The Host-Microbe Relationship

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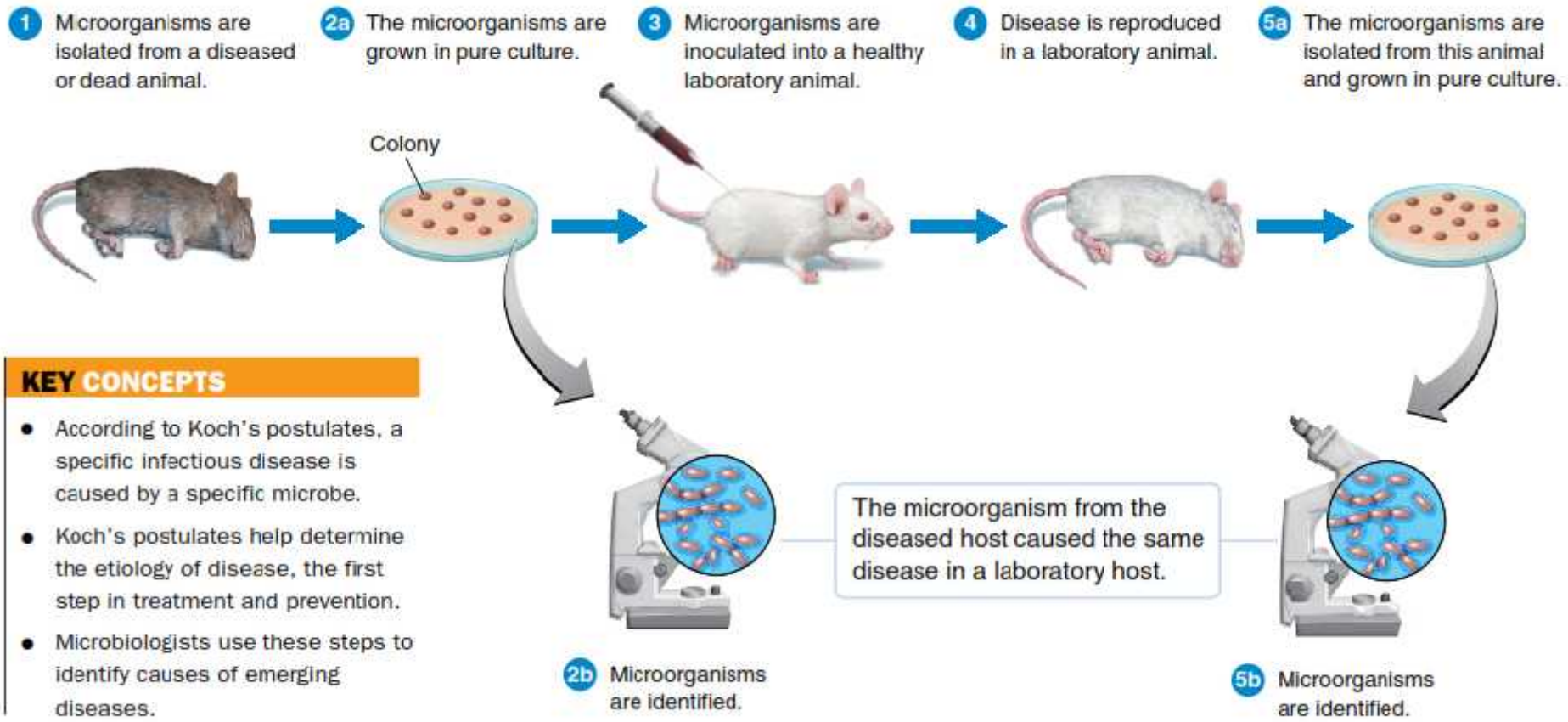
Epidemics of infectious disease are often compared with forest fires. Once fire has spread through an area, it does not return until new trees have grown up. Epidemics in humans develop when a large population of susceptible individuals is present. If most individuals are immune, then an epidemic will not occur.

