

Biology 6 – Test 4 Study Guide

Chapter 14 – Pathology

- A. Overview of terms
 - a. Pathology – study of disease
 - b. Etiology – cause of disease
 - c. Pathogenicity – how a pathogen overcomes host defenses to produce disease
 - d. Pathogenesis – development and progression of disease
 - e. Epidemiology – occurrence and spread of disease
- B. Microbial - Host relationships
 - a. Normal Flora
 - i. Resident flora – permanent microbes in the body.
 - 1. Most are commensals, some mutualistic.
 - 2. Located on skin, mucous membranes of urinary and respiratory systems, intestines
 - ii. Transient flora – temporary microbes
 - b. Symbiosis – relationship between two organisms
 - i. Mutualism – both benefit. E.g. *E. coli* break down food and release vitamin K. Also may outcompete pathogens: *microbial antagonism*.
 - ii. Commensalism – one benefits, other unharmed. E.g. organisms that live on our skin.
 - iii. Parasitism – one benefits, other is harmed. Diseases caused by these. Some are *opportunistic* – causes disease in different environment. E.g. *E. coli* outside of intestine can be harmful, or breakage in skin lets in *Staph*, or weakened immune system lets in *Pneumocytis*.
- C. Etiology - Koch's Postulates
 - a. Postulates (Fig. 14.3)
 - i. Same pathogen must be present in every case of disease.
 - ii. Pathogen must be able to be isolated and cultured in pure media.
 - iii. Cultured pathogen must be able to cause disease again.
 - iv. Same pathogen must be able to be isolated from the organism given disease.
 - b. Exceptions
 - i. Pathogen may not be able to be cultured in pure media (e.g. viruses, *Rickettsia*).
 - ii. Diseases with multiple causes (e.g. nephritis, UTI)
 - iii. Pathogen causes multiple diseases/symptoms (e.g. *Mycobacterium tuberculosis*)
- D. Pathogenesis
 - a. Types of infections
 - i. Duration and severity
 - 1. Subclinical – no symptoms (e.g. Hepatitis A)
 - 2. Acute – quick and severe (e.g. flu)
 - 3. Chronic – slow but continuous (e.g. tuberculosis)
 - 4. Latent – has an inactive phase (e.g. HIV)
 - ii. Placement
 - 1. Local – confined to one area
 - 2. Focal – localized to one area but toxins/pathogens can affect other areas
 - 3. Systemic – affects entire body
 - iii. Sequence
 - 1. Primary infection – the first infection of a healthy person
 - 2. Secondary infection – the second pathogen. Usually opportunistic

- b. Disease progression – general stages (Fig. 14.5)
 - i. Incubation – initial infection but no symptoms yet
 - ii. Prodromal – early/mild symptoms
 - iii. Illness – most acute symptoms, immune system overrun. Acme is the peak.
 - iv. Decline – begin recovery. Symptoms subside, immunity recovers
 - v. Convalescence – recovered. Body regains strength.
- E. Epidemiology
 - a. Spread of infection
 - i. Occurrence (Fig. 14.4)
 - 1. Incidence - # of people who got the disease during a period of time
 - 2. Prevalence - # of people who have the disease at a given point in time
 - ii. Degree of spreading
 - 1. Endemic – localized to a certain geographic region and considered “normal”. Sometimes seasonal (e.g. chickenpox)
 - 2. Epidemic – an outbreak at higher than normal rates (e.g. Diphtheria in former USSR 1990s)
 - 3. Pandemic – world wide. E.g. 1918 flu or current AIDS
 - iii. Reservoirs – sources of infection
 - 1. Human – e.g. HIV
 - 2. Animal – usually vectors such as arthropods
 - 3. Non-living – soil and water are main ones
 - iv. Transmission (Fig. 14.6-8)
 - 1. Contact
 - a. Direct – requires touching of individuals
 - b. Indirect - use nonliving intermediate called a *fomite*
 - c. Droplet – in a liquid droplet (e.g. sneezing)
 - 2. Vehicle – uses medium (e.g. water, air, food)
 - 3. Vector – uses a living organisms
 - a. Mechanical – passive transfer
 - b. Biological – transfer is necessary for lifecycle of pathogen
 - b. Nosocomial infections – spread through hospitals (Fig. 14.9)
 - i. Common microbes and infections (Tab. 14.5)
 - ii. Compromised host – wounds, lowered immunity
 - iii. Chain of transmission – hospital practices may spread disease
 - 1. Multiple modes of transmission
 - 2. Equipment and procedures contribute to transmission
 - iv. Prevention: wear gloves, masks. Wash hands. Proper disposal of fluids, needles, etc.
 - c. Methods of investigation
 - i. Descriptive – describes occurrence of disease to trace back to origin. E.g. John Snow (1850) solved cholera outbreak by mapping individuals and finding common water source.
 - ii. Analytical – cause and effect relationship of disease. E.g. Florence Nightingale found factors contributing to epidemic typhus (poor sanitation and food)
 - 1. Handout on hot tub rash
 - iii. Experimental – potential causative agents are tested to see if they cause disease. Not ethical in humans.
- F. Public Health Organizations
 - a. Center for Disease Control and Prevention (CDC) – US organization
 - i. Charge
 - 1. Provide safety guidelines

