Chapter 29 Lecture Notes: Parasitism, pathogenicity and resistance

I. Symbiosis – relationship in which 2 organisms spend a portion or all of their lifecycles associated with one another
   A. Commensalism – relationship in which one symbiont (the commensal) benefits, while the other (the host) is not affected
   B. Mutualism – relationship in which both symbionts benefit
   C. Parasitism – relationship in which one of the symbionts lives at the expense of the other (the host); pathogenesis is a consequence of microbial parasitism

II. Some definitions
   A. Infection
      1. Entry of a host by a microorganism capable of causing disease (and subsequent establishment); infection does NOT equal disease
      2. Outcome of infection depends upon
         a) number of infecting organisms
         b) virulence (see below) of the organism
         c) host defenses
   B. Infectious disease – change in the normal structure or function of any part of the body caused by a infectious organism
   C. Colonization – persistence of microbe in the body; colonization does NOT equal disease
   D. Pathogen - any organism that produces a disease
   E. Pathogenicity – ability of a organism to cause disease
   F. Virulence – degree or intensity of pathogenicity
      1. Dependent upon
         a) Infectivity - the ability of an organism to establish an infection
         b) Invasiveness – the ability of an organism to spread to adjacent tissues
         c) Pathogenic potential – the ability of an organism to cause morbid symptoms
      2. Measured by
         a) lethal dose 50 (LD50) – number of pathogens that will kill 50% of the experimental group of organisms within a specific period (Fig 29-2)
         b) infectious dose 50 (ID50) – number of pathogens that will infect 50% of the experimental group of organisms within a specific period
   G. Virulence factor
      1. product of pathogen that contributes to virulence
      2. what defines a virulence factor? this is currently under debate
      3. how to find virulence factors? must consider that they may only be expressed in the host
H. Koch’s postulates
R. Koch definitively proved that *Bacillus anthracis* caused the disease anthrax in cows and *Mycobacterium tuberculosis* caused the disease tuberculosis using Koch's postulates.
1. The suspected pathogen should be present in ALL cases of the disease and NOT present in healthy animals.
2. The suspected pathogen should be grown *in vitro* in pure culture.
3. Cells from a pure culture of the putative pathogen should cause disease in healthy animals.
4. The putative pathogen should be reisolated from the infected animal.

III. Determinants of infectious disease – what do pathogens do that causes disease OR what do pathogens do to survive and grow in the niche of the human body?

A. Be transferred to the host from source
   1. Direct contact transmission - from host to host without intermediate
      a) sneeze
      b) body contact
      c) coughing
      d) touching
      e) sexual contact
   2. Airborne transmission – pathogen is suspended in the air and has traveled > 1 meter from source
      a) sneeze
      b) dust
   3. Vehicle transmission – a single inanimate object (fomite) serves to spread pathogen to multiple hosts
      a) food, water
      b) surgical instruments
   4. Vector transmission – an organism (vector) transmits pathogens from one host to another
      a) external (mechanical) – passive transport of pathogens on organisms feet or other external body part
      b) internal – pathogen in carried within the organism
B. Enter the host

1. Host defenses
   a) resident microflora compete with transient organisms for attachment and nutrients
   b) skin
      (1) epidermis is composed of densely packed epithelial cells covered by keratin which prevent entry into lower layer
      (2) dry, acidic conditions limit growth
      (3) sloughing off of cells removes organisms
   c) hair follicles and sweat glands produce lysozyme and lipids that kill bacteria
   d) mucus membranes
      (1) line the "internal tubes" that are open to the environment (i.e. the gastrointestinal tract)
      (2) composed of an epithelial layer which secretes mucus (see below)
      (3) tight junctions between cells prevent entry into lower layers
      (4) sloughing off of cells removes organisms
   e) mucus (mucin)
      (1) composed of polysaccharides and proteins (see below) that form a physical and chemical defense of the epithelial layer
      (2) sIgA - antibody that binds to both bacteria and mucin to trap bacteria in mucin layer, which is later sloughed off
      (3) antimicrobial secretions: lysozyme, lactoferrin (binds iron), and lactoperoxidase (produces superoxide radicals to damage microbes)
   f) body area specific – see attached

2. Routes of entry inside the human body
   a) through skin – usually via cut or lesion or bite
   b) through mucus membranes that line the GI, respiratory, genitourinary tract, and conjunctiva
      (1) via microbial proteins that
         (a) degrade cell to cell junctions
         (b) disrupt the cells
      (2) via passive mechanisms such as lesions or ulcers, tissue damage by other organisms
      (3) via passage through the cells via endocytosis- can be mediated by bacterial proteins
   c) deposited into the tissues beneath the skin and mucus membranes via deep punctures, injections, bites, or surgery