—Andrew Cliff and Peter Haggett, British Geographer

Koch's Postulates: Understanding Disease



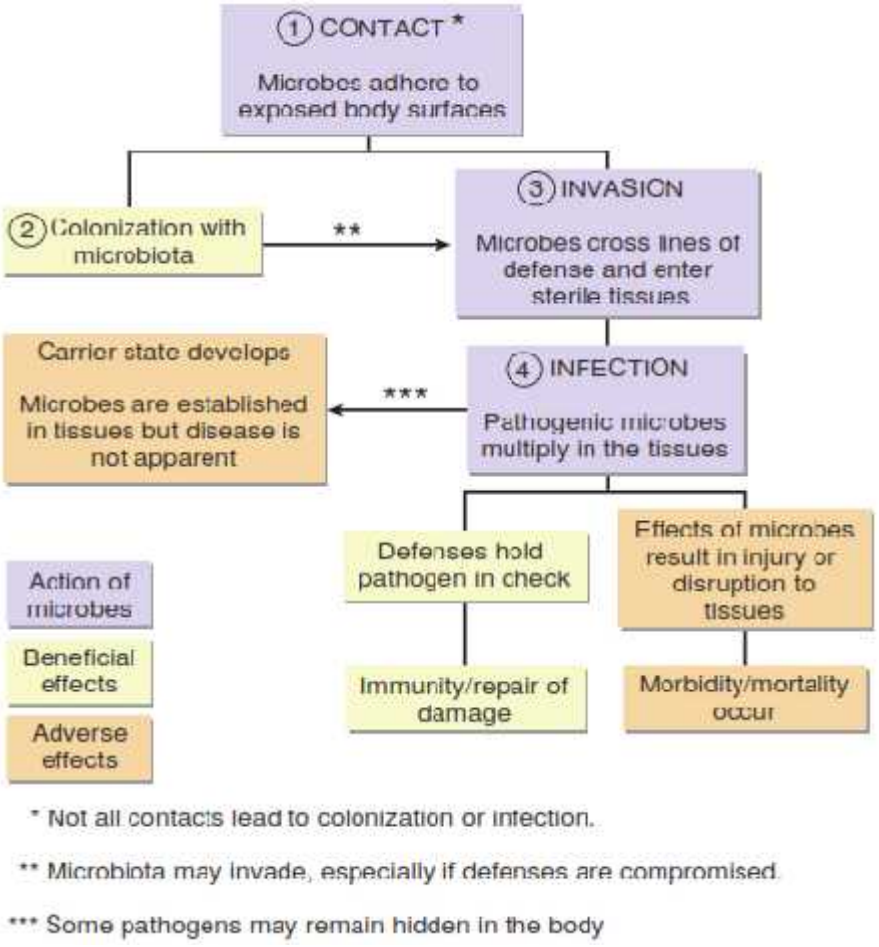
KEY CONCEPTS

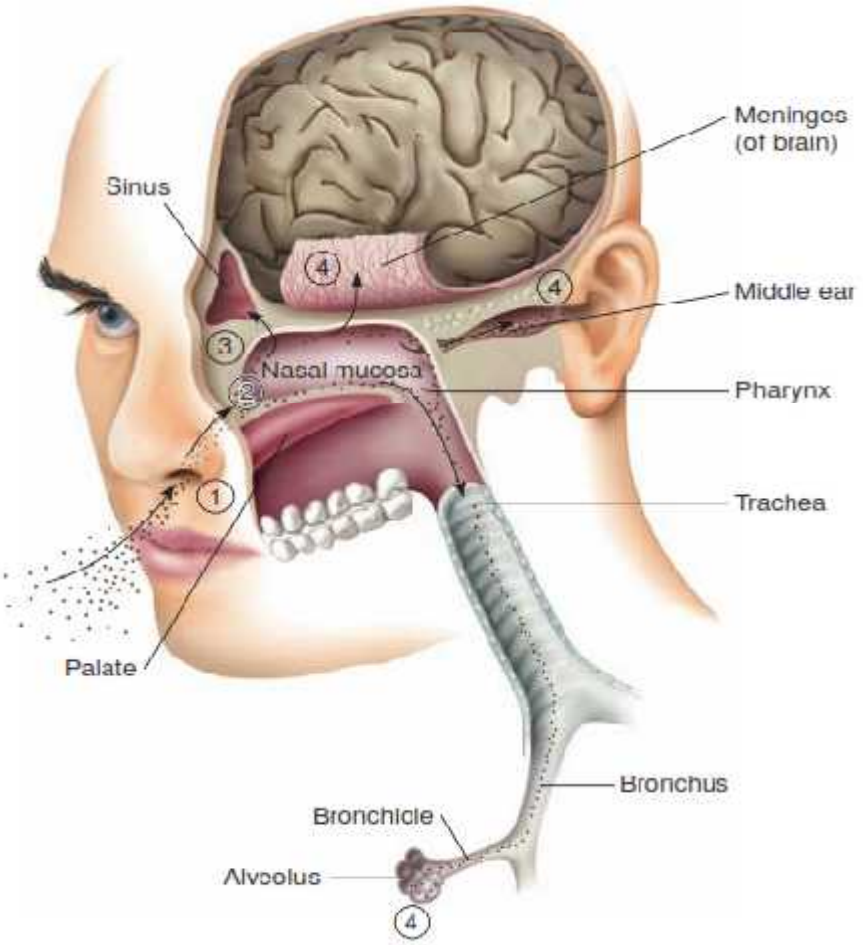
- According to Koch's postulates, a specific infectious disease is caused by a specific microbe.
- Koch's postulates help determine the etiology of disease, the first step in treatment and prevention.
- Microbiologists use these steps to identify causes of emerging diseases.

Associations between Microbes & Humans

Case of contact with a pathogen such as *Streptococcus pneumoniae* (the pneumococcus).

