Pathophysiology ("Patho") Notes

1: Introduction to Pathophysiology / Altered cell and tissue biology

Learning Outcomes

Introduction to Pathophysiology

- Define pathophysiology and demonstrate an understanding of the scope of science of pathophysiology.
- Define and use appropriately the various pathophysiological terms.

Altered Cellular and Tissue Biology

- Describe cellular structure, components, organelles and their functions (review).
- Define and distinguish cellular adaptation versus cellular injury.
- Describe the cellular adaptations made in each of the following processes: atrophy, hypertrophy, hyperplasia, dysplasia (atypical hyperplasia), and metaplasia.
- Discuss physiologic versus pathogenic cellular adaptations.
- Describe the mechanisms of cellular injury that can occur as a result of the following causes: hypoxia, chemicals, free radicals, infectious agents, asphyxial injuries, immunologic and inflammatory responses, genetic factors, nutritional imbalances, and physical trauma.
- Describe the cellular damage incurred in reperfusion (reoxygenation) injury.
- Describe the characteristics of the following intentional and unintentional injuries: blunt force injuries, sharp force injuries, gunshot wounds, and asphyxial injuries.
- Define the following terms associated with blunt force injuries: contusion, hematoma, abrasion, laceration, and fracture.
- Define the following terms association with sharp force injuries: incised wound, stab wound, puncture wound, and chopping wound.
- Define the following terms associated with gunshot and asphyxial injuries: entrance wound, exit wound, suffocation, strangulation, drowning, and chemical asphyxiation.
- Define necrosis.
- Identify and describe the mechanism and resulting damage of coagulative, liquifactive, caseous, fat, and gangrenous necrosis.
- Compare and contrast cellular necrosis with apoptosis.
- Describe the cellular mechanisms of normal degenerative changes of aging.
- Describe the clinical manifestations of somatic death

Definitions: Altered Cellular and Tissue Biology

Term	Definition
Actin Filament	- Twisted protein fibers that are responsible for cell movement.
Acute Disease	- Symptoms/signs of the disease developing quickly, within short period.
Anaplasia	- Undifferentiated cells, with variable nuclear and cellular structures. No structure.
Anoxia	- Lack of oxygen supply to tissues.
Atrophy	- Decreases in cell size resulting in reduced tissue mass. - Examples: 1. Decrease or stoppage of exercise leading to smaller muscle mass (as occurs in bed-bound patients) 2. Smaller breast size after menopause
Autopsy (post-mortem examination)	- Examination of the body/organs after death. Performed to determine the exact cause of death.
Biopsy	- Excision of a part of the living tissue. - Ex. taking a piece of a tumor to examine.
Centriole	- Complex assembly of microtubules that occurs in pairs.
Chronic Disease	- Symptoms/signs of the disease developing gradually, persisting for longer time.
Complications	- New, secondary or additional problems.
Cytoskeleton	- Supports organelles and cell shape and plays a role in cell motion.
Cytoplasm	- Semifluid matrix that contains the nucleus and other organelles.
Dysplasia	- Cells vary in size and shape within a tissue - No obvious order or structure;
Etiology	- The cause of a disease. - Broad categories of etiology include:

	A. Identifiable (80%): infection, hereditary, immune, malnutrition. B. Idiopathic: No known cause. C. Iatrogenic: drug/intervention induced. D. Nosocomial: Hospital related.
Exacerbation	Periods when symptoms become worse and more severe.
Hyperplasia	- Increase in number of cells resulting in increased tissues mass. - Example: Mammary glands in lactation.
Hypertrophy	- Increase in cell size resulting in increased cell mass. - Example: Skeletal and heart muscles of weight lifters.
Hypoxemia	- Lack of oxygen due to reduced blood flow (more specifically arterial blood)
Hypoxia	- Insufficient oxygen delivery to cells resulting in tissue injury. - May be related to decreased oxygen content in inspired air, decreased hemoglobin for oxygen binding, or due to cardiovascular or respiratory disease.
Intermediate Filaments	- Intertwined proteins fibers that provide support and strength
Ischemia	- Insufficient blood flow to tissues. - May lead to subsequent cell injury or death.
Latent state	- No apparent clinical symptoms or signs. - Can flare up at any time. - Example: Shingles (Herpes-Zoster) caused by Varicella-Zoster virus (VZV).
Metaplasia	- Mature cell type is replaced by a different mature cell type which can lead to cancer - Example: stratified squamous epithelium replaces pseudostratified columnar epithelium in trachea in response to chronic smoking.

