RAMSADAY COLLEGE

NORMAL MICROBIAL FLORA OF THE HUMAN BODY

DEPARTMENT: MICROBIOLOGY

SEMESTER : 6th

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WHAT IS NORMAL MICROFLORA?

❖ The term “normal microbial flora” denotes the population of microorganisms that inhabit the skin and mucous membrane of healthy normal persons.

❖ The genomes of these microbial symbionts are collectively defined as the microbiome.

❖The **“normal microbiota” provides a first line of defense against microbial pathogens**, assist in digestion, play a role in toxin degradation, and contribute to maturation of the immune system.

❖The skin and mucous membranes always harbor a variety of microorganisms that can be arranged into two groups:

1) The **resident microbiota** consists of relatively fixed types of microorganisms regularly found in a given area at a given age; if disturbed, it promptly reestablishes itself and
2) The **transient microbiota** consists of nonpathogenic or potentially pathogenic microorganisms that inhabit the skin or mucous membranes for hours, days or weeks. They are derived from the environment, does not produce disease, and does not establish itself permanently on the surface.

If the resident microbiota is disturbded, transient microorganisms may colonize, proliferate and produce disesae. The microorganisms that are constantly present on body surfaces are commensals. Their flourishing in a given area depends on the physiological factors such as

1) Temperature
2) Moisture
3) The presence of certain nutrients and some inhibitory substances

TABLE 10–1 Normal Bacterial Microbiota

Skin

Staphylococcus epidermidis
Staphylococcus aureus (in small numbers)
Micrococcus species
α-Hemolytic and nonhemolytic streptococci (eg, *Streptococcus mitis*)
Corynebacterium species
Propionibacterium species
Peptostreptococcus species
Acinetobacter species
Small numbers of other organisms (*Candida* species, *Pseudomonas aeruginosa*, etc)

Nasopharynx

Any amount of the following: diphtheroids, nonpathogenic *Neisseria* species, α-hemolytic streptococci; *S epidermidis*, nonhemolytic streptococci, anaerobes (too many species to list; varying amounts of *Prevotella* species, anaerobic cocci, *Fusobacterium* species, etc)
Lesser amounts of the following when accompanied by organisms listed above: yeasts, *Haemophilus* species, pneumococci, *S aureus*, gram-negative rods, *Neisseria meningitidis*

Gastrointestinal tract and rectum

Various Enterobacteriaceae except *Salmonella, Shigella, Yersinia, Vibrio,* and *Campylobacter* species
Glucose non-fermenting gram-negative rods
Enterococci
α-Hemolytic and nonhemolytic streptococci
Diphtheroids
Staphylococcus aureus in small numbers
Yeasts in small numbers
Anaerobes in large numbers (too many species to list)

Genitalia

Any amount of the following: *Corynebacterium* species, *Lactobacillus* species, α-hemolytic and nonhemolytic streptococci, nonpathogenic *Neisseria* species
The following when mixed and not predominant: enterococci, Enterobacteriaceae and other gram-negative rods, *Staphylococcus epidermidis*, *Candida albicans*, and other yeasts
Anaerobes (too many to list); the following may be important when in pure growth or clearly predominant: *Prevotella, Clostridium,* and *Peptostreptococcus* species

ROLE OF NORMAL MICROBIAL FLORA

Normal flora play an **important role in maintaining health and normal function**. These are:

- **members of the resident microbiota in the intestinal tract synthesize vitamin K and several B vitamins which aid in the absorption of nutrients**
- On mucous membranes and skin, the resident microbiota may prevent colonization by pathogens and possible disease through **"bacterial interference".** The mechanism of bacterial interference may involve:

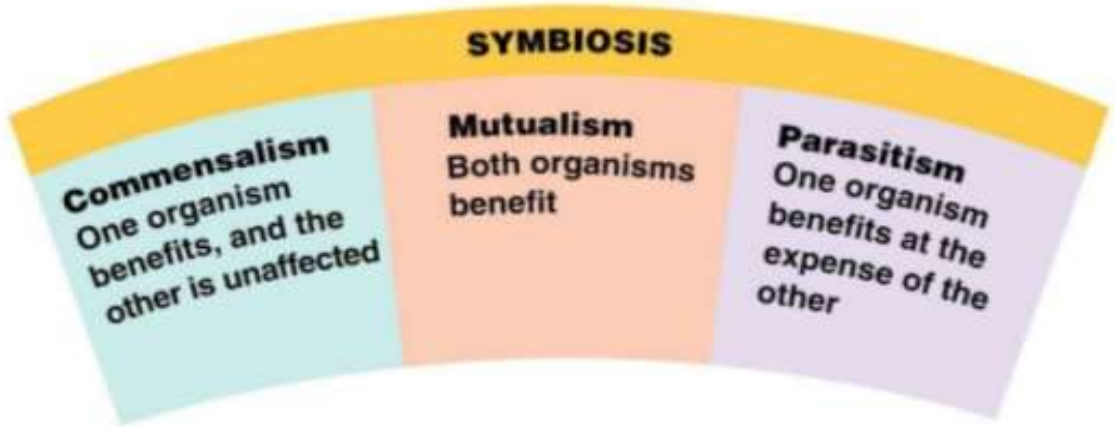
a) **competition for receptors or binding sites on the host cells, thus prevent or interfere with colonisation/invasion of the body by pathogens.**
b) **competition for nutrients**
c) **mutual inhibition by metabolic or toxic products**
d) **mutual inhibition by antibiotic materials or bacteriocins which exhibit harmful effect on pathogens**

- They become pathogenic when host defense failed.

Host - flora interactions

- Members of the normal flora form part of the host and include:

Saprophytes — Commensals
Facultative pathogens and — True pathogens



NORMAL MICROBIAL FLORA OF THE SKIN

- **The skin is the human body's largest organ, colonized by a diverse array of microorganisms, most of which are harmless or even beneficial to the host**.

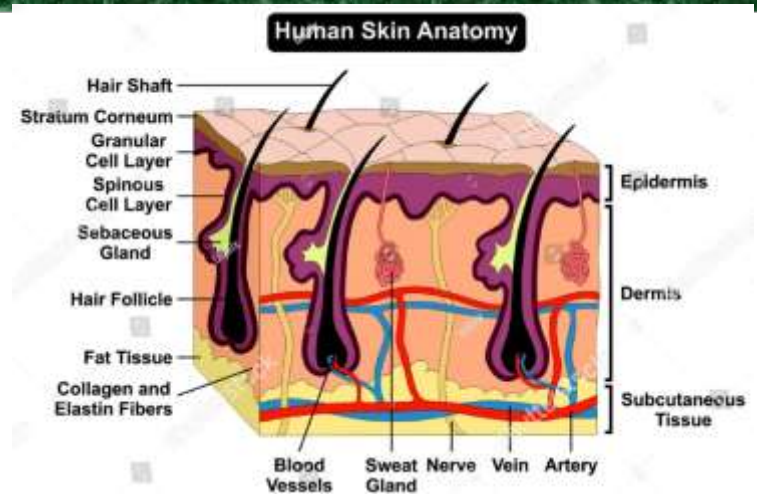
- Because of its constant exposure to and contact with the environment, the skin is particularly apt to contain transient microorganisms.

- The predominant resident microorganisms of the skin are:

- aerobic and anaerobic diphtheroid bacilli (eg, ***Corynebacterium***, ***Propionibacterium***)
- nonhemolytic aerobic and anaerobic staphylococci (***Staphylococcus epidermidis*** and other coagulase-negative staphylococci, occasionally ***Staphylococcus aureus*** and ***Peptostreptococcus*** species)
- Gram positive, aerobic, spore-forming bacilli that are ubiquitous in air, water, and soil
- α-hemolytic streptococci (viridans streptococci) and Enterococci (***Enterococcus*** species)
- Gram negative coliform bacilli and ***Acinetobacter.***