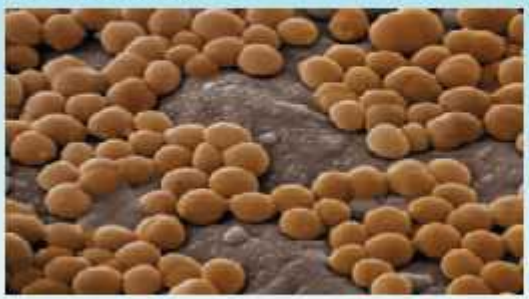
This bacterium can be harbored harmlessly in the upper respiratory tract, but it may also invade and infect the ear, cranium, and lower respiratory tract



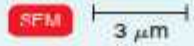


SYMBIOSIS

Commensalism: One organism benefits, and the other is unaffected

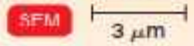


(a) *Staphylococcus epidermidis* bacteria on the skin

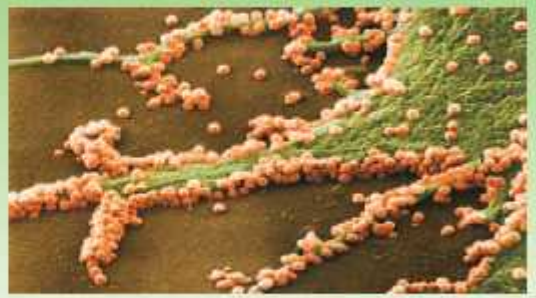


Mutualism: Both organisms benefit

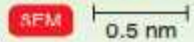
(b) *E. coli* bacteria (red) in the large intestine

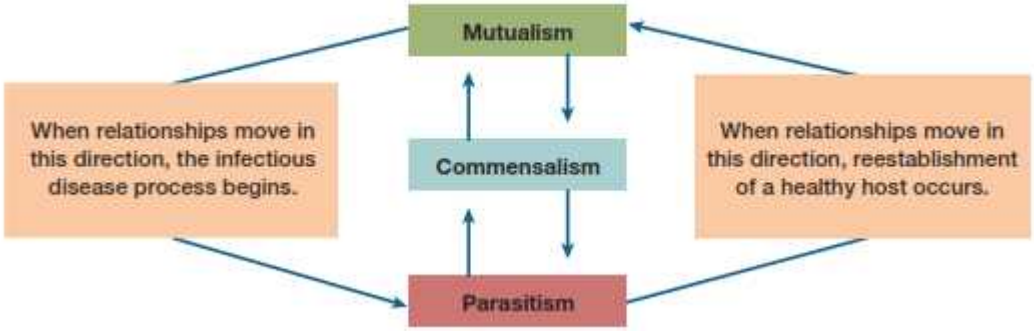


Parasitism: One organism benefits at the expense of the other



(c) Influenza viruses (orange) on a host cell (green)





Term	Definition
Microbiota	Community of microbes that live in and on an individual; can vary substantially between environmental sites and host niches in health and disease
Normal flora	Microbiota
Microbiome	Aggregate collection of microbial genomes in the microbiota
Core microbiome	Commonly shared microbial species among individuals at specific body sites; although typically represented by a limited number of species, these comprise the largest proportion of the microbial population
Secondary microbiome	Microbial species that contribute to the unique diversity of individuals at specific body sites; typically present in proportionately small numbers

Term	Definition
Functional redundancy	Required functions (e.g., metabolism of nutrients, regulation of the immune response) that are provided by the diverse members of the microbiota
Taxonomic diversity	The diverse number of species that comprise the microbiota
Prebiotic	Food ingredient that supports the growth of one or more members of the microbiota
Probiotic	Live organism that when ingested is believed to provide benefit to the host

Sites That Harbor Normal Resident Microbes

- Skin and its contiguous mucous membranes
- Upper respiratory tract
- Gastrointestinal tract (various parts)
- Outer opening of urethra
- External genitalia
- Vagina
- External ear and canal
- External eye (lids, lash follicles)

Sterile (Microbe-Free) Anatomical Sites and Fluids

All Internal Tissues and Organs

Heart and circulatory system	Bones
Liver	Ovaries/testes
Kidneys and bladder	Glands (pancreas, salivary)
Lungs	Sinuses
Brain and spinal cord	Middle and inner ear
Muscles	Internal eye