2. Recommendations on drugs and vaccines
3. Storing drugs and vaccines in cases of emergency
- ii. *Morbidity and Mortality Weekly Report (MMWR)*
- b. World Health Organization (WHO) – International
 - i. Similar charge as CDC but on a global scale. Have many direct activities as well
 - ii. Publishes *Weekly Epidemiological Record*.

Chapter 15 – Pathogenicity

- A. Host Entry
 - a. Portals
 - i. Mucous membranes – on most inner linings (e.g. respiratory, gastrointestinal, enitourinary, conjunctiva)
 - ii. Skin – outer lining.
 - iii. Parenteral – directly deposited on target tissue. Usually due to wounds, surgery, animal bites.
 - b. Dosage
 - i. ID₅₀ – pathogen dose necessary to infect half of population.
 - ii. LD₅₀ – toxin dose necessary to kill half of population.
 - c. Adherence
 - i. Use pili, fimbriae, capsule, cell wall etc. for binding.
 - ii. May use adhesins to specifically bind receptors in tissue specific adherence. (Fig. 15.1)
 - iii. Biofilms – mass of pathogens in cooperative adherence. First organisms attached secrete materials that assist others to help form the biolayer. E.g. dental plaques on teeth.
- B. Tissue Penetration – most pathogens must enter a cell to thrive.
 - a. Entry
 - i. Endocytosis – adherence can trigger endocytosis in host cell. Invasins may be involved that help rearrange cytoskeleton to facilitate entry and intracellular movements. (Fig. 15.2)
 - ii. Tissue degradation – enzymes secreted that dissolve barriers.
 1. E.g. hyaluronidase – produced by *strep* breaks down hyaluronic acid, a sugar that holds cells together. This is the cause of gangrene.
 2. E.g. collagenase - produced by *Clostridium* breaks down protein collagen which holds together connective tissue.
 - b. Evasion
 - i. Structures
 1. Capsules – resists phagocytosis by white blood cells.
 2. Cell wall – proteins and waxes in cell wall also resist phagocytosis.
 - ii. Enzymes
 1. Induce clots – coagulases produced by *staph* allow clots to form and shield the pathogen from host defenses.
 2. Break down antibodies – certain proteases break down antibodies.
 - iii. Antigenic variation – surface proteins are changed to avoid immune detection. Due to built-in variation and high mutation rate.
- C. Tissue Damage
 - a. Use up resources – nutrients are taken from host. E.g. mechanism of siderophores that scavenge iron.
 - b. Direct damage – physical destruction by movements, digestion.
 - c. Toxins

- i. Exotoxins – secreted proteins
 - 1. A-B toxins (Fig. 15.5)
 - a. B binds host cell receptor, A inhibits protein synthesis.
 - b. E.g. diphtheria toxin – nerve, heart, kidney cells.
 - 2. Membrane-disrupting – may lyse cell by forming protein channels in membrane, or direct interference of phospholipids bilayer.
 - 3. Superantigens – provoke intense immune response.
- ii. Endotoxins – lipopolysaccharides (LPS) of cell wall
 - 1. In Gram- bacteria only. Released upon death of bacterium.
 - 2. Effects
 - a. Stimulate macrophages to release cytokines. This may result in fever, chills, shock etc. (Fig. 15.6)
 - b. Activates blood clotting.

