The Nature of Bacterial Host-Parasite Relationships in Humans

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Bacteria are consistently associated with the body surfaces of animals. There are many more bacterial cells on the surface of a human (including the gastrointestinal tract) than there are human cells that make up the animal. The bacteria and other microbes that are consistently associated with an animal are called the **normal flora**, of the animal. These bacteria have a full range of **symbiotic interactions** with their animal hosts. In biology, **symbiosis** is defined as "life together", i.e., that two organisms live in an association with one another. Thus, there are at least three types of relationships based on the quality of the relationship for each member of the symbiotic association.

Types of Symbiotic Associations

1. **Mutualism**. Both members of the association benefit. For humans, one classic mutualistic association is that of the lactic acid bacteria that live on the vaginal epithelium of a woman. The bacteria are provided habitat with a constant temperature and supply of nutrients (glycogen) in exchange for the production of lactic acid, which protects the vagina from colonization and disease caused by yeast and other potentially harmful microbes.
2. **Commensalism**. There is no apparent benefit or harm to either member of the association.

3. **Parasitism**. In biology, the term **parasite** refers to an organism that grows, feeds and is sheltered on or in a different organism while contributing nothing to the survival of its host. In microbiology, the mode of existence of a parasite implies that the parasite is capable of causing damage to the host. This type of a symbiotic association draws our attention because a parasite may become pathogenic if the damage to the host results in disease.

Bacterial Pathogenesis

A **pathogen** is a microorganism (or virus) that is able to produce disease.
Pathogenicity is the ability of a microorganism to cause disease in another organism, namely the **host** for the pathogen. As implied above, pathogenicity may be a manifestation of a host-parasite interaction. In humans, some of the normal bacterial flora (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae)* are
potential pathogens that live in a commensal or parasitic relationship without producing disease. They do not cause disease in their host unless they have an opportunity brought on by some compromise or weakness in the host's anatomical barriers, tissue resistance or immunity. Furthermore, the bacteria are in a position to be transmitted from one host to another, giving them additional opportunities to colonize or infect. There are some pathogens that do not associate with their host except in the case of disease. These bacteria may be thought of as **obligate pathogens**, even though some may rarely occur as normal flora, in asymptomatic or recovered carriers, or in some form where they cannot be eliminated by the host.

Opportunistic Pathogens

Bacteria which cause a disease in a compromised host which typically would not occur in a healthy (noncom promised) host are acting as **opportunistic pathogens**. A member of the normal flora can such as *Staphylococcus aureus* or *E. coli* can cause an **opportunistic infection**, but so can an environmental organism such as *Pseudomonas aeruginosa.* When a member of the normal flora causes an infectious disease, it sometimes referred to as an **endogenous bacterial disease**, referring to a disease brought on by bacteria 'from within'. Classic opportunistic infections in humans are dental caries and periodontal disease caused by normal flora of the oral cavity.

Bacterial pathogenesis

Virulence factor: genetic traits of bacterium that enhance its ability to cause a disease.

Virulent bacteria: bacteria having mechanisms that promote their growth in host at the expense of the host tissue or organ function.

Determinants of Virulence

Pathogenic bacteria are able to produce disease because they possess certain **structural** or **biochemical** or **genetic** traits that render them pathogenic or **virulent**. (The term **virulence** is best interpreted as referring to the **degree of pathogenicity**.) The sum of the characteristics that allow a given bacterium to produce disease are the pathogen's **determinants of virulence**. Some pathogens may rely on a single determinant of virulence, such as toxin production, to cause damage to their host. Thus, bacteria such as *Clostridium tetani* and *Corynebacterium diphtheriae*, which have hardly any invasive characteristics, are able to produce disease, the symptoms of which depend on a single genetic trait in the bacteria: the ability to produce a toxin. Other pathogens, such as *Staphylococcus aureus*, *Streptococcus pyogenes* and *Pseudomonas aeruginosa*, maintain a large repertoire of virulence determinants and consequently are able to produce a more complete range of diseases that affect different tissues in their host.

Opportunistic bacteria: A member of flora that has the potential of becoming pathogenic to host, only under certain conditions. "Immune-suppression and reduction of other flora populations by antibiotics, are examples for these conditions."