- **Factors that may be important in eliminating nonresident microorganisms from the skin are:**

1) **Low pH**
2) **The fatty acids in sebaceous secretion and**
3) **The presence of lysozyme**



- Neither profuse sweating nor washing and bathing can eliminate or significantly modify the normal resident flora.
- The number of superficial microorganisms may be diminished by vigorous daily scrubbing with soap containing hexachlorophene or other disinfectants, but the flora is readily replenished from sebaceous and sweat glands.
- **In addition to being a physical barrier, the skin is an immunologic barrier. Keratinocytes continuously sample the microbiota colonizing the skin surface through Pattern Recognition Receptors (eg. Toll-like receptor, mannose receptors, NOD-like receptors). The activation of keratinocyte pattern recognition receptors by pathogen-associated molecular patterns initiates the innate immune response, resulting in the secretion of antimicrobial peptides, cytokines and chemokines.**
- Despite being constantly exposed to large numbers of microorganisms, the skin can distinguish between harmless commensals and harmful pathogenic microorganisms but the mechanism for this selectivity is not clear.

NORMAL MICROBIAL FLORA OF THE CONJUNCTIVA

- ✓ The conjunctiva is relatively free from organisms due to the flushing action of tears, which contain antibacterial lysozyme.

- ✓ The predominant organisms of the conjunctiva are:
- ❖ Diptheroids (***Corynebacterium xerosis***)
- ❖ ***Staphylococcus epidermidis***
- ❖ Non-hemolytic Streptococci
- ❖ ***Neisseriae*** and gram-negative bacilli resembling haemophili (***Moraxella*** species) are also frequently present.

NORMAL MICROBIAL FLORA OF THE MOUTH AND UPPER RESPIRATOEY TRACT

✓**The flora of the nose consists of prominent corynebacteria, staphylococci (*S epidermidis, S aureus), and streptococci.***

✓ **Vaginally delivered infants harbor bacterial communities** (in all body habitats) that are most similar in composition to the **vaginal communities of the mothers**; **C-section babies lack bacteria from the vaginal community (eg, *Lactobacillus, Prevotella, Atopobium, and Sneathia spp.).*** Infants **delivered via C-section harbor bacterial communities** (across all body habitats) that are most similar to the **skin communities of the mothers (eg, *Staphylococcus, Corynebacterium, or Propionibacterium spp.).***

✓Within 4–12 hours after birth, **viridans streptococci** become established as the most prominent members of the resident flora and remain so for life. These organisms probably originate in the respiratory tracts of the mother and attendants.

✓**Early in life**, aerobic and anaerobic staphylococci, gram-negative diplococci (neisseriae, *Moraxella catarrhalis),* diphtheroids, and occasional lactobacilli are added. **When teeth begin to erupt**, the anaerobic spirochetes, *Prevotella* species (especially *Prevotella melaninogenica), Fusobacterium* species, *Rothia species, and Capnocytophaga species* establish themselves along with some anaerobic vibrios and lactobacilli. ***Actinomyces species are normally* present in tonsillar tissue and on the gingivae in adults, and various protozoa may also be present**. **Yeasts (*Candida* species) occur in the mouth**.

✓ In the pharynx and trachea, a similar flora establishes itself, but few bacteria are found in normal bronchi. Small **bronchi and alveoli are normally sterile. The predominant organisms in the upper respiratory tract, particularly the pharynx, are nonhemolytic and α-hemolytic streptococci and neisseriae. Staphylococci, diphtheroids, haemophili, pneumococci, mycoplasmas, and prevotellae are also encountered.**

The Role of the Normal Mouth Microbiota in Dental Plaque and Caries

Soon after an infant is born, the mouth is colonized by microorganisms from the surrounding environment. Initially the microbiota belongs mostly to the genera *Streptococcus, Neisseria, Actinomyces, Veillonella, and Lactobacillus*, as well as some yeasts. Most microorganisms that initially invade the oral cavity are aerobes and obligate anaerobes. When the first teeth erupt, anaerobes (*Porphyromonas, Prevotella, and Fusobacterium* spp.) become dominant due to the anoxic nature of the space between the teeth and gums. As the teeth grow, *Streptococcus parasanguis and S. mutans* attach to enamel surfaces.

