

Pathogenicity and Infection

- refer to some aspects of the interaction between bacteria and infected humans or host-parasite relationship
- interaction involves
 1. human factors which are mostly immunological
 2. bacterial factors

Pathogenicity

- the ability or the potential of an organism to cause disease
- varies among the a. genera b. species c. strains

- based on pathogenicity bacteria are described as
 - a. non-pathogenic bacteria
 - b. pathogenic bacteria
 - c. opportunistic pathogens

Pathogenesis

- the processes in pathogenicity includes
 - a. the initiation of the infectious process
 - b. mechanisms that lead to signs and symptoms or manifestation of the associated disease
 - mechanisms occur in the
 1. infected person
 2. infecting organism

Some properties of pathogenic bacteria which enhance pathogenicity

1. **transmissibility** or **communicability** from one host or reservoir to a fresh host
 - enhanced by the organisms' ability to
 - a. be shed in large numbers in body fluids or secretions
 - b. survive unfavourable physical conditions
2. **infectivity** involves the organism's ability to
 - a. attach itself
 - b. survive and penetrate a healthy first line of defenses including the skin and mucous membranes

infectivity is

- more difficult in some parts with intact barriers
- easier where the surface is broken
- influenced by
 - a. the number of the infecting bacterial cells
 - b. phase of growth
 - c. properties of the organism which enable it to harm or destroy tissues during infection

Possible results of pathogenesis

1. resolution
2. obvious illness due to the organism can be
 - localized lesion at the site of entry due to inflammation
 - systemic illness or disease involving multiple parts
3. latent or asymptomatic or sub-clinical infection
 - can progress later into symptomatic illness
4. unnoticed signs and symptoms
5. chronic carriage

chronic carriage

- may develop after
 - a. recovery from the associated illness
 - b. asymptomatic or unnoticed infection
- characterized by small number of viable organisms present in a particular part with no associated manifestations
- significance includes
 - a. possible source of infection leading to symptomatic illness in the carrier or susceptible person through transmission
 - b. may lead to long term complications associated with infection by the organism
- majority are detectable by laboratory tests

Virulence

- the capacity of an organism to harm human tissues or to cause disease or the degree of pathogenicity
 - measurement of pathogenicity in relation to host's resistance within a group of species
- influenced by similar human factors and bacterial factors as pathogenicity
- varies among
 - a. various pathogenic genera
 - b. species
 - c. strains
- based on virulence pathogenic bacteria are described as
 - a. avirulent
 - b. virulent
 - c. highly virulent

Bacterial virulence factors

- mostly determined by
 - a. genetic composition
 - b. biochemical properties
 - c. structural components
- numerous with different mechanisms of action
 - number and types depend on the pathogen
 - each factor can be possessed by several bacteria
 - each factor can act in one or more ways
 - one or more factors can act in one disease process
- can be broadly grouped based on mechanisms of action

1. adherence factors or adhesins

- enable a bacterial cell to adhere to the cells of tissue surface in humans
- adherence factors include
 - a. pili or fimbriae on bacteria which possess them
 - b. binding molecules on a bacterial cell surface
 - binding molecules on a bacterial cell surface include components of a capsule and some surface antigens

2. Aggressins or aggressive factors

- enable the pathogenic organisms to overcome or evade host defense mechanisms
- include
 - a. capsules
 - b. surface proteins and carbohydrates
 - c. enzymes

capsule

- prevents the interaction between the bacterial cell surface and phagocytic cells that would lead to recognition that precedes phagocytosis

Aggressins which act intra-cellularly

- found in some bacteria which infect intra-cellularly
- enable the intra-cellular pathogen to
 1. reside and multiply within phagocytic cells
 2. escape intra-cellular destruction by interference with various mechanisms including
 - a. phagosome and lysosome fusion
 - b. activity of lysosomal enzymes

