

Pathogenesis of bacterial infection

The pathogenesis of bacterial infections includes initiation of the infection process and the mechanism leads to the development of signs and symptoms of disease

The characteristics of bacterial that are pathogens

Includes

Transmissibility

Adherence to host cells: it is a process by which a bacteria stick to surface of host cells, it is a major step in the infection.

Invasion: the process whereby bacteria, animal parasite fungi and viruses enters host cells or tissue and spread in body

Toxigenicity : the ability of microorganism to produces a toxin that contributes to the development of the disease.

Pathogen: microorganism capable of causing disease

Virulence: the quantitative ability of an agent to causes disease. Virulent agent causes disease when introduced into the host in small numbers, virulence involves invasion and toxigenicity

Opportunistic: an agent capable of causing disease only when the hosts resistance impaired (e.g. when the patient is immune-compromised)

Identifying bacteria that causes disease

Humans and animals have abundant normal flora that usually do not produce disease

1884, Robert Koch's proposed a series of postulates that have been applied broadly to like many specific bacterial species with a particular disease Koch's postulates

- ☒ The organism is found in all cases of the disease and its distribution in the body corresponds to that of the lesion observed.
- ☒ The organism should be cultured outside the body in a pure culture for several generation
- ☒ The organism should be reproduced the disease in other susceptible animals

Nowadays a fourth postulates would be added

- ☒ Antibodies to the organism usually developed during the course of the disease
- ☒ Modern day's microbial genetics has opened a new frontiers to study pathogenic bacteria and differentiate them from nonpathogenic

Contraindication

Treponema palidum * not cultured

Mycobacterium leprea

Niessleria gonorrhoea (human source)

The application of Koch's postulate leads to classify bacteria into

Pathogens e.g. *Mycobacterium tuberculosis*

Opportunistic e.g. yeasts and molds

Non-pathogens

Degree of pathogenicity

Primary pathogens: have high possibility to producing disease e.g. *Bordetella pertussis*

Opportunistic pathogens require some host comprised e.g. *Pseudomonas aeruginosa*

First line defense against microbial infection

Epithelial barriers

Skin, vaginal and conjunctiva epithelium

A simple mechanical barrier to microbial invasion is provided by intact epithelium, the most effective of which is the skin. Transmitted of infection. Organisms can gain access to the underlying tissue only by breaks or by way of hair follicles, sebaceous glands, and sweat glands,

Vagina protected by low pH and normal flora

Lysosomes and flushing action of tears protect conjunctiva

Respiratory epithelium

Respiratory protect by epithelium and IgA

Cilia escalate mucus and particles away from lungs

Gastrointestinal epithelium low pH, bile salts and digestive enzymes

Urinary tract infection

Low pH and flushing action of urine are protective

Some bacteria that commonly causes disease to animals and incidentally infect humans e.g. Salmonella and campylobacter sp. Their transmission by food products to human

Other bacteria produces infection to human by mistake in the normal life cycle of the organism e.g. Yersinia pestis has a well established life cycle in rodents and rodents flea, and their transmission is by flea

Bacillus anthracis (anthrax) it lives in the environment eventually can cause infection to animal and its transmitted to human by products of animal such as skin hair, bone etc from animals

The clinical manifestation of disease (e.g. diarrhea, cough, genital discharge) produced by microorganism often promote transmitting of agents
vibrio cholera can cause severe diarrhea which may contaminate water, ingestion of contaminated water will lead to the infection

M.T.B it infects human only and it transmitted by aerosols

Many bacteria are transmitted from one person to another on hands. S. aureus where found in nose (carrier) he/she may rub his nose and transmitted the bacteria to other persons, where infection is results

Many opportunistic pathogens that cause nosocomial infection are transmitted from one person to another.