Microtubule	- Tubule of protein molecules present in cytoplasm, centrioles, cilia and flagella
Mitochondria	- Cell organelle in which energy is generated during oxidative phosphorylation. “Power house of the cell”
Neoplasia	- "New growth" - commonly called a tumor.
Nuclear Envelope	- A double membrane that surrounds the nucleus in the cell. - Separates nucleus from cytoplasm.
Nuclear Pore	- Openings embedded with proteins that regulate passage into and out of the nucleus.
Nucleolus	- Centre of nucleus and site of ribosome synthesis.
Nucleus	- Command center of cell.
Pathophysiology	- Science that provides understanding of the mechanisms of disease (impaired physiology). - Functional changes in cells, tissues and organs by disease and/or injury that lead to the signs and symptoms of the disease.
Pathogenesis	- Pattern of changes associated with the development of diseases (natural course of the disease from exposure to recovery).
Pathology	- Science of diseases. Abnormal states or structural alterations in cells, tissues and organs.
Macroscopic (Gross) Pathology	- Investigation at the organ or system level.
Microscopic Pathology	- Investigation at the cellular or tissue level.
Peroxisomes	- Vesicles that contain enzymes that detoxify potentially harmful chemicals.
Plasma Membrane	- Phospholipid bilayer surrounding the cell, in which proteins are embedded.
Precipitating Factors	- Elements that trigger actual development of a disease. Example: Poor diet and exercise can precipitate diabetes.
Predisposing Factors	- Tendencies that promote a disease. Example: Genetic factor leading to diabetes.

Prognosis	- The expected outcome of the disease, such as recovery, chronic state, survival rate. - Prognosis affects treatment decisions for patients and health practitioners.
Remissions	- Manifestations of the disease subsiding or are absent. Example: Leukemia following successful chemotherapy.
Ribosomes	- Cell organelles; small complexes of RNA and protein for protein synthesis.
Rough ER	- Cell organelle; internal membranes studded with ribosomes that carry out protein synthesis.
Secretory Vesicle	- Vesicle fusing with the plasma membrane, releasing materials to be secreted from the cell (performs exocytosis).
Sequelae	- Residual outcomes of primary condition. Example: a scar following a burn.
Smooth ER	- Cell organelle; a system of internal membranes that aid in the manufacturing of carbs and lipids.
Subclinical state	- Pathologic changes with no obvious manifestations.
Syndrome	- Collection of signs and symptoms that affect more than one organ/system.

Altered Cellular and Tissue Biology

Types/Causes of Cellular injury

1. **Oxygen deficit**: Hypoxia and ischemia
2. Free Radicals
3. Chemical Injury
4. Physical Injury
5. Nutritional Injury
6. Mechanical Injury
7. Infection
8. Immunological/inflammatory injury
9. Genetic defects

