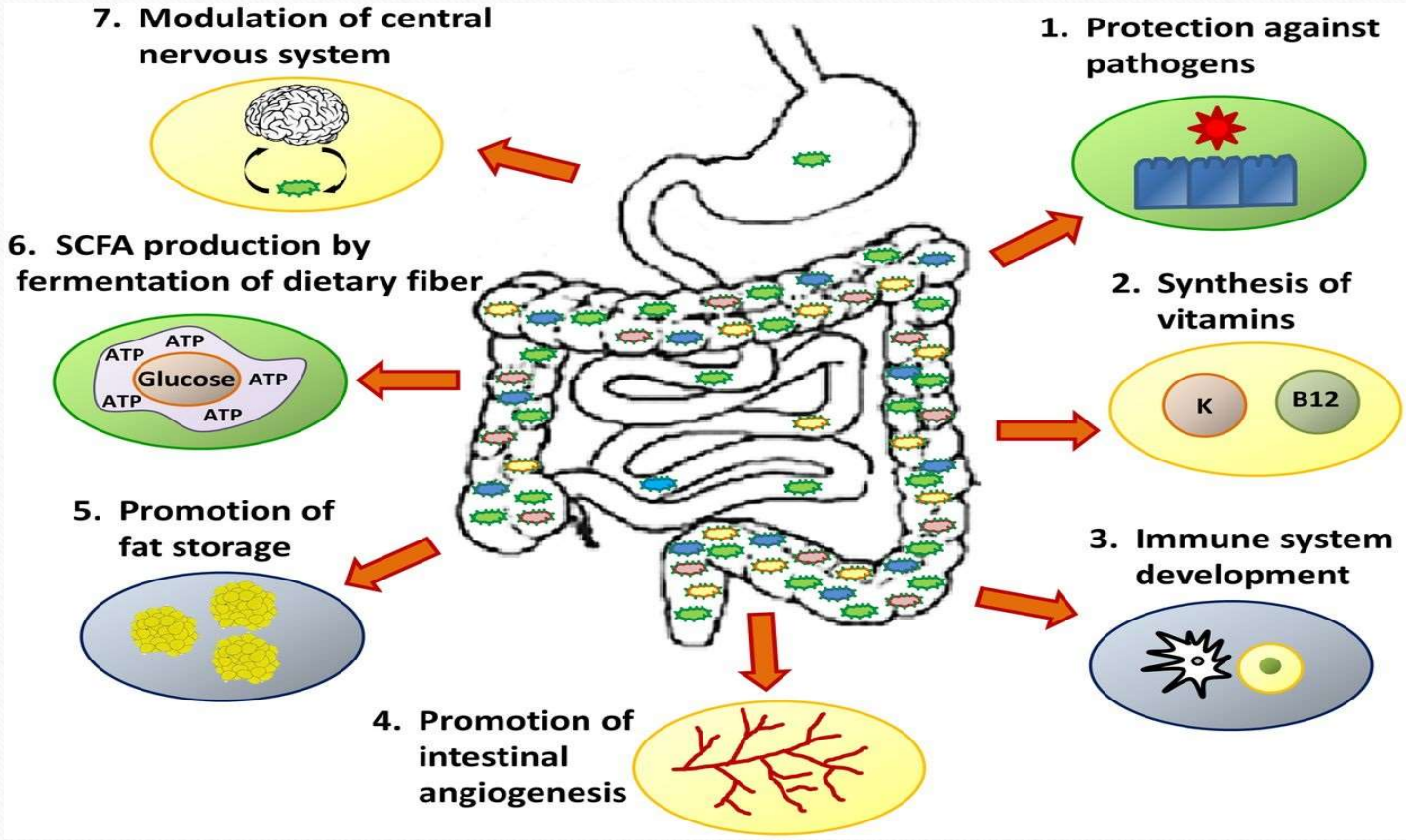

Fig. Role of human microbiota

Microbiome: health and disease

- Under homeostatic conditions, various members of the human microbiome viz., the symbiotic, commensal, pathobiontic and pathogenic members are in balance, referred to as symbiosis.
- Microbial dysbiosis i.e., imbalance within microbiome either due to reduced microbial diversity or due to changes in the relative proportions of taxa within a given community and result in proportional increases in pathobionts and pathogenic bacteria. Thus is associated with multiple disease states and can cause major health consequences.
- Pathobiont -Any potentially pathological (disease-causing) organism which, under normal circumstances, lives as a non-harming symbiont.