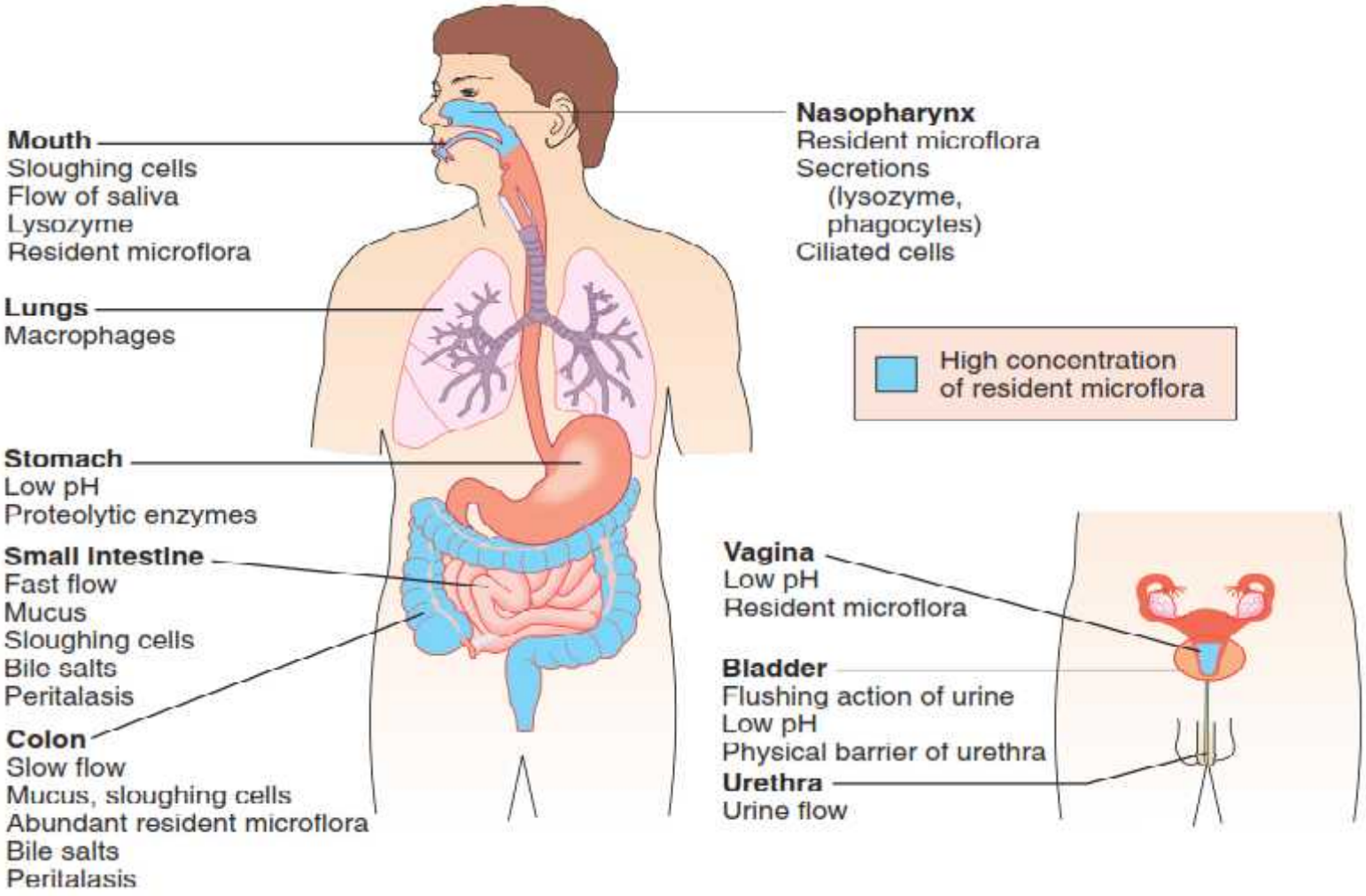
Fluids within an Organ or Tissue

Blood
Urine in kidneys, ureters, bladder
Cerebrospinal fluid
Saliva prior to entering the oral cavity
Semen prior to entering the urethra
Amniotic fluid surrounding the embryo and fetus