Systemic responses to bacterial infection: These are symptoms and signs due to toxins of bacteria and host cytokines produced in response to infection (mainly are: IL-1, IL-6, TNF).

Inoculum size: the minimal number of bacterial cells sufficient for disease production, under normal host conditions,e.g., 100-200 Shigella; 108 Vibrios; 106 Salmonella.

1. Bacterial entry into human body (Transmission) Via:

*Oral route (ingested).

*Airways (inhaled)

*Blood (injected or through traumatized vessels)

*Traumatic skin injury to reach soft tissues and bone (and blood as well)

*Arthropod bite.

*Sexual transmission to urogenital system.

Steps of bacterial pathogenesis :1.Host Defences:

Gut peristalsis , defecation ,respiratory tract, ciliary action, Coughing, sneezing, urogenital tract, urination.

2. Colonization:

Environmental conditions determine the bacteria that colonize a site.e.g. *Legionella* grows in the lungs but does not readily spread because it cannot tolerate high temperatures (e.g., 35°C).Colonization of sites that are normally sterile requires the presence of a defect in a natural defense mechanism or a new portal of entry.e.g. Patients with cystic fibrosis have reduction in the ciliary muco-epithelial function and altered mucosal secretions; as a result, their lungs are colonized by *S. aureus* and *P. aeruginosa.* In normal person, this doesn't occur !!

3. Adhesion

Adherence of the microbe to epithelial surface of the host; so the organism will not be removed e.g. by peristalsis and defecation (from the gut) ciliary action, coughing and sneezing (respiratory tract) or urination (urogenital tract).this adherence allows bacteria to colonize the tissue. specific interactions between external constituents on the bacterial cell (adhesins) and on the host cell (receptors) occur i.e. an adhesin-receptor interaction.-Many of these adhesin proteins are present at the tips of fimbriae (pili) and bind tightly to specific sugars on the target tissue. This sugar-binding activity defines these proteins as lectins.Specific interactions between external

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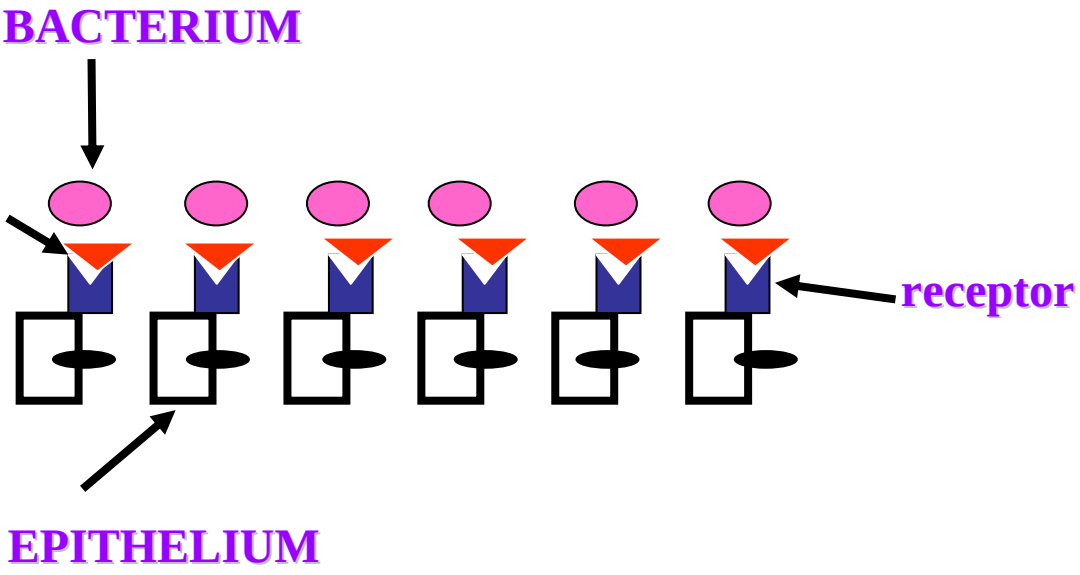