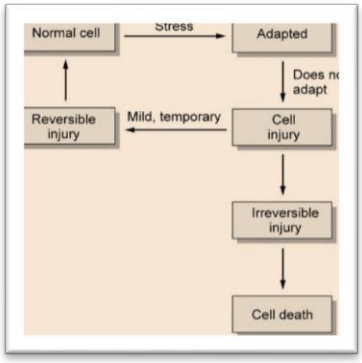


Figure 1: Cellular response to adaptation

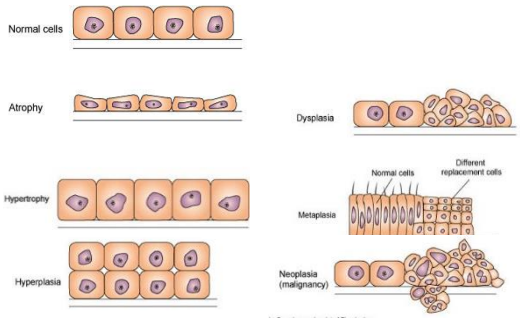


Figure 2: Cellular adaptation

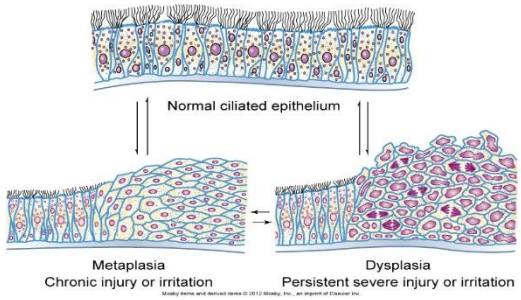


Figure 3: Cellular response in epithelium (e.g. trachea) to chronic, persistent injury or irritation (e.g. smoking)

1. Hypoxic Injury

- *Definitions: Hypoxia, Anoxia, Hypoxemia, Ischemia*
- Gas exchange takes place in the alveoli (between air and blood) and at tissues (between blood and cells)
- Hypoxic injury can occur as a result of:
  - **Lack of oxygen in the air**
    - E.g. High altitude, being trapped in an enclosed space such as an elevator or underground.
  - **Problems with oxygen transport**:
    - E.g. Conditions affecting RBC formation and structure, and subsequent oxygen carrying capacity.
    - E.g. decreased RBCs production (erythropoiesis).
  - **Disease of the respiratory and/or cardiovascular system**:
    - Blood is not getting pumped/circulated adequately.
    - Poor gas (oxygen) exchange in the lungs and/or delivery to tissues.
  - **Narrowing of an artery or vein**
    - E.g. atherosclerosis.
  - **Obstruction of an artery or vein**
    - E.g. blood clot (thrombosis).

Myocardial Infarction (MI)

- Acute obstruction of coronary artery leading to myocardial cell death.
- There is hypoxia, which progresses to anoxia if blood flow is not restored.
  - In response to hypoxia, the heart modifies its method of oxygen uptake and utilizes myoglobin stores [*Remember:* Myoglobin = hemoglobin in heart]
  - Myoglobin stores are limited and eventually run out.

- The heart becomes anoxic and cardiac cells decrease their metabolism to conserve energy until eventually no ATP is produced.
- The Na-K pump fails due to lack of ATP.
- Na and water leak into cell causing it to swell and burst.

- **Diagnostic Testing**
  - Troponin and cardiac enzyme test, ECG
    - Elevated troponin I is a marker for MI, however, depending on the timing in relation to onset of chest pain, levels may not be elevated. For this reason, Troponin is repeated in 4 hours for patients with suspected MI.
    - Elevated Troponin I after 4 hours is indicative of MI
  - ECGs are critical to determine treatment approach.
    - Do an ECG for any suspected MI*
    - *In practice, ECGs are completed on most adults presenting with sudden onset chest pain, especially with cardiac features, to rule out MI
    - Extra consideration should be taken for persistent, generalized, radiating pain in women with no apparent cause of onset as women with MI often present atypically from males
      - This includes generalized abdominal pain, back pain, neck, that is not reproducible with specific movements or is related to a specific diagnosis or injury

- *Reperfusion*:
  - Restoration of blood flow to an obstructed area.
  - This occurs via collateral circulation.

- **Reperfusion Injury**:
  - Cellular damage caused by restoration of blood flow to obstructed area
  - Occurs due to an increase in intracellular calcium and formation of free radicals:
    - Calcium damages mitochondria → Therefore no ATP production
    - Calcium increases cellular enzyme activities causing membrane damage, nucleus damage, and further decrease in ATP production.
    - Free radical causes further cell membrane damage and release of calcium stores contributing to mitochondrial calcium overload.
  - Cells attempt to detoxify radicals but they may fail:
    - Toxic free radicals can be stabilized by donating or accepting an electron from another molecule (antioxidants).
    - With significant free radical formation, there are not enough antioxidant molecules to stabilize all the unstable oxygen species.