Attributes of microbial pathogenicity

Entry

Pathogens use human environmental contact sites as points of entry,

Bites of insects, *Yersinia pestis* and malaria parasites
needle

the other sites of entry into human hosts include digestive tract, the respiratory tract, the urogenital tract, and the conjunctiva

aerosols can transmit organism from host to host

Adherence

The first major interaction between a pathogenic microorganism and its host entails attachment to eukaryotic cell surface. Adherence requires the participation of two factors: a receptor on host cells and an adhesion to the invading microbe. e.g. influenza viruses attach specifically to neuraminic acid containing glycoprotein receptor

Pili of many gram negative bacteria bind directly to sugar residues that are part of glycolipids or glycoproteins on host cells

Bordetella pertussis adheres specifically to cilia of respiratory epithelial cells and one of its toxins directly inhibits ciliary actions

Surface proteins, lipoteichoic acids and polysaccharides capsule may act as adhesions

Some organisms secrete an enzyme IgA protease that cleaves human IgA

Viruses have a single adhesion protein structure, specific receptors

Invasion of the hosts

Getting into cells

Many pathogenic bacteria are contented to fight of there entry to the mucosal surface

Adherence to cellular surface may only be the first step in other infections. Host cell invasion is a specialized strategy for survival and multiplication used by a number of pathogens

Cell invasion is an essential step for viruses and obligate intracellular bacterial pathogens like *Rickettsia* (typhus) and *chlamidia* (trachoma). Some bacteria and many parasites are facultative intracellular parasites . these organisms are capable of life both inside and outside host cells , *typhoide* (salmonella)

Establishment of pathogens after entry and the consequences of infections

Toxins

Exotoxins a number of microorganisms synthesize protein molecules that are toxic to there hosts and are most often secreted into there environment or found associated with the microbial surface

Membrane active exotoxins many bacteria elaborate substances that causes haemolysis of erythrocytes one of the virulent property

Hydrolytic enzymes

Many bacteria produces one or more enzymes that are non toxic but facilitate tissues invasion or help to protect organism against the body defense mechanisms, e.g. collagenase and hyauronidase may facilitate spread in tissue

Normal microbial flora

The term normal flora or endogenous flora is used to describe microorganisms that are frequently found in particular sites in normal, healthy individuals

The normal flora may have an asymptomatic relationship that benefits the hosts or may simply live as a commensal with a neutral relationship to the hosts

Transient: establish themselves briefly but tend to be excluded by competition from residents or by the host's innate or immune defense mechanism

Carrier

state is often used when potentially pathogenic organisms are involved e.g. *S. pneumoniae* which causes pneumonia or *Neisseria meningitidis* causes meningitis usually isolated from throat (healthy person) and can cause serious infection

Origin of normal flora

The healthy fetus is sterile until the birth membranes rupture. During and after birth the infant is exposed to the flora of the mother's genital tract, to the skin and respiratory flora of those handling it and the organisms in the environment

factors determining the nature of the normal flora

physiological conditions such as local pH influence colonization

adherence factor

ability to compete for nutrients is an advantage (production of hydrogen peroxides as their metabolic products or volatile fatty acids, antibiotics and bacteriocins)

Normal flora of different sites

Blood, body fluids and tissues

All these sites are sterile normally. Occasionally organisms may be displaced across epithelial barriers as a result of trauma such as transient bacteremia

Skin

The skin plays host to a abundant flora that varies somewhat according to the number and activity of sebaceous and sweat glands

It is common on a moist skin areas axillae, perium and between toes

Staphylococcus epidermidis, *Propionibacterium*, and diphtheroids

Normal flora on skin not easily removed

There are factors that eliminate the normal flora of skin

- ☒ Low pH
- ☒ The fatty acids in sebaceous secretions
- ☒ Presence of lysozyme
- ☒ Neither profuse sweating and nor washing and bathing can eliminate or modify the normal flora
- ☒ Daily scraping with soap containing hexachlorophene

Conjunctival sac

In healthy person a very scanty flora of nonpathogenic corynebacteria and *S. epidermidis*