Enzymes and enzyme-like substances

- enable the organism to invade and multiply in human tissues

- increase invasiveness

include

- hyaluronidase or spreading factor
- coagulase
- kinases or fibrinolysins
- lipases
- proteases

3. Bacterial toxins

- properties of some pathogenic bacteria
- classified as
 - exotoxins
 - endotoxins

Exotoxins

- diffusible products released by some Gram positive bacteria mostly and a few Gram negative organisms
 - structurally proteins some are enzymes
 - majority are heat labile a few are heat stable
 - liberated from the cytoplasm of live bacteria
 - strongly antigenic
 - can be converted to toxoids
 - highly specific for certain tissues
 - high potency
 - effectively neutralized by antitoxin
 - synthesis of the majority is encoded by extra-chromosomal genes

Mechanisms of action of bacterial exotoxins

- different and depend on the specific exotoxin
- may involve
 - a. inhibition of protein synthesis
 - b. interference with normal nervous response to stimuli
 - c. activity on the intestinal tract
 - d. enzymatic activity

Endotoxins

- composed of lipopolysaccharides liberated from the cell wall of dead or disintegrating Gram negative bacteria
- characteristics include
 - heat stable
 - not convertible to toxoids
 - lack specific receptors
 - moderately toxic and low in potency
 - poorly or non-antigenic
 - not effectively neutralized by antitoxin
 - synthesis directed by chromosomal genes

Effects of endotoxins

- generalized with variable manifestations
 1. low concentration in the blood causes release of pyrogens which cause fever
 2. high concentration interferes with normal physiological mechanisms in multiple systems leading to severe manifestations
 - a. abnormalities in immunological and haematological processes
 - b. hypotension and endotoxic shock and associated complications

Other bacterial properties which contribute to virulence

A Ability to obtain iron

- characteristic of most pathogenic bacteria
- organisms release small carrier protein molecules which obtain iron from the infected tissues
- iron is essential for the nutrition of pathogenic bacteria
 - availability supports the organisms' growth and virulence
- production of many extra cellular products involved in virulence including some exotoxins maybe influenced by availability of iron

B. Plasmids

- genes may code for
 - a. resistance to antimicrobial agents
 - genes referred to as R-factors
 - resistance leads to continued growth and spread of infection despite treatment
 - b. formation of sex pili and ability to transfer genetic material to other organisms
 - c. other characteristics which contribute to virulence including exotoxin production

c. **Change of surface antigens**

- some pathogenic bacteria undergo mutation during infection
 - acquire new antigenic determinants on the cell surface
 - process enables the organism to
 - a. avoid recognition by the immune defense mechanisms
 - b. evade elimination

Infection

- a process necessary for an organism to cause disease
- sometimes used to mean disease
- involves
 1. sustained presence of an organism in an anatomic part
 - can be on the surface including the skin or mucous membranes or in the inner tissues
 2. establishment and multiplication at the site or colonization
- with or without disease manifestation

Host and tissue specificity

- some organisms are known to be
 1. restricted in the type of animals they infect
 2. highly specific in the tissues they infect primarily and in disease production
- reasons for host-parasite or tissue specificity are not clearly identified

Sources of infection and reservoirs

- reservoirs are
 - normal growth habitats of organisms
 - can be
 - a. an anatomic site on an animal including humans
 - b. in the environment including water and soil
- specific infections associated with disease manifestation in humans can be classified according to the source of the organism involved as exogenous or endogenous

exogenous infections

- organisms involved originate from sources outside the infected person including
 - a. patients
 - b. human carriers
 - c. animals
 - d. environment

endogenous infections

- organisms involved originate from a site within the individual mostly
 - a. pathogenic organisms in asymptomatic carriers
 - b. potential pathogens particularly among the normal flora