Dental Diseases

Only a few of the symbiotic bacteria in the oral cavity can be considered true opportunistic dental pathogens, or odontopathogens. These few odontopathogens are responsible for the most common bacterial diseases in humans: **tooth decay and periodontal disease.**

Dental Plaque

➢The human tooth has a natural defense mechanism against bacterial colonization that complements the protective role of saliva. The hard enamel surface selectively absorbs acidic glycoproteins (mucins) from saliva, forming a membranous layer called the acquired enamel pellicle.

➢This pellicle, or organic covering, contains many sulfate (SO_4^{2-}) and carboxylate (—COO^-) groups that confer a net negative charge to the tooth surface. Because most bacteria also have a net negative charge, there is a natural repulsion between the tooth surface and bacteria in the oral cavity. Unfortunately, this natural defense mechanism breaks down when dental plaque forms.

➢**Dental plaque is one of the densest collections of bacteria in the body**—perhaps the source of the microorganisms seen under a microscope by Antony van Leeuwenhoek in the seventeenth century.

➢**Dental plaque formation begins with the initial colonization of the pellicle by *Streptococcus gordonii, S. oralis, and S. mitis* (figure 39.32).**

➢**These bacteria selectively adhere to the pellicle by specific ionic, hydrophobic, and lectin like interactions. Once the tooth surface is colonized, subsequent attachment of other bacteria results from a variety of specific coaggregation reactions.**

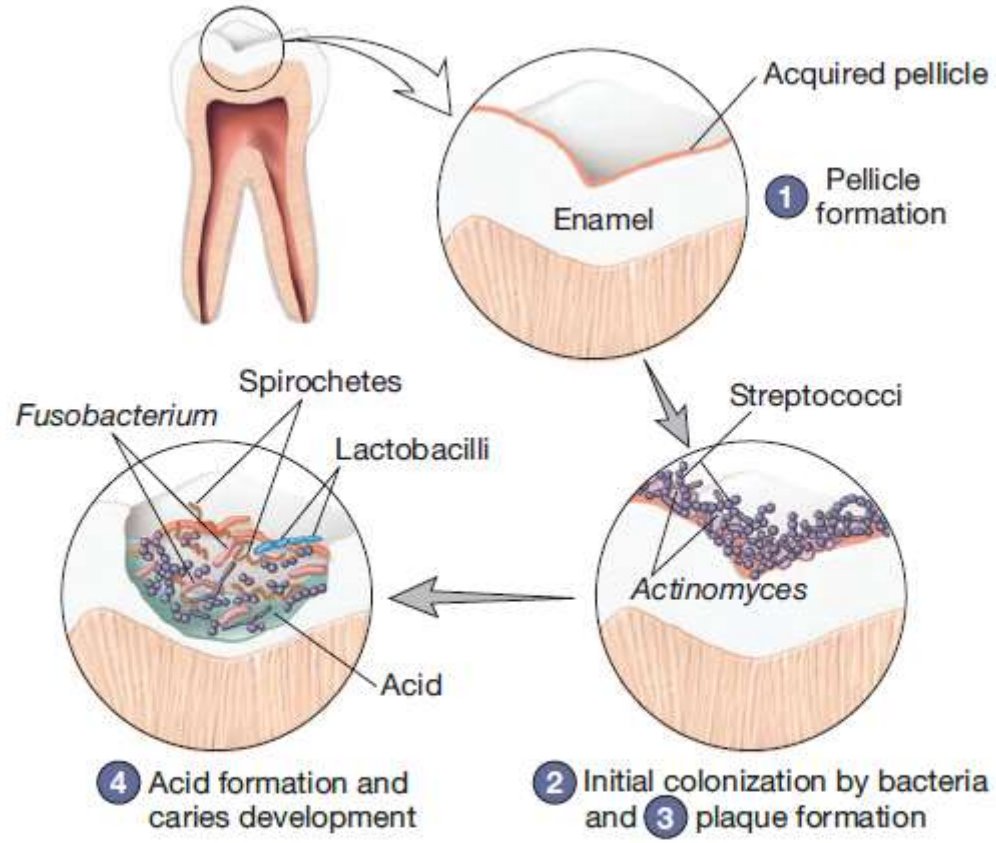


Figure 39.32 Stages in Plaque Development and Cariogenesis. A drawing of a microscopic view of pellicle and plaque formation, acidification, and destruction of tooth enamel.