Chapter 16 – Innate Immunity (Non-specific Defenses)

- A. Barriers - physical and chemical protection
 - a. Skin – protective layer + oil glands (Fig. 16.2)
 - b. Mucous membranes – acids, mucous, saliva, tears (Fig. 16.3)
 - c. Competition with normal flora.
- B. Cellular
 - a. Cell types (Tab. 16.1)
 - i. Granulocytes – have granules. Some release chemicals, others are phagocytic
 - ii. Agranulocytes – no granules. Some release chemicals, others are phagocytic, lymphocytes are used in specific defense.
 - b. Phagocytosis
 - i. Steps: chemotaxis, adherence, ingestion, digestion, excretion (Fig. 16.7).
 - ii. Some will hold on to antigens to activate specific defenses.
- C. Inflammatory Response
 - a. Caused by direct damage to tissue. Symptoms include swelling, redness, pain.
 - b. Mechanism (Fig. 16.8)
 - i. Damaged tissue releases chemicals that lead to *vasodilation* and leaky vessels. E.g. histamine released by mast cells in connective tissue.
 - ii. White blood cells migrate to site of damage by squeezing through leaky walls by *diapedesis* (includes margination and emigration). Some cells fight infection, platelets help clot broken vessels.
 - iii. Abscess forms with pus from concentration of cells and debris.
 - iv. Repair – scab forms. Epidermis regenerates. Scar tissue replaces irreplaceable cells.
 - c. Chronic inflammation
 - i. Continuous inflammation response due to persistent damaging agent.
 - ii. Granulomas can form – a pocket containing the walled-off agent. E.g. tubercles in tuberculosis.
- D. Fever – raised body temperature
 - a. Mechanism
 - i. Phagocyte stimulation releases IL-1 which stimulates hypothalamus to raise thermostat set point. Other cytokines (e.g. TNFs) may also stimulate hypothalamus. (Fig. 15.6)
 - ii. Temperature raised by blood vessel constriction, increase metabolism, shivering.
 - b. Purposes – slow pathogen growth, stimulate macrophages, speed tissue repair.

- c. Complications – heart dysfunction, metabolic side effects (dehydration, acidosis, electrolyte imbalance)
- E. Complement System
 - a. Components – made of proteins that activate and work with one another. Activation through cascades.
 - b. Pathways of action (Fig. 16.9)
 - i. Opsonization – enhancement of phagocytosis by coating bacteria.
 - ii. Inflammation – stimulates mast cell release of histamine and a chemoattractant for macrophages.
 - iii. Cytolysis – membrane attack complex (MAC) forms and creates pores in membrane of pathogen. (Fig. 16.10)
 - c. Pathways for activation – these allow for multiple ways to initiate cascade.
 - i. Classical – uses antibodies to recognize antigens (Fig. 16.12)
 - ii. Alternative – uses protein factors to recognize lipocarbohydrates. (Fig. 16.13)
 - iii. Lectin – uses lectin to recognize carbohydrates. (Fig. 16.14)
- F. Interferon
 - a. Small proteins that induce transcription.
 - b. α -IFN and β -IFN produced by infected cells as a distress signal. (Fig. 16.15)
 - i. Txn and tln of IFN triggered by infection.
 - ii. IFN is released and sensed by uninfected cells. Usually by cell signaling (receptor, signal transduction, response)
 - iii. Uninfected cell produces antiviral proteins (AVP) which inhibit viral replication.
 - c. γ -IFN produced by lymphocytes. Stimulates neutrophils and macrophages.