2. Free radicals

- Molecules with unpaired, negatively charged electron in their outer orbit.
- Free radicals come from many sources such as:
  - Aging, respiration, metabolism
  - Infection, cancer
  - Reperfusion, inflammation
  - Drugs, chemicals, radiation.
- Unstable and highly reactive, therefore called reactive oxygen species (ROS).
- Free radical injury has many effects, including:
  - Lipid peroxidation.
  - Alteration to proteins → impaired enzymatic activity and folding
- Free radicals must accept or donate an electron from another molecule to become stable, and they do this by binding to other molecules
  - This binding can be injurious if these ROS bind to molecules such as proteins, lipids, and carbohydrates, as well as those key to survival such as molecules of cellular membranes and nucleic acids (DNA)
  - ROS set of a chain reaction as they bind to stable molecules, in turn making these previously stable molecules unstable free radicals.

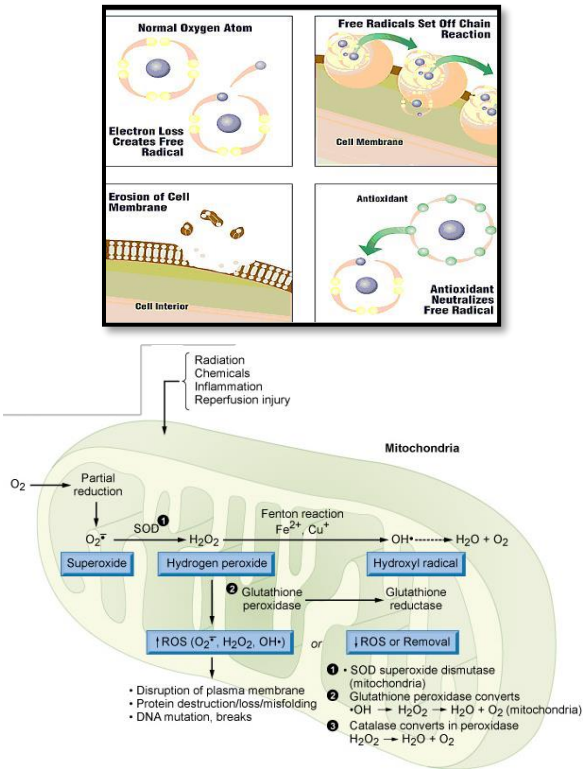


Figure 4: Formation and detoxification of free radicals

- Peroxisome is the cell that detoxifies the free radical by adding something to make them safe and "stable".
- Antioxidants can also act as binding molecules to stabilize free radicals and prevent their binding to other body molecules.
  - Free radicals can be eliminated by Antioxidants (vitamins A,C,E), spontaneously, or via enzymes. These enzymes include:
    - Superoxide dismutase (in the *mitochondria*) $O_2 + 2H \rightarrow H_2O_2$
    - Catalase (in *peroxisomes*): $2\ H_2O \rightarrow 2\ H_2O + O_2$
    - Glutathione peroxidase (in *cytoplasm*): H_2O_2 or $2\ OH + 2\ GSH \rightarrow 2\ H_2O + GSSH$
- **Antioxidants stabilize, peroxisomes detoxify**

- *Oxidative Stress*: When excess ROS production overwhelms endogenous antioxidant systems leading to cellular injury.

3. Chemical Injury

- Chemicals can cause cellular injury by direct (binding to molecular components of the cell) and indirect (lipid peroxidation or formation of free radicals).
- **Examples**:
  - Alcohol, ethylene glycol, lead, carbon tetrachloride (CCL_4), cyanide and carbon monoxide (CO).

a) Alcohol toxicity

- **Ethanol (alcohol)** turns into acetaldehyde in the liver by alcohol dehydrogenase.
  - This leads to the formation of free radicals and acetic acid by the liver
    - Creates a state of acidosis
  - Acetic acid leads to fatty change
  - Acetate can further breakdown to acetyl CoA and enter the Krebs cycle
    - Leads to build-up of ketone bodies

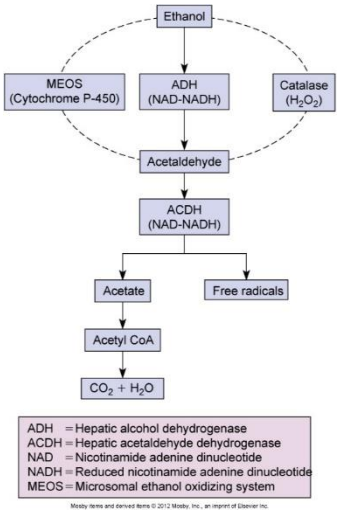


Figure 5: Metabolism and detoxification of ethanol (alcohol)