➢***S. mutans and S. sobrinus*** **become established on the tooth surface by attaching to these initial colonizers (figure 39.32).** ***S. mutans and S. sobrinus*** **produce extracellular enzymes that polymerize the glucose moiety of sucrose into a heterogeneous group of extracellular, water-soluble, and water-insoluble polysaccharides. These act like a cement that binds bacterial cells together, forming a plaque ecosystem that is also a biofilm**.

➢The fructose by-product can be used in fermentation. **Once plaque becomes established, the surface of the tooth becomes anoxic**. This leads to the growth of strictly anaerobic bacteria (*Bacteroides melaninogenicus, B. oralis, and Veillonella alcalescens),* Especially between teeth and in the dental-gingival crevices (**figure 39.33).**

Figure 39.33 The Microscopic Appearance of Plaque. Scanning electron micrograph of plaque with long filamentous forms and "corn cobs" that are the mixed bacterial aggregates.

In addition, bacteria produce lactic and possibly acetic and formic acids from sucrose and other sugars. Because plaque is not permeable to saliva, the acids are not diluted or neutralized, and they demineralize the enamel to produce a lesion on the tooth. It is this chemical lesion that initiates dental decay.

Dental Decay (Caries)

❖**Caries is a disintegration of the teeth beginning at the surface and progressing inward.**

❖**As fermentation acids move below the enamel surface, they dissociate and react with the hydroxyapatite of the enamel to form soluble calcium and phosphate ions. As the ions diffuse outward, some reprecipitate as calcium phosphate salts in the tooth's surface layer to create an outer layer overlying a porous subsurface area.** Between meals and snacks, the pH returns to neutrality and some calcium phosphate reenters the lesion and crystallizes. The result is a demineralization-remineralization cycle.

❖**When an individual eats foods high in sucrose for prolonged periods, acid production overwhelms the repair process, and demineralization is greater than remineralization.** This **leads to dental decay or caries (Latin, rottenness). Once the hard enamel has been breached, bacteria can invade the dentin and pulp of the tooth and cause its death** (figure 39.33).

Control of dental caries:

No drugs are available to prevent dental caries. The main strategies for prevention include

1) minimal ingestion of sucrose, good nutrition with adequate protein intake
2) Reduction of acid production in the mouth by limitation of available carbohydrates
3) daily brushing, flossing, and rinsing with mouthwashes; and
4) professional cleaning at least twice a year to remove plaque.
5) the use of fluorides in toothpaste, drinking water, and mouthwashes or fluoride and sealants applied professionally to the teeth protects against lactic and acetic acids and reduces tooth decay.

Periodontal Disease

Periodontal disease refers to a diverse group of inflammatory diseases that affect the periodontium and is the most common chronic infection in adults.

Figure 39.34 **Periodontal Disease.** Notice the plaque on the teeth (arrow), especially at the gingival (gum) margins, and the inflamed gingiva.

The **periodontium is the supporting** structure of a tooth and includes the cementum, the periodontal membrane, the bones of the jaw, and the gingivae (gums). The gingiva is dense, fibrous tissue and its overlying mucous membrane that surrounds the necks of the teeth.

The gingiva helps to hold the teeth in place. Disease is initiated by the formation of **subgingival plaque,** the plaque that forms at the dentogingival margin and extends down into the gingival tissue. A number of bacterial species contribute to tissue damage.