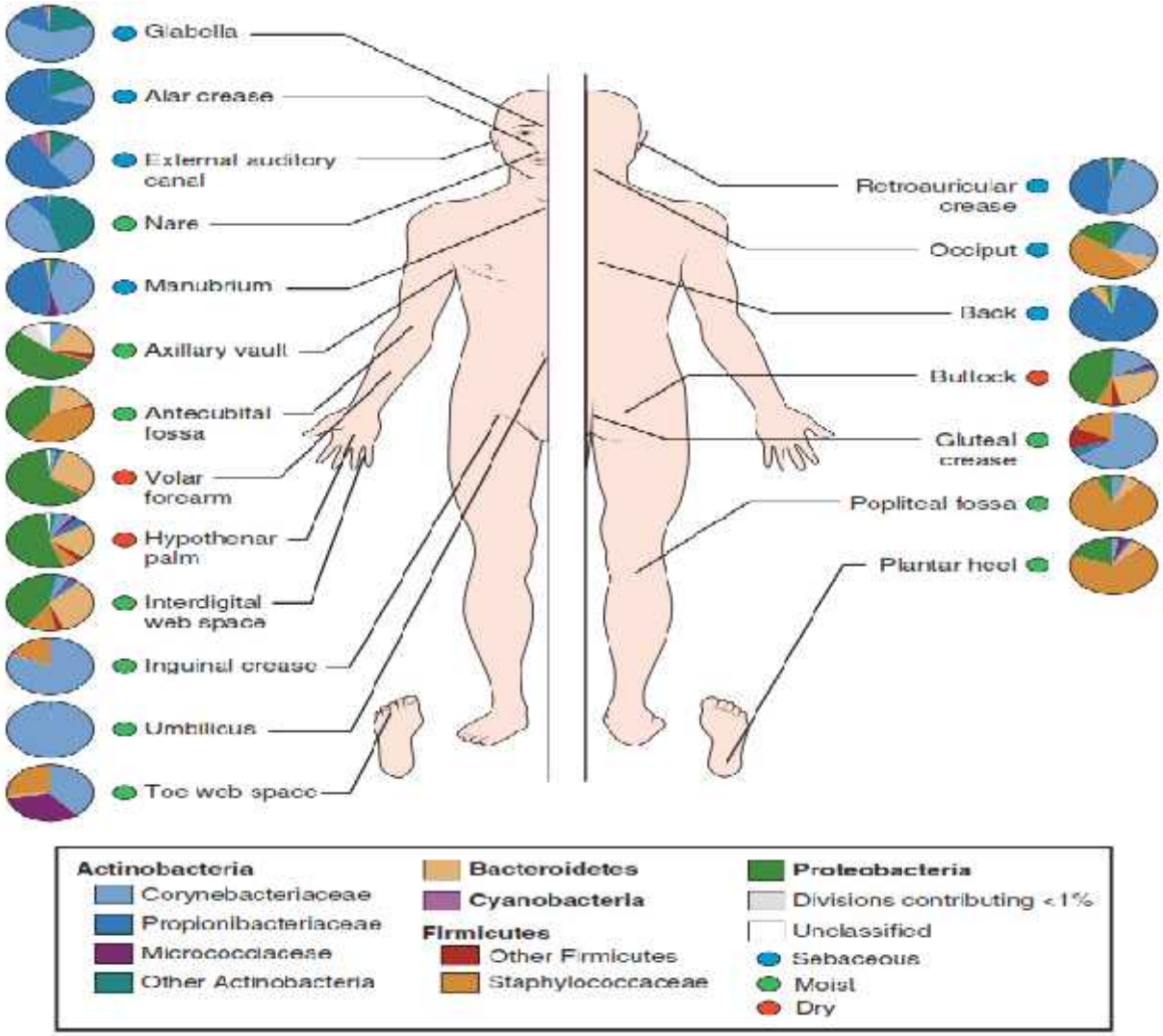
Normal Flora

- Is found on body surfaces contiguous with the outside environment
- Is semi-permanent, varying with major life changes
- Can cause infection
  - if misplaced, e.g., fecal flora to urinary tract or abdominal cavity, or skin flora to catheter
  - or, if person becomes compromised, normal flora may overgrow (oral thrush)
- Contributes to health
  - protective host defense by maintaining conditions such as pH so other organisms may not grow
  - serves nutritional function by synthesizing: K and B vitamins

Protective Characteristics Associated with The Mucosal Linings of Different Internal Body Surfaces



Topographical Distribution of Bacteria on Skin Sites



As at other body sites, the distribution of the skin microbiome is dependent on the microenvironment of the sampled site, such as sebaceous or oily (blue circles), moist (green circles), and dry, flat surfaces (red circles).

Life on Humans: Sites Containing Well-Established Microbiota & Representative Examples