- **Manifestations**:
  - CNS depression, metabolic acidosis
  - Inhibition of gluconeogenesis
  - Fetal alcohol syndrome (FAS)
    - Ethanol can cross the placental barrier and affect the developing fetus
    - Children are affected both physically and cognitively

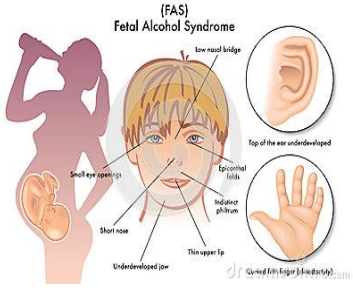


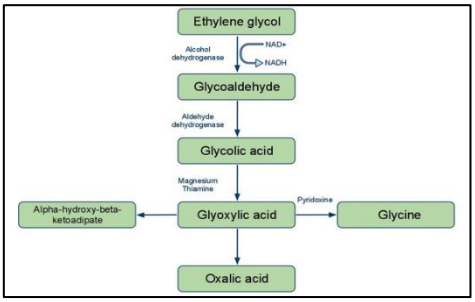
Figure 6: Fetal alcohol syndrome

  - **Acute toxicity manifests mainly by CNS depression, chronic toxicity manifests mainly by liver damage**.

b) *Ethylene Glycol Toxicity*

- Found in antifreeze, toxicity is usually via ingestion.
- Metabolized to glycolic acid leading to severe acidosis and acute renal injury.
- Direct effect on CNS with altered mental status
    - The person will feel drowsy for the first hour following intoxication

Figure 7: Ethylene glycol (antifreeze) toxicity



- Eventually oxalic acid can be made which is a toxic metabolite
    - This leads to the formation of calcium oxalate crystal in urine (renal stones).
- Serum levels of ethylene glycol peak within 1-4 hours
    - CNS depression occurs during the 1st hour
- Patients develop heart failure or pulmonary edema within 12 hours
    - Renal tubular necrosis within 24-72 hours (late stage).

c) *Lead Toxicity*

- Lead is a heavy metal, absorbed by inhalation or ingestion (paint, dust, occupational)
    - When in the body, lead mimics other metal cofactors (calcium, iron, zinc) in enzymatic reactions.
    - As a result, it inhibits 2 enzymes involved in heme synthesis: delta-ALAD (δ-aminiolevulinic acid dehydratase) and ferrochelatase.
    - Lead also interferes with neurotransmitter activity.
- Toxicity can be acute or chronic.
    - Not super common anymore with lead free toys, pencils, paints and car gas.
- **Manifestations include**:
    - **Anemia (Iron Deficiency):** Lead can replace iron in hemoglobin and inhibits the synthesis of RBCs
    - Lead can also replace calcium in bone (teeth), blood, and impair nerve conduction, muscle contraction etc.

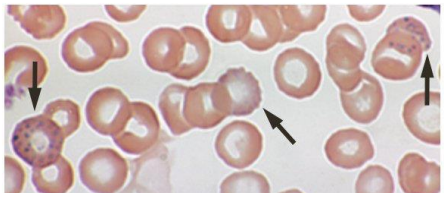


Figure 8: Blood smear of person with lead toxicity

- Calcium is a co-factor for blood coagulation so risk for bleeding is expected.
- In the cell, calcium is in the cisternae of the endoplasmic reticulum
- Intracellular free calcium stimulates contraction of muscles. Lead replaces this and those mechanisms are impaired.

- Blue gums (lead lines), dense metaphyseal lines on x-ray.
- Peripheral neuropathy (nerve conduction inhibited)
  - Manifested as wrist/foot drop in adults, poor hand-eye coordination in children.
- Lead crosses the placenta which can lead to miscarriages, stillbirths, low birth weight, and cognitive impairments.