Modes of transmission and spread of pathogenic bacteria

determined largely by the site infected and the infecting organism

1. Respiratory tract infections

- for the majority bacteria are carried in infected secretions and are released through
 - a. sneezing
 - b. coughing
 - c. speakingin droplet spray of secretions
- infected secretions reach the susceptible person directly or via contaminated items

2. Skin and wound infection

- spread through contact with the infected part or material from that part or via contaminated
 - a. hands
 - b. clothing
 - c. other

3. Sexually transmissible infection

- via sexual contact either through mucosal to mucosal surface or in secretions

4. Gastrointestinal tract infections

- majority of bacteria are ingested
- some of the bacteria are passed out in faeces and cause contamination of
 - a. water
 - b. hands
 - c. food or other items from which re-ingestion may occur
- constituting the faecal-oral transmission

5. **Bacteria in the blood circulatory system**

- a. **arthropod-borne or vector-borne infections**
 - spread by blood sucking arthropods during feeding
- b. **from infected pregnant female to expected baby or transplacental transmission**
- c. **through transfusion of infected blood**

Laboratory acquired accidental infections

- potential sources include
 - a. **infected specimens**
 - b. **artificial cultures**
 - c. **laboratory animals**

BACTERIAL NORMAL BODY FLORA

- a variety of micro-organisms which are
 1. harboured in some specific anatomic parts of humans
 2. not associated with disease due to their presence in those parts under normal circumstances
- can be classified as
 - a. transient flora
 - b. resident flora

Transient flora:

- inhabit the skin or mucous membranes for a limited period
 - can be hours or days or weeks
- derived from the immediate environment
- may cause disease when there is a disturbance in the defense mechanisms in that part

Resident flora

- relatively fixed types of micro-organisms regularly found in specific anatomic parts
- re-establish themselves if disturbed
- first lot is acquired by the newborn baby during passage through the birth canal
- subsequently organisms are acquired from other humans and inanimate sources in the environment

Distribution of resident flora

- partly influenced by
 - a. general physiological characteristics including
 - body temperature in various parts
 - pH of secretions
 - oxygen
 - moisture
 - nutrients in specific parts
 - b. other characteristics including age sex
hormonal activity especially in females
- associated with fluctuations throughout life

Anatomic parts considered free of resident normal flora

1. lower respiratory tract including
 - trachea bronchi bronchioles and alveoli
 - various defense mechanisms clear the micro-organisms that may enter
 - a. ciliated epithelium that moves the mucous upwards
 - b. phagocytic cells mainly polymorphs and macrophages that carry-out phagocytosis of microorganisms
 - pleural cavity and fluid are normally sterile

2. Gastrointestinal tract

a. Oesophagus

- naturally considered free of resident flora
- may contain bacteria from ingested food or saliva from the mouth as transient flora

b. Stomach

- acidity plays a protective role by keeping the number of the organisms at a minimum

c. Upper part of the small intestine

- close to and therefore similar to the stomach

3. Genito-urinary tract

- upper part including kidneys ureters and the bladder

4. others

- a. circulatory system and pericardial space and fluid
 - blood and pericardial fluid are free of normal flora
- b. central nervous system including the cerebrospinal fluid (CSF)
- c. peritoneal cavity and fluid
 - any organism isolated from properly collected specimen from a) b) and c) is clinically significant

Parts considered to harbour numerous normal resident microbial flora

1. Skin

- exposed to the environment therefore harbours transient as well as resident flora in large numbers
 - influenced in some parts by micro-environmental factors including availability of moisture
- organisms include
 - a. Gram positive cocci including species of *Staphylococcus*
 - b. Gram positive bacilli mainly diphtheroids

- some physiological mechanisms including
 1. secretions with low pH
 2. sebaceous secretions that contain fatty acids and lysozyme or an enzyme-like substance which is bacteriolytic
 - keep the number and types of normal flora in check
 - also make it unfavourable for most other bacteria
- sweating and washing do not eliminate the resident normal flora
- number may be reduced temporarily by vigorous scrubbing with soap or antiseptic but the flora re-establishes itself soon after