The result is an initial inflammatory reaction known as **periodontitis,** which is caused by the host's immune response to both the plaque bacteria and the tissue destruction. This leads to swelling of the tissue and formation of periodontal pockets. Bacteria colonize these pockets and cause more inflammation, which leads to formation of a periodontal abscess, bone destruction (periodontosis), inflammation of the gingiva (gingivitis), and general tissue necrosis (**figure 39.34).** If the condition is not treated, the tooth may fall out of its socket.

Control of periodontal disease requires removal of calculus (calcified deposit) and good mouth hygiene.

NORMAL MICROBIAL FLORA OF LOWER RESPIRATORY TRACT

The **lower respiratory tract does not have normal microbiota**. This is because microorganisms are removed in at least three ways:

1) a continuous stream of mucus is generated by the goblet cells. This entraps microorganisms, and the ciliated epithelial cells continually move the entrapped microorganisms out of the respiratory tract,
2) alveolar macrophages phagocytize and destroy microorganisms.
3) Finally, a bactericidal effect is exerted by the enzyme lysozyme, present in nasal mucus.

NORMAL MICROBIAL FLORA OF GASTROINTESTINAL TRACT

The very acidic pH (2 to 3) of the gastric contents kills most microorganisms. As a result, the stomach usually contains less than 10 viable bacteria per milliliter of gastric fluid. These are mainly: ***Streptococcus, Staphylococcus, Lactobacillus, Peptostreptococcus*** **spp. and yeasts such as** ***Candida spp.***

Microorganisms may survive if they pass rapidly through the stomach or if the organisms ingested with food are particularly resistant to gastric pH (e.g., mycobacteria).

The **small intestine is divided into three anatomical areas: duodenum, jejunum, and ileum.**

1) The duodenum (the first 25 cm of the small intestine) contains few microorganisms because of the combined influence of the **stomach's acidic juices and the inhibitory action of bile and pancreatic secretions that are added here**. Of the bacteria present, Gram-positive cocci and rods comprise most of the microbiota.
2) ***Enterococcus faecalis*, lactobacilli, diphtheroids, and the yeast *Candida albicans* are occasionally found in the jejunum.**
3) In the distal portion of the small intestine (ileum), the microbiota begins to take on the characteristics of the colon microbiota. **It is within the ileum that the pH becomes more alkaline**. As a result, anaerobic Gram-negative bacteria and members of the family *Enterobacteriaceae* become established.

The **large intestine or colon** has the largest microbial community in the body. Microscopic counts of feces approach 10^{12} organisms per gram wet weight. Over 1,000 different bacterial species have been identified in human feces. These microorganisms consist primarily of anaerobic, Gram-negative bacteria and Gram-positive rods.

The metagenomic profile of colonic bacteria in healthy adults includes 60–80% firmicutes, 20–40% bacteriodetes, with the remaining largely proteobacteria and actinobacteria.

Under normal conditions, the resident microbial **community is self-regulating. Competition and mutualism between different microorganisms and between the microorganisms and their host maintains a status quo.**

Gastrointestinal tract	Mouth and oropharynx	*Streptococcus* spp. (including *S. pneumoniae*) 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*
	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.

NORMAL MICROBIAL FLORA OF 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 (*S. epidermidis, E. faecalis, and Corynebacterium* spp.) usually are cultured from the distal portion of the urethra.

In contrast, **the adult female genital tract**, because of its large surface area and mucous secretions, has a complex microbiota that constantly changes with a woman's menstrual cycle. **The culturable microorganisms are acid-tolerant lactobacilli, primarily *Lactobacillus acidophilus*, often called *Döderlein's* bacillus. They ferment glycogen produced by the vaginal epithelium, forming lactic acid. As a result, the pH of the vagina and cervix is maintained between 4.4 and 4.6, inhibiting other microorganisms.** In addition to *L. acidophilus*, metagenomic sequencing has identified a variety of anaerobic Gram-negative and Gram-positive bacteria in the female genitourinary tract. Some of these include those that normally inhabit moist skin areas.

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.

THANK YOU