Chapter 17 – Adaptive (Specific) Immunity

- A. Main components
 - a. Features of Adaptive Immunity
 - i. Recognition of foreign particles. Antigens are foreign and recognized by antibodies or T-cell receptors (Fig. 17.1)
 - ii. Specificity and diversity – we can make up to 100 million different antibodies/T-cell receptors. Each can recognize a specific shape.
 - iii. Memory – we can be trained to respond more quickly to a second exposure of an antigen.
 - b. Main Parts
 - i. Humoral Immunity – fights small pathogens (viruses, bacteria, toxins)
 - 1. Uses B cells.
 - 2. Antibody is main weapon. Soluble factor.
 - ii. Cell-Mediated Immunity – fights larger organisms (infected cells, eukaryotes)
 - 1. Uses T cells.
 - 2. T-cell receptor is main weapon. Fights “hand-to-hand.”
 - c. Differentiation
 - i. Both B cells and T cells are derived from stem cells (Fig. 17.8).
 - ii. Lymphocytes that recognize self-antigens are destroyed in the fetus. This is clonal deletion
 - iii. T cells mature in thymus gland which is mostly active in children.
- B. Humoral Immunity
 - a. Clonal Selection (Fig. 17.5)
 - i. 10^8 antibodies. Each B cell makes one type of antibody. Binding of an antigen to the one cell that has the correct antibody. Makes it divide.

- ii. Activated B cell will produce memory and plasma cells.
 - iii. Memory cells remain in body for a long time in case of subsequent exposure to antigen.
 - iv. Plasma cells produce antibodies (2000/sec)
 - b. Antibody Structure
 - i. Y shaped (Fig. 17.3)
 - 1. Made of two heavy and two light chains. Each has a constant (C) and variable (V) region.
 - 2. V regions make up the antigen binding sites.
 - 3. Fc domain is stem formed from heavy C regions
 - ii. 5 Classes – IgG, M, A, D, E (Table 17.1)
 - c. Antibody Action (Fig. 17.7)
 - i. Agglutination – clumping of pathogen. Eases phagocytosis of small sized objects.
 - ii. Opsonization – coats pathogen for better phagocytic recognition.
 - iii. Neutralization – surrounds pathogen or toxin preventing it from attaching or entering cell.
 - iv. Cytotoxicity – coated pathogen will be recognized by cytotoxic lymphocytes.
 - v. Complement – classical system activated by antibodies.
 - vi. Inflammation – complement will induce inflammation.
 - d. Immune Response (Fig. 17.16)
 - i. Initial exposure triggers primary response. May not be protective.
 - ii. Second exposure triggers stronger secondary response. Usually more protective.
- C. Cell-Mediated Immunity
- a. Communication
 - i. Cell-cell contact via receptors. E.g. CD4 and CD8 receptors.
 - ii. Chemicals – uses cytokines
 - b. Cell types and functions
 - i. Antigen presenting cells (APC) (Fig. 17.13-14)
 - 1. Displays an antigen on MHC (major histocompatibility complex), a protein that marks cell as “self” and to display an antigen.
 - 2. Dendritic or macrophages
 - ii. Clonal selection – a T cell will become activated by being bound by an antigen and differentiate into the cell types below.
 - 1. Helper – produce cytokines
 - a. T_H1 – these produce cytokines to activate cell-mediated immunity
 - b. T_H2 – cytokines that stimulate some B cells.
 - c. Activation (Fig. 17.10)
 - i. APC presents antigen and binds T_H receptor.
 - ii. IL-1 induces T_H to produce IL-2
 - iii. This causes further clonal selection of T_H .
 - 2. Cytotoxic – destroys cells on contact (Fig. 17.11)
 - a. Binds to cells with MHC presenting antigen.
 - b. Perforin released. This, like complement, makes holes in membrane and lyses cell.
 - 3. Memory – long-lived.
- D. Humoral and Cell-mediated Immunity working together (Fig. 17.19)
- a. Antibody production
 - i. T_H binds APC
 - ii. T_H also binds B cell and acts as a bridge.
 - iii. IL-2 stimulates B cell clonal selection

- b. Antibody-dependent cell-mediated toxicity (ADCC) (Fig. 17.15)
 - i. Pathogen is first coated with antibody
 - ii. Macrophages, NK, etc. bind to Fc and release toxic compounds.