Significance of skin flora includes

- increased risk of
 - a. contamination of specimens collected from or through the skin
 - b. introduction into and infection of inner tissues through clinical invasive procedures involving passage through the skin
 - c. initiation of a focus of infection associated with devices inserted through the skin and left in place for a long time
 - d. wound infection
- proper cleansing required prior to procedures which involve the skin

2. **Nose** similar flora as the skin

- *Staphylococcus aureus* is a significant normal flora in the nasal cavity in some people
 - occasionally a source of infection leading to disease

3. **Mouth**

- majority are Gram positive cocci mainly alpha haemolytic streptococci or viridans streptococci
- others
 - Lactobacilli Actinomyces
 - Bacteroides Fusobacterium Veillonella
 - specific spirochaetes

4 Pharynx or upper respiratory tract

- as oral cavity flora plus others including
 - Streptococci
 - *Haemophilus* species
 - *Moraxella catarrhalis*

Significance of mouth and URT flora

- potential causative agents of disease locally and in other parts
 - disease causation may or may not be associated with abnormal immunological defense mechanisms

- alpha-haemolytic streptococci are associated with
 - dental caries and other infections in the mouth
 - infections in other tissues including bacterial endocarditis
- other normal flora associated with infections in the mouth include
 - Actinomyces species
 - spirochaetes acting together with other factors and other organisms
 - Bacteroides and other strict anaerobic organisms in the mouth occasionally cause disease in internal tissues including abscesses

5. Large intestine

- numerous normal flora
 - more than 100 different species
 - consists of bacilli and cocci
 - strict anaerobes
 - facultative anaerobes
 - strict aerobe

Significance of large intestinal flora includes

1. risk of causing disease
 - a. in adjacent tissues as a result of disturbance
 - occasionally in association with trauma

- ▷ relocation to other parts increases the risk of disease causation
 - more frequently associated with infections involving the
 - urinary tract
 - peritoneal cavity
 - pelvic tissues
- treatment or investigative procedures which involve the large intestine are performed applying necessary precautions to minimize chances of relocating the organisms

6. Lower urethra

- generally contains a small number of organisms as normal flora
 - detectable in urine specimens occasionally as contaminants

7. Lower female genital tract

- dominant flora changes according to the pH which is under hormonal influence and age
 - soon after birth the majority of the flora are lactobacilli as the pH is acidic
 - mixed flora of cocci and bacilli develops with age

- at puberty lactobacilli re-establish in large numbers and maintain the acidic pH through activity on glycogen
 - a protective mechanism
- mixed flora recurs later as the age increases
- generally organisms from the large intestine may form part of the vaginal flora due to close proximity including
 - *Escherichia coli*
 - species of *Clostridium*
 - anaerobic streptococci
 - group B beta-haemolytic streptococci

Significance of vaginal flora

- protection by lactobacilli through the low pH
- group B streptococci can be transmitted to a newborn during vaginal delivery resulting in infection
- some flora derived from the large intestinal tract flora are significant causative agents of
 - . urinary tract infection
 - . infections associated with reproduction in females

Significance of normal flora in general

Beneficial effects

- competition for micro-environments more effectively than some regular pathogens enables prevention of colonization by regular pathogens
- stimulation of the immune system
- metabolic activity which may be protective
- production of nutrients
 - vitamin K produced by some normal flora in the large intestine

Harmful effects normal flora include

- potential causative agents of disease
 - a. as opportunistic pathogens including
 - . dental caries and mouth infection
 - . infections involving injured tissue
 - . infections associated with physiological changes and other abnormalities which reduce the immunological defense mechanism
 - b. when relocation from the usual occupied site
 - c. as a result of prolonged administration of broad spectrum antibiotics leading to overgrowth or super infection by the flora which are not susceptible to the agent
- contribute in the spread of antibiotic resistance