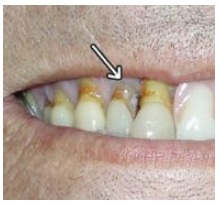


Figure 9: Blue gum line in lead toxicity

d) Carbon monoxide

- Produced from incomplete combustion of organic materials
- Binds to Hb and forms carboxyhemoglobin (COHb)
- This is known as the silent killer (so is hypertension). *No taste or smell* but it is fatal. The carbon is tightly bound to Hb, so does not release oxygen in the tissues. Tissues get hypoxic and die.

e) Cyanide

- Binds/ inactivates cytochrome oxidase in mitochondria.
- Disrupts mitochondrial cellular respiration.
- Causes respiratory failure.

4. Physical injury

- **Thermal:**
  - *Hyperthermia (>38.5°C):* High heat damages protein and stops enzyme activity (eg. Heat stroke)
  - *Hypothermia (<35°C):* Excessive exposure to cold, alcohol intoxication. (cooling of the surgical field to decrease circulation and reduce bleeding, if overdone → hypoxic tissue.
  - *Burns*
- **Radiation:** UV
  - Exposure creates thymine dimers leading to faults in DNA replication when the cell divides and subsequent mutations.
  - A method for killing bacteria.

- **Pressure:**
  - Air pressure
    - Explosion e.g. Blast injuries: complex physical trauma.
    - Water pressure.
- **Surgery:**
  - Deliberate tissue injury.
  - Potential damage to the cells as a post-operative complication.

5. Nutritional Injury
   - **Nutritional Deficits**
     - *Malnutrition*: not enough intake of any nutrient (CHO, Fat, Protein, Minerals)
     - *Dehydration*: Water loss (may also result in electrolyte imbalance)
     - *Hypoalbuminemia*: Albumin = 60% of plasma proteins; therefore, it is largely responsible for the oncotic pressure, so low albumin leads to edema/ascites since fluid is not retained in blood vessels.
     - *Hypoglycemia*: Low blood glucose level → low glucose inside cells →reduce energy production.
     - *Vitamin deficiencies* (Vitamins ADEK and folic acid).
   - **Nutritional Excess**
     - Excess nutrients can also cause injury e.g. Hypervitaminosis D, hypercalcemia.
6. Mechanical Injury
   a. *Blunt force:*
      - Application of mechanical energy to the body resulting in the tearing, shearing, or crushing of tissues e.g. MVAs
      - **Manifestations**:
        - **Contusion / hematoma** = bruise.
        - Stages:
          I. Trauma to the site = rupture of BV → blood (RBCs; low oxygen) in subcutaneous tissue (hematoma) → blue/purple skin.
          II. Lysis of the escaped RBCs → free Hb which is decomposed further → hemosiderin (brownish skin).
          III. Hemosiderin turns into biliverdin → (yellowish skin)
        - **Abrasion**, **laceration**, **fractures**.

   b. *Penetrating injuries*
      - Stab wounds, gunshot wounds. If gunshot went into body it is damaging mechanically, can rupture BV→ internal hemorrhage.

- Ruptured spleen = almost fatal (storage site for blood)

c. *Asphyxial Injuries*

- Effects due to hypoxia
    - Suffocation (choking).
    - Strangulation (hanging, ligature, manual strangulating).
    - Chemical asphyxiants (cyanide and hydrogen sulfide).
    - Drowning.

d. *Gunshot wounds*

- Effects
    - Tissue disruption.
    - Bleeding, hypovolemic shock.
    - Pneumothorax.
- KE = ½ MV^2
    - Wounds produced by missiles of higher mass (M) and/or velocity (V) produce greater tissue disruption
        - I.e. faster & heavier = more damage

7. Infectious Injury
    - *Note: Details of infectious agents in Microbiology course*
    - **Bacteria**
        - Produce toxins (endotoxin or exotoxin).
    - **Viruses**
        - Decrease the ability to synthesize proteins.
        - Change the cell's antigenic properties.
    - **Other microbes**
8. Immunologic and Inflammatory Injury (Details in Microbiology course)
    - Induced by:
        - **Cells:** phagocytic cells (neutrophils, macrophages, monocytes)
            - Alterations in cell membrane
            - Changes in membrane permeability
                - These changes cause unintentional injuries and problems that will need to be repaired
        - **Mediators:** substances release by immune inflammatory cells
            - Histamine, cytokines, antibodies, complement, and proteases

    - Histamine from basophils circulates in body leading to itching, edema
- **Remember Inflammation = tissue response to ANY injury

9. Genetic Injury
    - Genetics play a substantial role in cellular structure and function including:
        - Cell shape
        - Protein structure and functions
        - Receptors and recognition
        - Transport mechanisms
    - **Examples**
        - *Sickle cell* disease (missense mutation in globin protein; abnormal Hb S; red cell hemolysis; anemia)
        - *G6PD* (X-linked; enzyme deficiency; red cell hemolysis; anemia)
        - *CML (chronic myeloid lymphoma); Philadelphia chromosome*
            - Chromosome 22 to chromosome 9 translocation.