This maintained by the high lags some content of lacrimal secretions and tears

Intestinal tracts

Mouth and pharynx containing large number of facultative and strict anaerobes

Streptococcus mutans.....carries

Gram negative diplococi of genera *Neisseria* and *Moraxella*

Streaked anaerobic and microaerophilic

Stomach have a few residences of organisms , because of the lethal hydrochloric acid and peptic enzymes on bacteria

Small intestinal flora is scanty but it increases towards the lower ileum

The colon carries the specific normal flora

Aerobic organism

Bactericides , *fusobacterium*, although *Clostridium* perfringens ,*E. coli enterococci*, yeasts ,

Bifidobacteria are predominant flora of breast fed infants

Respiratory tract

50% of people carries *S. aureus* in there nose

naso-pharynx is often a site of carriage of potential pathogens such as

S pneumonia , meningococcal, haemophilus species

The respiratory tract below the level of larynxes protected in health by action of the epithelial cilia and by movement of mucociliary blanket

S, viridians with low potentially pathogen

Genitourinary tract

Bladder and upper urinary tract are sterile in health

The vagina has a flora that varies according to hormonal influences at a different ages

Before puppetry and after menopause

Lactobacillus

Anaerobic gram negative rods

Gram positive cocci

And yeasts can survive in acidic pH which produced by lactobacilli, these conditions develops because glycogen is deposit in vaginal epithelial cells under the influence of estrogen hormone and metabolized to lactic acid by lactobacilli. This process result in The pH of the vagina is 4-5 which is acidic good for lactobacilli but not of the other organisms

Role of the resident flora

The microorganism that are constantly present on body surfaces are commensally

Certain normal flora There presence maintaining health and normal function. E.g. normal flora of intestine synthesize a vitamin K and aid in the absorption of nutrient

On mucus membrane and skin prevents the colonization by pathogens and possible disease through bacterial interference, through the competition for receptors or

binding sites on host cells, competition for nutrient , mutual inhibition by metabolic or toxic products, mutual inhibition by antibiotic materials or bacteriocine or other mechanism

Role of the normal flora in disease

Many species among the normal flora are opportunistic in that they can causes infection if they reach protected areas of body in sufficient numbers of if local or general host defense mechanism is compromised

1. E. coli can reaches the urinary bladder by ascending though urethra an causes urinary tract infection
2. S. viridans from oral cavity may reaches the blood stream as a results of physiologic trauma or injury (tooth extractions) causing damage to heart valves initiating bacterial endocarditis
3. compromised defense system increase the opportunity for invasion
4. mouth flora play major role in dental carries
5. Bactericides are the commonest residence in the large intestine and are quite harmless in that location if it introduce into free peritoneal cavity or into pelvic tissues as a results of trauma they can causes suppuration and bacteremia

so the normal flora are harmless but may produce disease if introduced into foreign location in large numbers and if predisposing factors are present

Beneficial effects of the normal flora

Exclusionary effect

The normal flora produces a conditions that tend to block the establishment of extraneous pathogens and there ability to infect the host.

1. *Bifidobacteria* in the colon of the breastfed infant produce an environment inimical to colonization by enteric pathogens this protective effect is added by ingested maternal IgA.
2. The normal vaginal flora has a similar protective effect. *Lactobacillus* vaginal flora can protect against transmitting in gonorrhoea
3. Antibiotic thereby with broad spectrum agents may also alter the normal flora of the gastrointestinal tract that antibiotic resistance organism multiply in the relative ecologic vacuum produced sometimes causing significant infections particularly immunocompromised patients. E.g. *Candida albicans* , Pseudomembran colitis results from overproliferation of toxin producing anaerobe *Clostridium difficile*.
4. exclusionary effect makes entrance of pathogens more difficult

Production of essential nutrients

some vitamins are produced by members of the normal flora e.g. vitamin K