Chapter 18 – Applications of Immunology

A. Immunization

- a. Overview
 - i. Active
 - 1. Give an antigen (vaccine), causing an immune response.
 - 2. Many require multiple challenges to produce stronger secondary/tertiary responses, gives long-term protection.
 - ii. Passive
 - 1. Give ready-made antibodies.
 - 2. No immune response, but gives temporary protection.
- b. Types of Vaccines
 - i. Traditional
 - 1. Attenuated whole-agent. Live but weakened strain. Can reproduce. Most effective but dangerous if it mutates. (e.g. polio, MMR)
 - 2. Inactivated whole-agent – chemically killed. (e.g. flu)
 - 3. Toxoids – inactivated toxins (e.g. tetanus, diphtheria)
 - 4. Subunit – antigenic fragment (e.g. hep B viral coat)
 - 5. Conjugated – put two kinds of compounds together. (e.g. protein and carbohydrate in children's *H. influenza B*)
 - ii. Newer Vaccines
 - 1. DNA – a plasmid is injected. It contains a gene that when *txn* and *tln* will produce a protein that gives immune response.
 - 2. Gene therapy – can use viral infections to insert a gene.
 - 3. Recombinant (GM) plants – contains gene. When eaten, supplies antigen.
 - iii. Safety
 - 1. Rare cases of vaccine causing the disease itself (e.g. attenuated polio)
 - 2. Unlikely but potential link to autoimmune diseases. Some believe boosting immunity may overstimulate it. Very unlikely cause of autism.
- c. Types of Passive Immunizations
 - i. Antisera – noncellular part of blood containing antibodies (e.g. snake venom treatments)
 - ii. Breast milk – contains IgG – immunoglobulin G.
 - iii. Purified antibodies – specific antibodies can be purified for maximum effect.

B. Diagnostics

- a. Natural Antibody Function
 - i. Precipitation – when antibodies bind antigen, a large complex is formed and precipitates out of solution (Fig. 18.4)
 - ii. Agglutination – used to clump larger particles that are already precipitated. E.g. red blood cells in blood typing. (Fig. 18.5)
 - iii. Neutralization – a toxin is neutralized by antibodies (Fig. 18.9)
- b. Fluorescence
 - i. Direct – fluorescent dye-labeled antibody binds to antigen and glows. (Fig. 18.11)
 - ii. Indirect – primary antibody binds antigen. Secondary fluorescently labeled antibody binds primary. This gives greater sensitivity.

- iii. FACS – fluorescence activated cell sorter. Sorts cells. (Fig. 18.12)
 - 1. Pool of cells is labeled with antibody.
 - 2. Dripped through a small opening allowing only one cell at a time.
 - 3. Laser detects fluorescence.
 - 4. Electrode charges droplet.
 - 5. As it falls it moves towards opposite charged plate and goes into correct collection tube.
- c. ELISA – enzyme linked immunosorbent assay. (Fig. 18.14)
 - i. Direct
 - 1. Antibody adsorbed to well.
 - 2. Sample added and antigen binds antibody.
 - 3. Antibody linked to an enzyme is added.
 - 4. Substrate added and when cleaved forms color.
 - ii. Indirect
 - 1. Cell/antigen adsorbed to well.
 - 2. Test serum with potential primary antibody added.
 - 3. Secondary antibody with linked enzyme (e.g. peroxidase, phosphatase) that recognizes primary Fc binds if primary is present.
 - 4. Substrate added. If cleaved by enzyme, color forms.
 - iii. Pregnancy test uses a direct method (video)
 - 1. Antibody to chorionic gonadotropin (hCG), a placental hormone, is adsorbed to test site.
 - 2. Antibody to a free antibody is adsorbed to control site.
 - 3. Labeled free antibody that can bind to hCG is deposited at end of stick.
 - 4. Urine deposited at end of stick and draws free antibody up stick.
 - 5. In control, free antibody always binds.
 - 6. In test site, only free antibody bound to hCG will bind.