3. Concept of preferred portal of entry – most microbes have a preferred portal of entry and may not cause the same disease (or any disease) if inoculated via another route
C. Attachment/adherence
   1. Host defenses
      a) mucin layer – see above
      b) immune response – see below
   2. Attachment via adhesins (Table 29-3)
      a) generally attachment of microbe is to specific cellular receptors which are tissue and host specific
      b) types of adhesins (adherence factors)
         (1) surface proteins
         (2) pili or fimbriae – either via pilin or specialized tip protein
         (3) capsule/glycocalyx
         (4) lipotechoic acid
   3. Intracellular residence (invasion) – some bacteria attach to eukaryotic cells and then are internalized via endocytosis
   4. Motility may be important for moving through the mucin layer, against body fluid flows to get to point of attachment

D. Growth inside the host
   1. Host defenses
      a) sequestering of nutrients such as iron
      b) immune response – see below
   2. Bacteria produces components to aid in the acquisition of nutrients
      a) siderophores – for high affinity uptake of iron
      b) hemolysins – lyse RBC
      c) cytolysins – lyse cells
      d) proteases – cleave proteins
      e) lipases – cleave fatty acids
   3. Locations – many pathogens have a specific niche(s) in the human body
      a) within the eukaryotic cells
      b) in tissues
      c) in blood

E. Spread in the body
   1. Host defenses
      a) immune response (see below)
      b) fibrin clots
      c) basement membranes
   2. Degradative enzymes that allow dissemination in tissues (Table 29-4)
   3. via blood stream
   4. via lymphatic system
F. Evading the host response

1. The host immune response in very, very, very brief detail
   a) antibodies – binds to microbial proteins and neutralize their action; bind to microbial cells to aid in phagocytosis by macrophages
   b) immune cells
      (1) neutrophils – phagocytic
      (2) macrophages – phagocytic
      (3) T cells (any types)
         (a) stimulate B cells to make antibodies
         (b) kill infected cells
      (4) B cells – make antibodies
   c) GALT and SALT (gut or skin associated lymphoid tissue) - concentration of immune cells beneath the gut or skin
   d) complement – a group of plasma proteins that activates the immune response by a signaling cascade that generates activated factors that
      (1) recruit other immune cells to the area
      (2) increase blood supply
      (3) coat bacteria to aid in phagocytosis by macrophages
      (4) lyse bacteria via the formation of a membrane associated complex
   e) inflammation
      (1) localized response to tissue injury characterized to pain, heat, redness, swelling
      (2) injured cells release a chemical signal $\rightarrow$ activation of endothelial cells lining the blood vessels $\rightarrow$ attraction and attachment of neutrophils to area vessels $\rightarrow$ passage of neutrophils through spaces in endothelium and into the interstitial fluids
   f) mannose binding protein – binds to mannose on bacteria and activates complement

2. Evasion mechanisms by microbes
   a) sIgA proteases – degrade sIgA
   b) capsule – prevents complement activation and phagocytosis
   c) C5a peptidase – interferes with signaling component of complement
   d) antigenic variation (i.e. alteration of pilin subunit type)
   e) molecular mimicry (i.e. sialic acid in capsule)
   f) toxic proteins kill macrophages and other immune cells
   g) take over of phagocytes by intracellular adapted pathogens

G. Damage the host

1. via exotoxins
   a) soluble, heat-labile proteins that damage the host
   b) synthesized by specific pathogens and frequently encoded by plasmids or prophage
   c) extremely lethal
d) have specific mechanisms of action (Table 29-5)
(1) inhibition of protein synthesis (*P. aeruginosa* exotoxin A, diphtheria toxin)
(2) inhibition of nerve synapse formation (tetanus toxin)
(3) disrupting membrane transport (cholera toxin)
(4) damaging plasma membranes (listeriolysin)
(5) overstimulation of the immune system (superantigen)

e) affect different cells and can be named to reflect this
(1) neurotoxin – nerve cells
(2) cytotoxin – general cells
(3) enterotoxin – intestinal cells

f) immunogenic (stimulate antibody production)

g) AB model of exotoxins (for some but not all) (Fig. 29-4)
(1) toxins are secreted by bacteria as a complex of A and B subunits
(2) A subunit = toxin
(3) B subunit = binds to host cell receptor and allow entry via endocytosis or formation of pore

h) Role in disease (see attached)

2. Endotoxin
   a) lipopolysaccharide of gram negative bacteria
   b) released when cell lysis and during cell division
   c) toxic component = lipid A
   d) heat stables
   e) toxic only at high doses
   f) weakly immunogenic
   g) generally similar among bacteria
   h) mechanism of action (Fig. 29-5)
   (1) activate intrinsic clotting pathway $\rightarrow$ disseminated intravascular coagulation $\rightarrow$ depletion of blood platelets and clotting factors $\rightarrow$ internal hemorrhaging
   (2) activate complement $\rightarrow$ overstimulation of complement mediated immune response system leading to vasodilatation and lowered blood pressure and extensive tissue damage
   (3) activate fibrinolytic pathway which contributes to internal hemorrhaging
   (4) activate kininogen system which caused vasodilation and lowered blood pressure

i) produces general systemic affects such as fever, shock (collapse of the circulatory system), inflammation

j) peptidoglycan and techoic acids may elicit a similar response as endotoxin