Bacterial Biofilm:
A **biofilm** produced by the bacteria is a special adaptation that facilitates colonization, especially of surgical appliances such as artificial valves or indwelling catheters. Bacteria in biofilms are bound within a sticky web of polysaccharide that binds the cells together and to the surface.Biofilm can protect its colonizers from the effect of antibiotics, host defenses, and other environmental factors.
Dental plaque is an example of a biofilm.
4. Invasion
Invasion is the ability of an organism to enter a cell with/without further passage into the systemic vasculature. Some bacterial pathogens reside on epithelial surfaces e.g. *Vibrio cholerae*. Other species are able to penetrate these barriers but remain locally e.g. *Shigella* . Others pass into the bloodstream or from there onto other systemic sites e.g. *Salmonella typhi* .
The invasive bacteria either destroy the barrier or penetrate into the cells of the barrier.
- Enteric bacteria use fimbriae to bind to M (microfold) cells of the colon and then inject proteins which stimulate M-cell membrane to surround and take-in the bacteria (membrane ruffling).
5. Tissue Destruction:
Bacteria cause tissue injury primarily by: 1) exotoxins
2) Endotoxins and non-specific immunity
3) specific humoral and cell mediated immunity
Also, the by-products of bacterial growth, especially fermentation, result in the production of acids, gas, and other substances that are toxic to tissue. Staphylococci produce enzymes to modify the tissue environ.:Hyaluronidase: digest connective t. matrix Fibrinolysin: digest formed fibrin. Lipases: open gaps in adipose tissues.

Streptococci also produce enzymes, including streptolysins S and O, hyaluronidase, DNAases, and streptokinases;these enzymes facilitate the development of infection and spread

Bacterial Exotoxins

bacterial produce protein that directly harm tissue or trigger destructive biologic activities.

Exotoxins are either cytolytic enzymes or receptor-binding proteins that alter a function or kill the cell.

5. Tissue Destruction

1)Toxins which act on the extracellular matrix of connective tissue include : proteases, collagenases and hyaluronidases.*E.g. Clostridium perfringens* produces collagenase, whilst *Staphylococcus aureus* produces a hyaluronidase.

5. Tissue Destruction

(2) A - B Toxins: consist of two components. One binds to cell surfaces (B) and the other passes into the cell membrane or cytoplasm (A) where it acts. E.g. *cholera* and *diphtheria*.

The biochemical targets of A-B toxins include :*Ribosomes (example *diphtheria*…….. *transport mechanisms (example *cholera*…….. *intracellular signaling cAMP production (example *tetanus*……..

(3) Membrane Damaging Toxins e.g. *Staphylococcus aureus* delta toxin

enzymatically digest the phospholipid (or protein) components of membranes (as detergents), holes are punched in the cell membrane and the cytoplasmic contents can leach out. The phospholipase ("toxin") of *C. perfringens* is an example

Superantigens are a special group of toxins:

They activate T cells by binding simultaneously to a T-cell receptor and a MHC II molecule on another cell without requiring antigen.

Effects on the immune system:

1) Non-specific activation of T cells ◊ Stimulating the release of large amounts of interleukins, as IL-1 & IL-2 ◊ autoimmune-like responses.

2) Stimulation of T cells can also lead to death of the activated T cells ◊ loss of specific T-cell clones and their immune responses.

The condition called toxic shock syndrome is due to *S. aureus* enterotoxins, and the erythrogenic toxin of *S. pyogenes*

Properties of the Host

The **host** in a **host-parasite interaction** is the animal that maintains the parasite. The host and parasite are in a dynamic interaction, the outcome of which depends upon the properties of the parasite and of the host. The **bacterial parasite has its determinants of virulence** that allow it to invade and damage the host and to resist the defenses of the host. The **host has various degrees of resistance** to the parasite in the form of the **host defenses.** Typically the **host defense mechanisms are divided into two groups**:

1. Innate Defenses. Defenses common to all healthy animals. These defenses provide general protection against invasion by normal flora, or colonization, infection, and infectious disease caused by pathogens. Innate defenses include anatomical and structural barriers, inflammation, phagocytosis and the presence of a normal bacterial flora. The innate defenses have also been referred to as "natural" or "constitutive" resistance, since **they are inherent to the host**.

