Chapter 8
Pathophysiology

Learning Objectives

- Discuss cellular adaptation
- Describe cellular injury, cellular death
- Describe factors of disease in human body
- Describe systemic manifestations resulting from cellular injury

Learning Objectives (Cont'd)

- Discuss familial diseases, associated risk factors
- Describe environmental risk factors
- Describe aging as risk factor for disease
Learning Objectives (Cont’d)

• Discuss process of analyzing disease risk
• Discuss combined effects of risk factors, interactions among risk factors
• Discuss hypoperfusion
• Define cardiogenic, hypovolemic, neurogenic, anaphylactic, septic shock

Learning Objectives (Cont’d)

• Describe multiple organ dysfunction syndrome
• Define immune response characteristics
• Discuss activation of immune system
• Discuss fetal, neonatal immune function

Learning Objectives (Cont’d)

• Discuss aging, immune function in elderly
• Describe inflammation response
• Discuss role of mast cells, inflammation response
• Describe plasma protein system
Learning Objectives (Cont'd)

- Discuss cellular components of inflammation
- Describe systemic manifestations of inflammation response
- Describe resolution, repair from inflammation
- Discuss aging effect on mechanisms of self-defense

- Discuss hypersensitivity
- Describe deficiencies in immunity, inflammation
- Discuss interrelations among stress, coping, illness
- Describe neuroendocrine regulation

Alterations in Cells & Tissues

- Cellular adaptation
  - Atrophy
    - Cell shrinkage
    - Pathologic
    - Physiologic
Alterations in Cells & Tissues (Cont’d)

- Cellular adaptation
  - Hypertrophy
    - Size increase of cell, tissue, organ
    - Due to workload increase demand
    - Usually temporary
  - Hyperplasia
    - Cellular division, increase number specific cell type
    - Physiologically occurs as part of normal growth
    - Pathologically occurs as tumors

Alterations in Cells & Tissues (Cont’d)

- Cellular adaptation
  - Dysplasia
    - Abnormal size, shape, organization
    - Can be reversed if irritation removed early
    - Many considered precancerous
  - Metaplasia
    - Transformation of 1 mature differentiated cell into another
    - Cartilage changes to bone

Cellular Injury

- Hypoxic
  - Reduction in oxygenated blood, hemoglobin loss
  - Red blood cell reduction
  - Respiratory, cardiac system ineffectiveness

- Chemical
  - Toxic substance
  - Common, environmental
  - Damage cell wall, sodium, water, calcium continue damage
Cellular Injury (Cont’d)

- Infectious
  - Bacteria
  - Viruses
  - Fungi

- Infectious
  - Protozoa
  - Parasites
  - Prions
  - Immunologic, inflammatory

- Infectious
  - Injurious genetic factors
  - Injurious nutritional imbalance
  - Injurious physical agents
Cellular Injury (Cont’d)

- Manifestations of cellular injury
  - Anabolism, catabolism
  - Cellular swelling
  - Lipid accumulation
  - Systemic manifestations

Cellular Death & Necrosis

- Apoptosis
- Autolysis
- Necrosis

Cellular Death & Necrosis (Cont’d)

- Necrosis
  - Coagulative
  - Liquefactive
  - Casous
  - Fat
  - Gangrenous
Cellular Environment

- Depend on environment for survival
  - Fluid, electrolytes balance necessary
- Water movement between intracellular fluid & extracellular fluid
  - Osmosis
  - Diffusion
  - Mediated transport
    - Active
    - Facilitated

Cellular Environment (Cont’d)

Osmosis

Cellular Environment (Cont’d)

Diffusion
Cellular Environment (Cont’d)

Capillary Filtration Forces

- Water movement between plasma & interstitial fluid
  - Result of pressure
  - Filtration
  - Hydrostatic pressure
  - Osmotic pressure
  - Oncotic pressure
  - Capillary & membrane permeability

Cellular Environment (Cont’d)

- Alterations in water movement
  - Edema
    - Fluid distribution problem
    - Increased hydrostatic pressure
    - Decreased plasma osmotic pressure
    - Increased capillary membrane permeability
    - Lymphatic obstruction
    - Clinical manifestations
Role of Electrolytes

- Sodium
  - Chief extracellular cation
  - Maintains water balance, neuromuscular irritability, acid-base balance

- Chloride
  - Major anion
  - Provide neutrality to sodium, other cations

Role of Electrolytes (Cont’d)

- Sodium & chloride balance
  - Normal sodium, 135-145 mEq/L, maintained by kidneys
    - Aldosterone
    - Renin
    - Natriuretic

Role of Electrolytes (Cont’d)

Renin-angiotensin-aldosterone system
Role of Electrolytes (Cont’d)

- Sodium & chloride balance
- Alterations in sodium, chloride, & water balance

Role of Electrolytes (Cont’d)