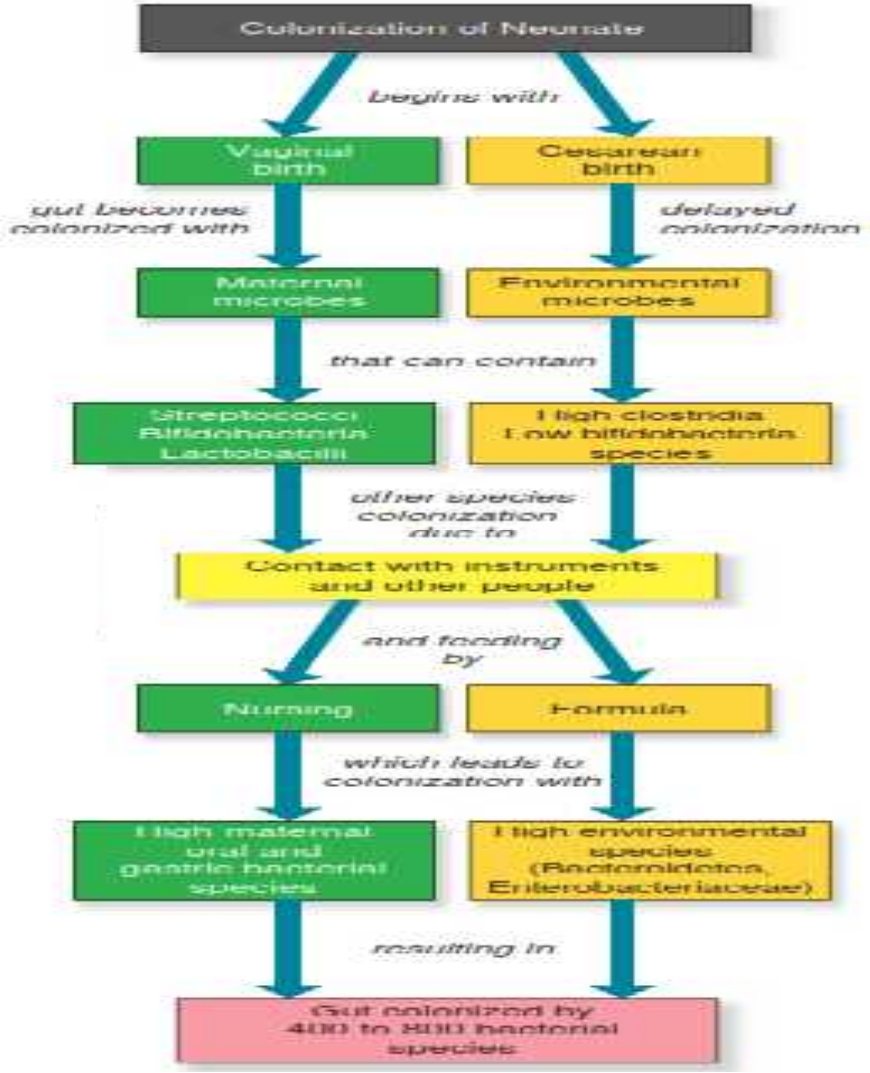
Anatomic Sites	Common Genera	Remarks
Skin	**Bacteria:** *Staphylococcus, Micrococcus, Corynebacterium, Propionibacterium, Streptococcus*	Microbes live only in upper dead layers of epidermis, glands, and follicles; dermis and layers below are sterile.
	Fungi: *Candida, Malassezia*	Dependent on skin lipids for growth
	Arthropods: *Demodix* mite	Present in sebaceous glands and hair follicles
Gastrointestinal Tract		
Oral cavity	**Bacteria:** *Streptococcus, Neisseria, Veillonella, Fusobacterium, Lactobacillus, Bacteroides, Actinomyces, Eikenella, Treponema, Haemophilus*	Colonize the epidermal layer of cheeks, gingiva, pharynx; surface of teeth; found in saliva in huge numbers
	Fungi: *Candida* sp.	Can cause thrush
	Protozoa: *Entamoeba gingivalis*	Inhabit the gingiva of persons with poor oral hygiene
Large intestine and rectum	**Bacteria:** *Bacteroides, Fusobacterium, Bifidobacterium, Clostridium,* fecal streptococci and staphylococci, *Lactobacillus,* coliforms (*Escherichia, Enterobacter*), *Proteus* sp.	Areas of lower gastrointestinal tract other than large intestine and rectum have sparse or nonexistent residents. Microbiota consist predominantly of strict anaerobes; other microbes are aerotolerant or facultative.
	Fungi: *Candida*	Yeast can survive this habitat, but not molds.
	Protozoa: *Entamoeba coli, Trichomonas hominis*	Feed on waste materials in the large intestine
Upper Respiratory Tract	Microbial population exists in the nasal passages, throat, and pharynx; owing to proximity, microbes are similar to those of oral cavity.	Trachea may harbor a sparse population; bronchi, bronchioles, and alveoli are essentially sterile due to local host defenses.
Genital Tract	**Bacteria:** *Lactobacillus, Streptococcus, diphtheroids* (*Corynebacterium* and relatives) *Escherichia, Gardnerella*	In females, microbes occupy the external genitalia and vaginal and cervical surfaces; internal reproductive structures normally remain sterile. Vaginal colonists respond to hormonal changes during life.
	Fungi: *Candida*	Cause of yeast infections
Urinary Tract	**Bacteria:** *Staphylococcus, Streptococcus, Corynebacterium, Lactobacillus*	In females, microbiota exist only in the first portion of the urethral mucosa; the remainder of the tract is sterile. In males, the entire reproductive and urinary tract is sterile except for a short portion of the anterior urethra.
Eye	**Bacteria:** coagulase-negative staphylococci, *Streptococcus, Neisseria*	The lids and follicles harbor similar microbes as skin; the conjunctiva has a transient population; deep tissues are sterile.
Ear	**Bacteria:** staphylococci, diphtheroids	The external ear is similar to the skin in content; areas internal to the tympanum are generally sterile.
	Fungi: *Aspergillus, Penicillium, Candida,* yeasts	

Effects of the Germ-Free State

Germ-Free Animals Display	Significance
Enlargement of the cecum; other degenerative diseases of the intestinal tract of rats, rabbits, chickens	Microbes are needed for normal intestinal development.
Vitamin deficiency in rats	Microbes are a significant nutritional source of vitamins.
Underdevelopment of immune system in most animals	Microbes are needed to stimulate development of certain host defenses.
Absence of dental caries and periodontal disease in dogs, rats, hamsters	Microbes are essential in caries formation and gum disease.
Heightened sensitivity to enteric pathogens (*Shigella*, *Salmonella*, *Vibrio cholerae*) and to fungal infections	Normal bacterial residents are antagonistic against pathogens.
Lessened susceptibility to amebic dysentery	Normal resident microbes facilitate the completion of the life cycle of the amoeba in the gut.
Less body fat	Normal microbiota help to break down indigestible carbohydrates and increase fat storage in the body.

The Origins of Microbiota in Newborns

A **newborn** presents a **rich and varied collection of habitats**. Exposure to the environment through the **birthing process, parents, health care workers, and visitors** leads to colonization of the newborn by numerous microbes



✓**Vaginal birth** is the point at which people first come into contact with **a vast array of microbes**.

✓Recent studies indicate **asthma, obesity**, and **type 1 diabetes** all appear more commonly in people delivered by **C-section** than they do in people delivered vaginally.