Pathological themes - Cellular injury

a) Mitochondrial damage
    - O_2 depletion
    - Impaired oxidative metabolism → decreased ATP production
    - ROS = Reactive oxygen species (free radicals)

b) Membrane damage:
    - *Plasma membrane damage*: failure of Na-K pump; increases cellular water
    - *Lysosomal membrane damage*: enzyme release, activation & digestion of cell components
    - *Mitochondrial membrane damage* → decreased ATP

c) Protein synthesis impairment:
    - Ribosomes separate from the swollen endoplasmic reticulum → decreases protein synthesis

d) Lipid peroxidation:
    - Causing damage to phospholipid cell membranes

Manifestations of Cellular injury - Accumulations

a) Water:

- Necessary for life, but when there is too much, this can lead to flooding
- Water accumulation = hydropic degeneration

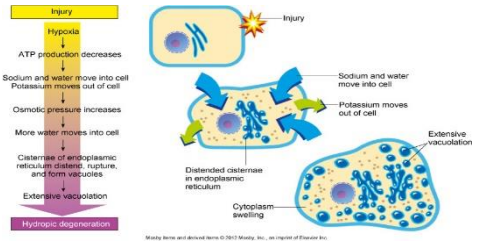


Figure 10: Cellular injury from water accumulation (hydropic degeneration)

b) Lipids and carbs

c) Glycogen

d) Proteins

e) Pigments

- Melanin, hemosiderin, bilirubin

f) Calcium

- Calcium is stored inside Cisternae of ER (inactive state) and is only released when needed (e.g. muscle contraction, cofactor in the activation of enzymes)
- Free Ca^{2+} activates enzymes → hormonal action, calcium mediated, kinases etc

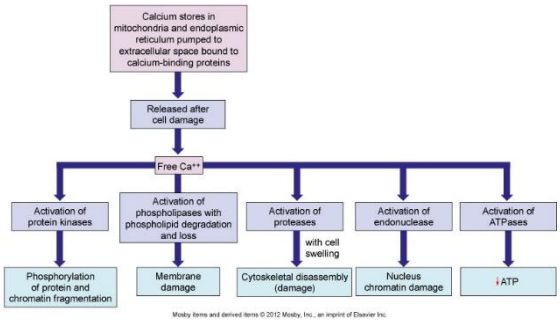


Figure 11: Cellular damage by excess free calcium

- Therefore, it is essential for the regulation of body processes to have calcium remain stored in the ER because if calcium were to be free it would continuously activate body processes (above)

g) Urate

Cell Death

- Happens when you can't reverse the changes through adaptation to injury/stress

Apoptosis

- Programmed cell death.
- Normal occurrence in the body:
  - Aging/senescence of cells e.g. RBCs killed every 120 days
  - Tissue involution following hormonal withdrawal
  - Elimination of self-reactive lymphocytes (immune tolerance) in Thymus
  - Breaking self-tolerance → autoimmune disease

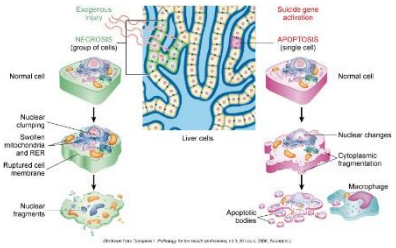


Figure 12: Cell death - Necrosis vs apoptosis

Autophagy

- Self-eating membrane extension, fusion with lysosomes
- Survival mechanism in deprivation and starvation
- Degenerative CNS disease and cancer