- Dehydration
  - Isotonic
  - Hypernatremic
  - Hyponatremic
- Overhydration

Electrolyte Imbalances

- Sodium
  - Primary function
  - Hypernatremia
  - Hyponatremia
Electrolyte Imbalances (Cont’d)

- **Potassium**
  - Maintenance of fluid, pH balance inside cells, normal neurologic functions, cardiac function, muscle contraction, glycogen storage in liver/skeletal muscle
  - Hyperkalemia
  - Hypokalemia

Electrolyte Imbalances (Cont’d)

- **Calcium**
  - Cell membrane stability & permeability, hormone secretion, muscle contraction, nerve impulse transmission
  - Hypercalcemia
  - Hypocalcemia

Electrolyte Imbalances (Cont’d)

- **Magnesium**
  - Helps absorb, use other electrolytes, cardiac muscle relaxation
  - Hypermagnesemia
  - Hypomagnesemia
Acid-Base Balance

- Acid
  - Hydrogen ion, proton donor
- Base
  - Hydrogen ion, proton acceptor
- Balance expressed by pH
  - 0 – most acidic, 14 – most alkaline

Acid-Base Balance (Cont'd)

- Hydrogen ion & pH
  - Inversely proportionate
  - More hydrogen, more acidic
  - Less hydrogen, more basic/alkaline
  - pH, expression of negative logarithm of hydrogen ion concentration in solution
    + Change in 1 pH unit, 10-fold change

Acid-Base Balance (Cont'd)

- Buffer systems
  - Carbonic acid-bicarbonate buffering
  - Protein buffering
  - Renal buffering
  - Other buffers
Acid-Base Balance (Cont’d)

- Acid-base imbalances
  - Mixed acid-base disturbances

- Respiratory Acidosis

- Respiratory Alkalosis
Acid-Base Balance (Cont’d)

- Acid-base imbalances
  - Compensation in acid-base disorders
    - Metabolic acidosis compensated by respiratory alkalosis, respiratory acidosis compensated by metabolic alkalosis
    - Determine direction of pH

Genetics & Familial Diseases

- Germ theory
  - Some disease processes caused by microorganisms
- Genetic factors
- Environmental Factors
- Age & gender

Analyzing Disease Risks

- Disease rates
  - Incidence
  - Prevalence
  - Mortality
Analyzing Disease Risks (Cont’d)

- Risk factor analysis
  - Causal
  - Noncausal
  - Combined effects & interaction of risk factors
    - Occurrences/characteristics associated with increased disease rate

Analyzing Disease Risks (Cont’d)

- Familial tendency
  - Genetic impact with environmental factors
- Age & age-related disorders
  - Heart disease
  - Alzheimer’s, degenerative diseases
  - Metabolic changes

Analyzing Disease Risks (Cont’d)

- Common familial diseases & associated risk factors
  - Immunologic disorders
  - Cancer
  - Endocrine disorders
  - Hematologic disorders
  - Cardiovascular disorders
Analyzing Disease Risks (Cont’d)

- Common familial diseases & associated risk factors
  - Renal disorders
  - Gastrointestinal disorders
  - Neuromuscular disorders
  - Psychiatric disorders

Hypoperfusion

- Inadequate oxygen available to tissue
- Fick principle
  - Oxygen volume available for organism
- Pathogenesis

Hypoperfusion (Cont’d)

- Decreased cardiac output
  - Fluid shifts from interstitial spaces into vascular space
    - Ion gradient change, loss of intravascular volume
  - When body cannot compensate, shock
- Cellular metabolism impairment
Types of Shock
- Cardiogenic
- Hypovolemic
- Neurogenic

Types of Shock (Cont'd)
- Anaphylactic
- Septic

Multiple Organ Dysfunction Syndrome
- Progressive impairment, 2+ organ systems
  - Uncontrolled inflammatory response
- Pathogenesis
  - Adaptive cellular process from injury, insult
  - Systemic inflammation
  - Primary
  - Secondary
Multiple Organ Dysfunction Syndrome (Cont’d)

- Clinical progression
  - Early identification of signs/symptoms, implement prevention strategies

Immune System & Resistance to Disease

- Resistance
  - Body’s ability to resist attacks

- Susceptibility
  - Vulnerability, weakness

- Natural/non-specific system
  - Responds, attacks immediately
  - Anatomic body barriers

Immune System & Resistance to Disease (Cont’d)

- Inflammation
- Acquired, adaptive system
  - Slower, targets specific antigens

- Defense
  - Anatomic barrier
  - Chemical, cellular reaction
  - Immune response
Characteristics of Immune Response

- Natural vs. acquired immunity
  - Natural
    - No immunologic memory
  - Acquired
    - Develops after birth, antigen exposure
    - Active acquired, after host naturally exposed to antigen
  - Passive
    - Mother passing, medical treatment