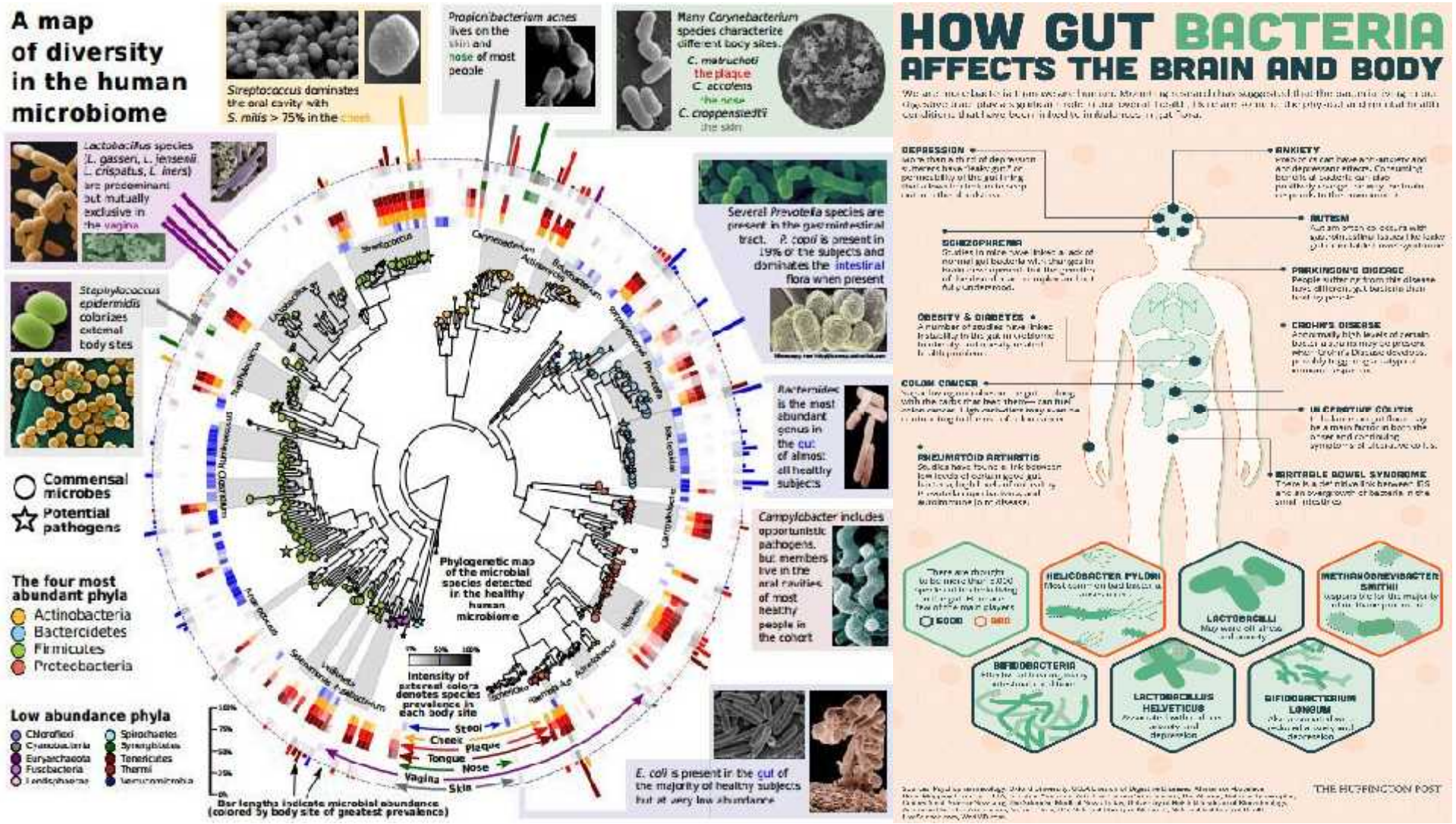
✓***Lactobacillus*** and ***Bacteroides*** are prevalent in the microbiota of infants **delivered vaginally**, but the microbiome of infants delivered by **C-section** more closely resembles that of the human skin, with abundant ***Staphylococcus aureus***.

✓In one study, **sterile gauze** was placed in the **mother's vagina** for one hour before C-section delivery. After birth, the gauze was swiped over the newborn's face and body. Over the next month, the microbiota of babies who received these vaginal swabs was tracked.