Necrosis

- Un-programmed cell death
- Cell changes include:
  - **Karyolysis**: Nuclear dissolution and chromatin lysis
  - **Pyknosis**: Clumping of the nucleus
  - **Karyorrhexis**: Fragmentation of the nucleus

Types of necrosis:

1. *Liquefaction necrosis*
   - Tissue transforms into a liquid viscous mass due to release of hydrolytic enzymes
     - Common in brain, liver and lungs
     - Due to bacterial infection

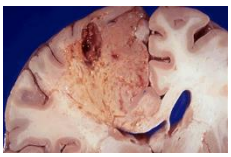


Figure 13: Liquifaction necrosis

2. *Coagulative necrosis*
   - Denaturation of structural proteins (coagulation) including lysosomal enzymes
   - Like an egg on a hot pan

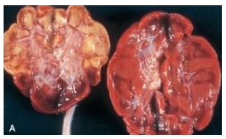


Figure 14: Coagulative necrosis

3. *Fat necrosis*
   - Tissue broken down into fatty acids by action of lipases
     - Liver, breast, pancreas and other abdominal organs
     - Common in liver. Lipases break down hepatocytes into fatty acids

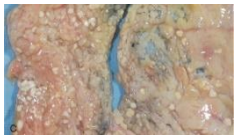


Figure 15: Fat necrosis

4. *Caseous necrosis*
   - Combination of coagulative and liquefactive necrosis
   - Thick, yellowish “cheesy” substance
     - Tuberculosis pulmonary infection

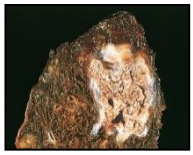


Figure 16: Caseous necrosis

5. *Infarction*
   - Area of dead tissues as a result of oxygen deprivation
   - E.g Myocardial infarction

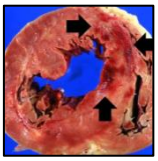


Figure 17: Infarction

6. *Gangrene*

- Area of dead tissues due to severe and persistent hypoxic injury
    - **Dry gangrene** (arterial occlusion; feet and toes; DM)
    - **Wet gangrene** (venous occlusion; most tissues/organs strangulated hernia)
    - **Gas gangrene:** hypoxia + gas production (Clostridium perfringens)

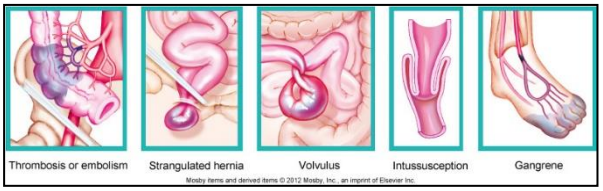


Figure 18: Types of gangrene

Aging

- Humans have normal life span and life expectancy
- **Aging vs disease**
    - Aging is a physiological process (not a disease). Atrophy, decline in number and size of cells, low blood supply, poor healing, poor skin elasticity…etc
- **Cellular aging**
    - Atrophy, decreased function/renewal, and organelle damage
- **Tissue and systemic aging**
    - Progressive stiffness and rigidity
    - Sarcopenia (muscle loss; decreased body mass with aging)
- **Frailty**
    - Complex clinical **syndrome**, common in elderly
    - Affects: mobility, balance, muscle strength, motor activity, cognition, nutrition, endurance and bone density
    - Person vulnerable to falls, fractures, functional decline

Somatic Death

- Death of the entire person

Manifestations:

- Post-mortem change is diffuse and does not involve the inflammatory response
    - Cessations of respiration and circulation
    - Pupil dilation
    - Gradual lowering of body temp
    - Loss of elasticity and transparency of skin
    - Muscle stiffening (rigor mortis)
    - Skin discoloration

Types of post-mortem changes:

- *Algor mortis*
  - Reduction in body temp
- *Livor mortis*
  - Purplish red discoloration of the skin
- *Rigor mortis*
  - Stiffness of body parts, visible within 2-4 hours, fully developed 6-12 hours after death
- **Post-mortem decomposition**
  - *Autolysis*
  - *Putrefaction*: obvious around 24-48 hours after death. Rotting or decaying of the body.
  - *Maceration*: aseptic autolysis of dead fetus in utero within amniotic fluid.

Helpful Hint

Think Al Gor(e) and his focus on temperature change to remember the relationship of algor mortis and reduction in body temperature