Characteristics of Immune Response (Cont’d)

- Primary vs. secondary immune response
  - Primary
  - Secondary
- Formation of lymphocytes

Characteristics of Immune Response (Cont’d)

- Humoral vs. cell-mediated immunity
  - Differentiation of lymphocytes into B cells
  - Minimal ability to recognize antigens
  - B cell activated by helper T cell, divide, antibodies formed, defense begins
  - Cell-mediated immunity, differentiation of lymphocytes into T cells
Characteristics of Immune Response (Cont’d)

Lymphatic Tissues: Sites of B-cell & T-cell Differentiation

Activation of Immune System

- Antigens & immunogens
- Blood group antigens
- ABO system
- Rh system

Activation of Immune System (Cont’d)

ABO System
Humoral Immune Response

- Function of B lymphocytes
- Phagocytosis
- Differentiate into memory cells, plasmablasts

Immunoglobulins

- Structure of immunoglobulins
- Classes of immunoglobulins
  - IgC
  - IgA
  - IgM
  - IgD
  - IgE

Immunoglobulins (Cont’d)

- Function of antibodies
  - Circulates in blood
  - Neutralization/destruction of antigen
  - Agglutination
  - Precipitation
  - Neutralization
  - Defend against viruses
  - Enable bacteria become susceptible to phagocytosis
Immunoglobulins (Cont'd)

- Antibodies as antigens
- Monoclonal antibodies
- Secretory immune system

Immunoglobulins (Cont'd)

- Cell-mediated immune response
  - Become T lymphocytes
  - T cells respond to antigen

Immunoglobulins (Cont'd)

- Cellular interaction in immune response
- Cytokines
- Antigen processing, presentation & recognition
Immunoglobulins (Cont’d)

- T-cell & B-cell differentiation & control
- Fetal & neonatal immune function
- Age

Inflammation

- Inflammation Process
Inflammation (Cont’d)

- Acute inflammatory response
  - Occurs immediately after injury
  - Mast cells
  - Degranulation of vasoactive amines & chemotactic factors
  - Synthesis of leukotrienes & prostaglandins

Inflammation (Cont’d)

Synthesis of Leukotrienes & Prostaglandins

Inflammation (Cont’d)

- Plasma protein systems [obj 21]
  - Complement system
  - Coagulation system
  - Kinin system
  - Control & interaction of plasma protein system
Inflammation (Cont’d)

- Cellular components of inflammation
  - Function of phagocytes
  - Polymorphonuclear neutrophils
  - Monocytes & macrophages
  - Eosinophils

Diapedesis of Phagocyte
Inflammation (Cont'd)

- Cellular products
  - Interleukins
  - Lymphokines
  - Interferon
  - Systemic responses of acute inflammation

Inflammation (Cont'd)

- Chronic inflammatory response
- Local inflammatory response

Inflammation (Cont'd)

- Phases of resolution & repair
  - Acute inflammation
  - Resolution
  - Debridement
  - Primary intention
  - Secondary intention
Inflammation (Cont'd)

- Phases of resolution & repair
  - Reconstructive phase
  - Maturation phase
  - Dysfunctional wound healing
  - Dysfunction during the inflammatory response
  - Dysfunction during the reconstructive phase

Inflammation (Cont'd)

- Wound Repair by Primary or Secondary Intention

- Aging & self-defense mechanisms
  - Neonates, aged have difficulty healing
Variances in Immunity & Inflammation

- Hypersensitivity, allergy, autoimmunity, alloimmunity
  - Hypersensitivity reaction
  - Allergy
  - Autoimmunity
  - Alloimmunity
- Targets of hypersensitivity
- Allergy

Variances in Immunity & Inflammation (Cont’d)

- Mechanisms of hypersensitivity
  - Substances initiate inflammation, damage to healthy tissue
  - Type I
    - IgE-mediated allergic reaction
  - Type II
    - Tissue-specific reaction
  - Type III
    - Immune complex-mediated reaction
  - Type IV
    - Cell-mediated reactions

Variances in Immunity & Inflammation (Cont’d)

- Immunoglobulin E-mediated allergic reactions
  - Production of antigen-specific IgE after exposure to antigen
  - Environmental
  - Histamine release, effects
  - Atopic individuals
Variances in Immunity & Inflammation (Cont'd)

Type I Hypersensitivity Reactions

- Tissue-specific reactions
  - Complement system
  - Phagocytosis
  - Cytotoxins
  - Disabling

Variances in Immunity & Inflammation (Cont'd)

Mechanism of Type II, Tissue-Specific Reactions
Variances in Immunity & Inflammation (Cont'd)

- Immune complex-mediated reactions
  - Antigen-antibody complex
  - Localized or systemic