Human Microbiome Projects (2007)
A typical human body contains 3×10^{13} body cells, and harbors as many bacteria cells—an estimated 4×10^{13} bacterial cells

MICROBIOME VERSUS MICROBIOTA

MICROBIOME	MICROBIOTA
The entire habitat of microorganisms, including the microorganisms (bacteria, archaea, lower and higher eukaryotes, and viruses), their genomes (i.e., genes), and the surrounding environmental conditions	The assemblage of microorganisms present in a defined environment
Describes both biotic and abiotic factors associated with microorganisms within a particular habitat	Describes only the biotic factor of microorganisms in the habitat
Mainly focuses on the genetic makeup of microorganisms	Mainly focuses on the type of microorganisms in the habitat


A map of diversity in the human microbiome
Streptococcus dominates the oral cavity with S. mitis > 75% in the cheek
Propionibacterium acnes lives on the skin and nose of most people
Many Corynebacterium species characterize different body sites.
C. matruchoti the plaque
C. accolens the nose
C. croppensiedtii the skin
Lactobacillus species (L. gasseri, L. jensenii L. crispatus, L. iners) are predominant but mutually exclusive in the vagina
Several Prevotella species are present in the gastrointestinal tract. P. copri is present in 19% of the subjects and dominates the intestinal flora when present
Staphylococcus epidermidis colonizes external body sites
Bacteroides is the most abundant genus in the gut of almost all healthy subjects
Commensal microbes
Potential pathogens
Campylobacter includes opportunistic pathogens, but members live in the oral cavities of most healthy people in the cohort
The four most abundant phyla
Actinobacteria
Bacteroidetes
Firmicutes
Proteobacteria
Phylogenetic map of the microbial species detected in the healthy human microbiome
Intensity of colored colors denotes species prevalence in each body site
Stool
Cheek
Plaque
Tongue
Nose
Vagina
Skin
Bar lengths indicate microbial abundance (colored by body site of greatest prevalence)
Low abundance phyla
Chloroflexi
Cyanobacteria
Euryarchaeota
Fusobacteria
Lentisphaerae
Spirochaetes
Synergistetes
Tenericutes
Thermi
Verrucomicrobia
E. coli is present in the gut of the majority of healthy subjects but at very low abundance
HOW GUT BACTERIA AFFECTS THE BRAIN AND BODY
DEPRESSION
ANXIETY
AUTISM
SCHIZOPHRENIA
PARKINSON'S DISEASE
OBESITY & DIABETES
CROHN'S DISEASE
COLON CANCER
ULCERATIVE COLITIS
RHEUMATOID ARTHRITIS
IRRITABLE BOWEL SYNDROME
HELICOBACTER PYLORI
LACTOBACILLI
METHANOBREVIBACTER SMITHII
BIFIDOBACTERIA
LACTOBACILLUS HELVETICUS
BIFIDOBACTERIUM LONGUM
THE HUFFINGTON POST

Basic Infectiological Terminology I (Pathogen)

Term	Explanation
Saprophytes	These microorganisms are nonpathogenic; their natural habitat is dead organic matter
Parasites	Unicellular or metazoan organism living in or on an organism of another species (host) on the expense of the host
– Commensals	Normal inhabitants of skin and mucosa; the normal flora is thus the total commensal population
– Pathogenic microorganisms	Classic disease-causing pathogens
– Opportunists or facultatively pathogenic microorganisms	Can cause disease in immunocompromised individuals given an "opportune" situation; these are frequently germs of the normal flora or occasionally from the surrounding environment, animals, or other germ carriers
Pathogenicity	Capacity of a pathogen species to cause disease
Virulence	Sum of the disease-causing properties of a strain of a pathogenic species
Incubation period	Time between infection and manifestation of disease symptoms; this specific disease characteristic can be measured in hours, days, weeks, or even years
Prepatency	A parasitological term: time between infection and first appearance of products of sexual reproduction of the pathogen (e.g., worm eggs in stool of a host with helminthosis)
Infection spectrum	The totality of host species "susceptible" to infection by a given pathogen
Minimum infective dose	Smallest number of pathogens sufficient to cause an infection
Mode of infection	Method or pathway used by pathogen to invade host

Basic Infectiological Terminology II (Host)

Term	Explanation
Contamination	Microbiological presence of microorganisms on objects, in the environment, or in samples for analysis
Colonization	Presence of microorganisms on skin or mucosa; no penetration into tissues; typical of normal flora; pathogenic microorganisms occasionally also show colonization behavior
Infection	Invasion of a host organism by microorganisms, proliferation of the invading organisms, and host reaction
Inapparent (or subclinical) infection	Infection without outbreak of clinical symptoms
Infectious disease (or clinical infection)	Infection with outbreak of clinical symptoms
Probability of manifestation	Frequency of clinical manifestation of an infection in disposed individuals (%)
Endogenous infection	Infection arising from the colonizing flora
Exogenous infection	Infection arising from invasion of host by microorganisms from sources external to it
Nosocomial infection	Infection acquired during hospitalization (urinary tract infections, infections of the respiratory organs, wound infection, sepsis)
Local infection	Infection that remains restricted to the portal of entry and surrounding area
Generalized infection	Lymphogenous and/or hematogenous spread of invading pathogen starting from the portal of entry; infection of organs to which pathogen shows a specific affinity (organotropism); three stages: incubation, generalization, organ manifestation
Sepsis	Systemic disease caused by microorganisms and/or their toxic products; there is often a localized focus of infection from which pathogens or toxic products enter the bloodstream continuously or in intermittent phases
Transitory bacteremia/viremia/parasitemia	Brief presence of microorganisms in the bloodstream
Superinfection	Occurrence of a second infection in the course of a first infection
Relapses	Series of infections by the same pathogen
Reinfection	Series of infections by different pathogens