2. Inducible Defenses. Defense mechanisms that **must be induced or turned on by host exposure to a pathogen** (as during an infection). Unlike the innate defenses, they are not

immediately ready to come into play until after the host is appropriately exposed to the parasite. The inducible defenses are synonymous with **acquired or adaptive immunity** and involve the immunological responses to a pathogen causing an infection. Adaptive immunity is generally quite specifically directed against an invading pathogen. The innate defenses are not so specific, and are directed toward general strategic defense. Innate defenses, by themselves, may not be sufficient to protect a host against pathogens. Such pathogens that evade or overcome the relatively **nonspecific innate defenses** are usually susceptible to the more **specific inducible defenses**, once they have developed.

Microbes and Human Life

Because of the presence of microbes in all walks of human life, there is constant interaction between microbes and humans. The vast majority of the bacteria in the body are rendered harmless by the protective effects of the immune system, and a few are beneficial. In fact, the relationship between microbes and humans is delicate and complex.

Benefits of Microbes

Microbes are useful for us in many ways in various industries.

Production of Foods

Microbes are a key component in both home and industrial food preparation.

+ Lactic acid bacteria are used to make yogurt, cheese, sour cream, buttermilk and other fermented milk products.
+ Vinegars are produced by bacterial acetic acid fermentation.
+ Yeast is used in the manufacture of beer and wine and for the leavening of breads. It is also involved in fermentations to convert corn and other vegetable carbohydrates into ethanol to make beer, wine, or gasohol; but bacteria are the agents of most other food fermentations.
+ Other fermented foods include soy sauce, sauerkraut, dill pickles, olives, salami, cocoa and black teas.

Medical, Pharmaceutical and Biotechnological Applications

Certain microbes can help us in the fight against other microbes. In human and veterinary medicine, that are used to treat and prevent infectious diseases, microbes are a source of antibiotics and vaccines.

+ Antibiotics are substances produced by microorganisms that kill or inhibit other microbes. They are used in the treatment of infectious disease. Antibiotics are produced in nature by molds such as Penicillium and bacteria such as Streptomyces and Bacillus.
+ Vaccines are substances derived from microorganisms and are used to immunize against disease. The microbes that are the cause of infectious disease are usually the ultimate source of vaccines.
+ Biotechnology Microbiology makes a significant contribution to biotechnology, an area of science that applies microbial genetics to biological processes for the production of useful substances. Microorganisms

play a central role in recombinant DNA technology and genetic engineering. Important tools of biotechnology are microbial cells, microbial genes and microbial enzymes.

Other benefits of microbes

+ The microbes that normally live in association with humans on the various surfaces of the body (called the normal flora), such as Lactobacillus and Bifidobacterium, are known to protect their hosts from infections and otherwise promote nutrition and health.
+ They help purify waste water in waste water treatment facilities.
+ They help reduce atmospheric nitrogen and transform it to ammonia important for agriculture.

Ecology

Microbes are involved in cycling vital elements such as carbon and nitrogen, breaking down wastes and dead organisms into simpler substances plants can use in photosynthesis. Other species are at the base of the food chain, especially in aquatic ecosystems. Even pathogens have a role in controlling the populations of their host species. Microbes are used to digest oil from oil spills.

property	Endotoxins	Exotoxins
Chemical nature	lipopolysaccharide	protein
Produced by	Gram negative bacteria	Many gram positive and few gram negative bacteria
Relation ship to cell	Part of outer membrane	Extracellular, diffusible
Molecular weight	10kD	50-1000kD
Vaccines	No toxoids formed and no vaccine available	Toxoids used as vaccines.
Heat stability	Stable at 100°C for 1 hour	Destroyed rapidly at 60°C(except Staphylococcal enterotoxin)
Antigenicity	yes	occasionally
potency	Low(>100 µg)	High (1 µg)
Specify	low	High
Enzymatic action	no	yes
Pyrogenicity	yes	occasionally
Detected by	Limulus lysate assay	Many tests;(precipitation, neutralization,..etc

The difference between Endotoxins and exotoxins