Mechanism of Type III, Immune Complex-Mediated Reactions

- Cell-mediated tissue reactions
  - Do not occur as result of antibody actions
  - Mediated by T lymphocytes
    - Cytotoxic
    - Transfer delayed hypersensitivity cells
**Variance in Immunity & Inflammation (Cont'd)**

**Mechanism of Type IV, Cell-Mediated Reactions**

- **Autoimmunity**
  - Mechanisms
    - Previously sequestered antigen exposed to body
    - Neoantigen development
    - Infectious diseases complications
    - Forbidden clone
    - Suppressor cell function

- **Alloimmunity**
  - Immune response to antigens of another individual

**Variance in Immunity & Inflammation (Cont'd)**

- **Autoimmune & isoimmune diseases**
  - Graves' disease
  - Rheumatoid arthritis
  - Myasthenia gravis
  - Immune thrombocytopenic purpura
  - Isoimmune neutropenia
  - Systemic lupus erythematosus
  - Rh & ABO alloimmunization
Variances in Immunity & Inflammation (Cont’d)

- Immunity & inflammation deficiencies
  - Congenital immune deficiencies
  - Acquired deficiencies
- Replacement therapies for immune deficiencies
  - Gamma-globulin therapy
  - Transplantation, transfusion
  - Gene therapy

Stress & Disease

- Concepts of stress
  - Hans Selye
- General adaptive syndrome
  - Stages
    - Alarm stage
    - Resistance, adaptation stage
    - Exhaustion stage

Stress & Disease (Cont’d)

- Psychologic mediators & specificity
  - Adrenal cortex
  - Pituitary gland
- Homeostasis as dynamic steady state
  - Body’s ability to maintain constant internal environment
  - Dynamic steady state
Stress Response

- Psychoneuroimmunologic regulation
- Neuroendocrine regulation
- Catecholamines

Stress Response (Cont’d)

- Cortisol
- Role of immune system

Stress, Coping, & Illness Interrelations

- Potential effect of stress based on effectiveness of coping
  - Effective coping skills, transient effect
  - Ineffective coping skills, significant effect
Chapter Summary

- Human body fascinating, complex organism
- Cell, basic unit of life
- Tissues, groupings of similar cells, perform common function
- Organs composed of tissues, work together to accomplish specific functions

Chapter Summary (Cont’d)

- Body organs work to maintain homeostasis of organism
- Structure, function changes of cells can be helpful/harmful to host, occur because of stimulus
  - Adaptation include atrophy, hypertrophy, hyperplasia, dysplasia, metaplasia

Chapter Summary (Cont’d)

- Most common cellular injury forms include hypoxia, chemical injury, infectious injury, immunologic & inflammatory injury, genetic factors, nutritional imbalances, physical agents
- Cellular death, result of spreading irreversible injury/necrosis, preprogrammed response for tissue regeneration/apoptosis
Chapter Summary (Cont'd)

- Viruses most common cause of infections in human organism
- Water in body distributed between intracellular, extracellular compartments
  - Proper distribution of fluid between these compartments essential for proper function

Chapter Summary (Cont'd)

- Movement of water/other substances between various compartments of body occurs by osmosis, diffusion, mediated transport
- Water balance affected by distribution, concentration of electrolytes
- Proper electrolyte balance essential for body systems function

Chapter Summary (Cont'd)

- Upsetting proper electrolyte balance generates signs/symptoms, primarily in central nervous system, peripheral nervous system, heart
- Body strives to maintain constant concentration of hydrogen ions
  - pH should be between 7.35 - 7.45
  - Greater than 7.45, alkalosis
  - Less than 7.35, acidosis
Chapter Summary (Cont’d)

- Acid-base derangements, respiratory or metabolic
  - Body compensates for change through carbonic acid–bicarbonate buffer system, protein buffering, renal mechanisms
- Hypoperfusion, inadequate tissue perfusion
  - Body must deliver oxygen, remove cellular waste products from tissues
  - Cardiac output, adequate blood flow determinant

Chapter Summary (Cont’d)

- MODS, progressive impairment 2+ organ systems
  - Uncontrolled inflammatory response from severe illness/injury
  - Sepsis, trauma, or severe burn injuries
  - Cause unknown
- Immune system has multiple mechanisms against foreign invaders
  - Anatomic barriers, chemical attacks/inflammatory response, adaptive mechanism

Chapter Summary (Cont’d)

- When immune system produces exaggerated response to stimulus, can be harmful
  - Hypersensitivity
- Ongoing research for effects of stress on body, link to disease
  - Communication between immune, nervous, endocrine systems believed to play role in disease progression, as relates to stress response
Chapter Summary (Cont’d)

- Understand cell interaction in various body tissues
  - Assists in understanding physiologic basis, condition of patient, best treatment approach

Questions?