

Infection = successful multiplication of a microorganism within a host.
(not all infections are diseases)

Infectious disease = signs and symptoms as a result of an infection and its associated damage or altered physiology.

Characteristics of infectious diseases

- Diseases are caused by living microorganisms which can usually be identified early in the illness;
- Most infections are self-limited or the microorganisms are sensitive to antibiotics;
- Transmission of pathogenic organisms to other people, directly or indirectly, may lead to an epidemic
- Many infections are preventable by hygienic measures, vaccination or chemoprophylaxis.

Pathogen: any microorganism that has the capacity to cause disease.

- prions
- viruses
- mycoplasma, rickettsia, chlamydia
- bacteria
- spirochetes
- fungi
- protozoans and helminthes

The pathogenic process

sequence of events in which many microbial components play a part allowing:

- the pathogen access to the appropriate site in the host
- provide a means for environmental signals to be transmitted to the bacterium to indicate that the conditions are right for expression of toxin and other virulence determinants
- protect the microbe against clearance by host defenses.

Virulence: a quantitative measure of pathogenicity.
(the likelihood of causing disease)

Infectious dose depends primarily on the "virulence factors"

Disease due to infection is the result of the interaction between a microorganism and the defense mechanisms of the body.

The **outcome** depends on:

1. the number and virulence of the organism
2. the physiological and anatomical effects that they induce
3. the effectiveness of the natural defense (innate immunity)

Microbe-mediated mechanism in infection:

- direct cell destruction (poliomyelitis, rabies)
- exotoxin (tetanus, cholera, botulism, diphtheria)
- endotoxin (meningococcal infection, Gram-negative septicemia, typhoid)

Host mediated mechanism in infection

- neutrophils and macrophages activation
- complement activation
- activation of clotting cascade
- immune mechanisms
- secondary autoimmune mechanisms

The attributes of microbial pathogens

- to make contact with an appropriate surface
- to reach niche or microenvironment on or within the host that permit to multiply and secure its potential transmission to a new susceptible host
- to express a virulence factor.

Microbial adherence

- is the initial interaction of a pathogen with its host
- is the route to cellular invasion by intracellular parasites
- is the first step in host cell killing and toxin delivery by microbial pathogens

Adhesins = molecules that mediate adherence of microbe to the host.

Receptors = host molecules where adhesins bind to.

Microbial toxins

1. Exotoxin - bacterial products that are:

- proteins
- are released from the bacterium during exponential growth
- are toxic for target cells

2. Endotoxin – LPS (lipopolysacharids)

- are intracellular
- are released only after lysis of the bacterial cells

3. Exoenzymes.

Classification of toxins

Criteria by which toxins may be classified after are:

1. cellular or tissue target of action (i.e. enterotoxins, neurotoxins, leukotoxins);
2. mechanism of action (proteolytic toxins, ADP-ribosylating toxins)
3. intracellular target (small-molecular-weight G proteins such as Rho)
4. major biologic effects (dermonecrotic toxin, edema-producing toxin, hemolytic toxin)
5. the microorganisms that produce them (pertussis toxin, cholera toxin).

Host defense mechanisms

1. Natural Barriers

- the skin and mucous membranes
- pH
- normal flora
- mucus
- mucocilliary movement
- peristalsis
- antimicrobial substances such as:
 - lysozyme
 - defensins
 - Ig A and Ig G
 - iron-binding proteins

2. Components of nonspecific immunity:

Soluble proteins	Cells
- complement	- phagocytes - neutrophils
- cytokines	- monocytes
	- macrophages
- acute phase reactants	- NK cells

Complement

Roles of complement activation are:

- microbial lysis
- chemotaxis – attraction of cells into an area of inflammation
- anaphylatoxin activity: increase vascular permeability, smooth muscle contraction, and mast cell degranulation
- regulate neutrophil and monocyte activities
- clearance of immune complexes.

Cytokines

- are glycoproteins secreted by macrophages, lymphocytes, endothelial cells
- may act in an autocrine, paracrine or systemic manner
- can be divided into several groups:
 - interferons (IFN α , β , γ)
 - tumor necrosis factor (TNF α , β)
 - interleukins (IL-1, IL-2....IL-8)
 - transforming growth factors
 - hematopoietic colony-stimulating factors (CSF)
- mediate the acute phase response that is not antigen-specific (inflammatory cytokines).

Acute phase response

- nonspecific reaction
- mediated by:
 - cytokines/chemokines
 - prostaglandins
 - phagocytes
 - lymphocytes
 - endothelial cells
- augments the concentration and function of humoral defensive components such as:
 - C reactive protein
 - serum amyloid A
 - haptoglobin
 - ceruloplasmin
 - fibrinogen
 - complement components
 - transferrin
 - procalcitonin
 - α fetoprotein
 - fibronectin
 - ferritin

These proteins play the following roles:

- increase the number and function of phagocytic cells
- facilitate the delivery of humoral and cellular components to sites of inflammation
- direct the pattern of antigen-specific immune responses.

The inflammatory response

- attraction of phagocytes by a chemotactic gradient of microbial products
- movement of phagocytes to the inflammatory site and contact with the microorganism
- phagocytosis (ingestion) of the microorganism
- development of an oxidative burst directed toward the microorganism
- fusion of the phagosome and lysosome with degranulation of lysosomal contents
- death and degradation of microorganism.

3. Specific Immune Responses

T cells and cellular immunity

Includes:

- destruction of infected cells by T cells
- destruction of intracellular pathogens by macrophages activated by T_{H1} cells.

There are 2 type of T_H cells:

- T_{H1} - is directed principally at intracellular pathogens
 - contribute to humoral immunity
- T_{H2} – initiates the humoral response

B cells and humoral immunity

Involves:

- production of antibodies by plasma cells
- binding of the antibodies to the pathogen
- elimination of the pathogen by accessory cells and molecules of the immune system.

IgM is produced early in the response and has a major role in protecting against infection in the bloodstream.

IgG is the most important defense factor to bacteria, viruses and toxins; can diffuse into the tissue (similar level intra- and extra-vascular).

IgA is produced into lamina propria of the mucosa and is transported across epithelial surfaces

IgE is produced in small amounts and binds avidly to the surface of mast cells.

IgD is present on B lymphocyte membrane and plays a role in forming memory cells.

CLINICAL MANIFESTATIONS OF INFECTION

Fever is an elevation of body temperature above the normal daily variation ($>37.5^{\circ}$).

Pyrogens – are exogenous or endogenous substances that cause fever.

Hematologic manifestation

Cardiac manifestation

Respiratory manifestation

Renal manifestation

Hepatic dysfunction

Upper G_1 bleeding

Abnormalities of mental status

Endocrinologic dysfunction