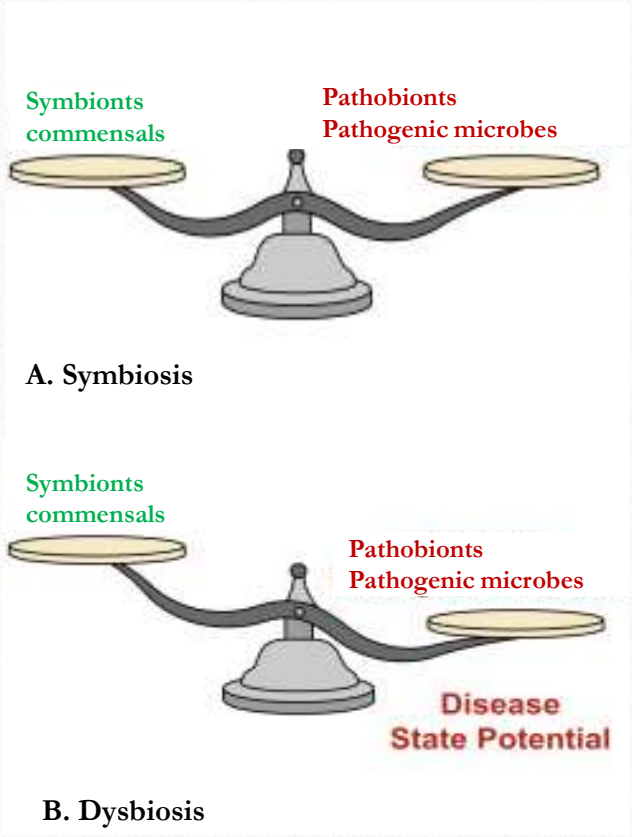

Fig. Microbe-host interaction

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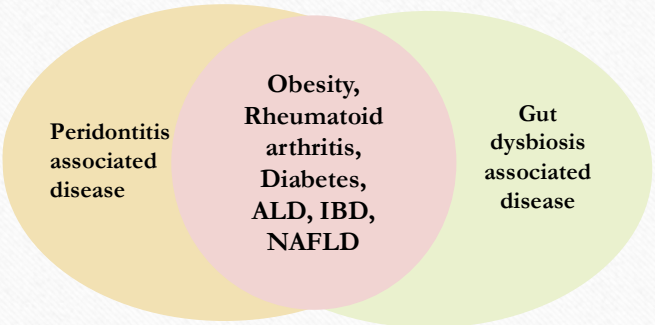
- The composition of the human microbiota is influenced by the use of antibiotics and by the lifestyle of the human host, including exercise, diet, hygiene preferences, etc.
- Any sort of dysbiosis of human microbiota affects the production of immune mediators and induces both chronic inflammation and metabolic dysfunction.
- For example, evidence suggests role of human oral microbiota in regulating oral diseases (dental cries, periodontal disease) as well as a wide range of systemic diseases.
- *Porphyromonas gingivalis* is associated with human periodontitis and gingivitis. It may often influence gut microbiota resulting in gut dysbiosis leading to a number of systemic diseases like, obesity, rheumatoid arthritis, diabetes Type 2, alcoholic liver disease (ALD), inflammatory bowel disease (IBD), nonalcoholic fatty liver disease (NAFLD), colon cancer, pancreatic cancer etc.



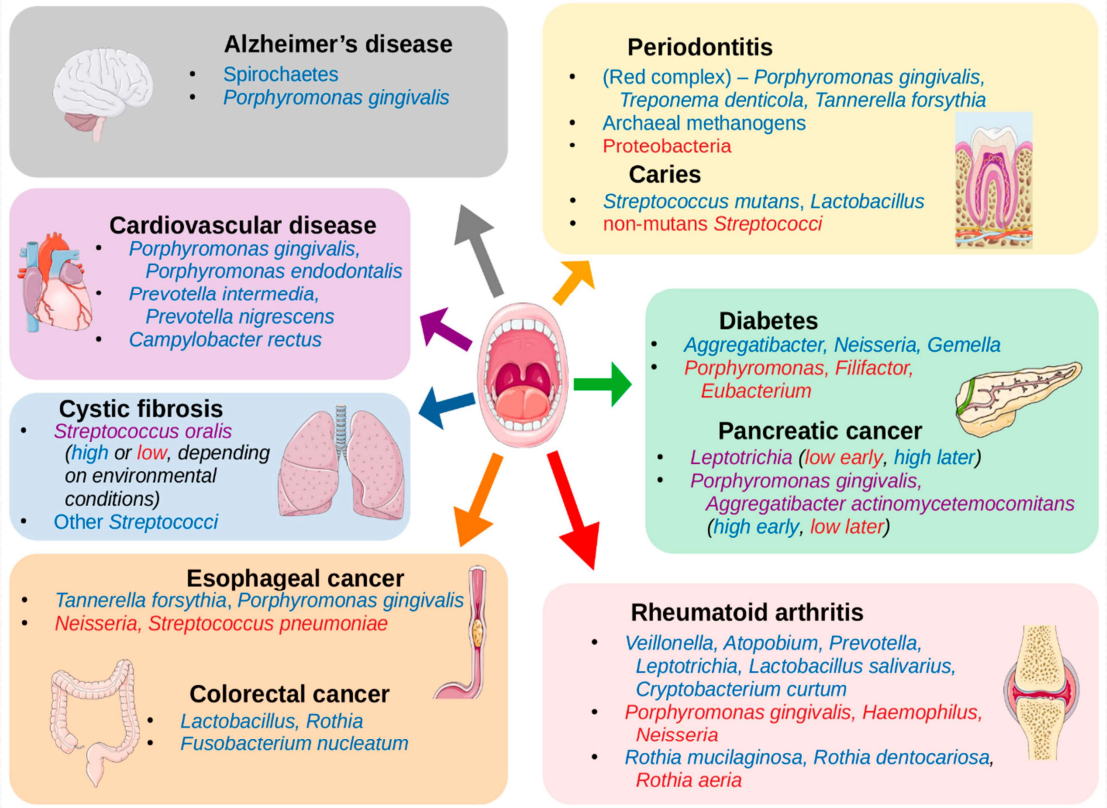


Fig. Oral and systemic diseases associated with the oral microbiome

- Microorganisms in blue - increased in abundance in the oral cavity in individuals presenting with the noted disease
- Microorganisms in Red- decreased.
- Microorganisms in Purple- may be either increased or decreased depending on the conditions or progression of the disease.

THANK YOU