Cell Injury

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Cellular Adaptation

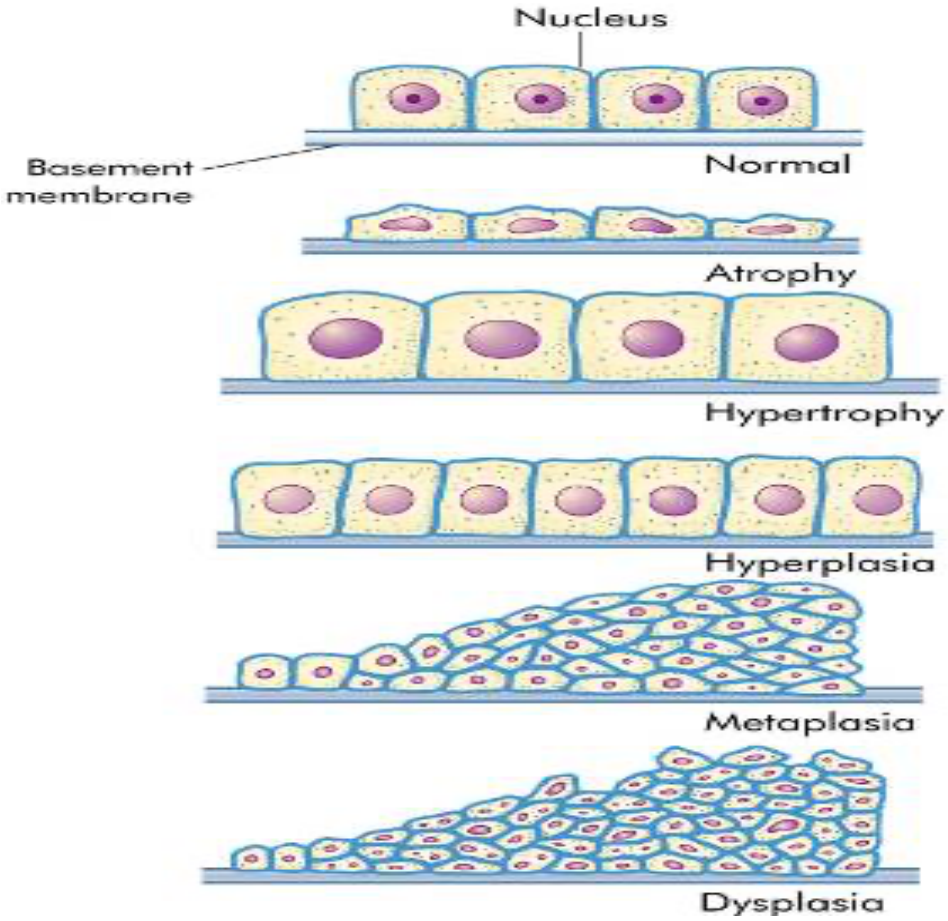
- Altered cell biology can happen with injury, aging, neoplasia, adaptations, deficiencies, poisoning
- Adaptations can be physiologic or pathogenic
- For example the normal change of the size of the uterus in pregnancy.
- Injuries can be reversible (sub-lethal) or irreversible (lethal)
- Cells adapt to the environment all the time, usually to protect themselves
- Cellular adaptations are a common part of most disease states

Atrophy is decrease or shrinkage of cell size

- Can affect any organ, but usually seen in skeletal muscle
- Physiologic atrophy (Shrinking thymus in childhood)
- Pathologic atrophy (decreased blood or nerve supply or nutrition, etc.)
- Disuse atrophy
  (Immobilized muscles)

Hypertrophy is increase in size of cells and ultimately the organ

- Heart, liver, spleen, etc
- The increased cell size is an accumulation of protein in the plasma membrane, myofilaments, endoplasmic reticulum and mitochondria and NOT with increased cell fluid.



Hyperplasia is an increase in the number of cells because of increased cell division

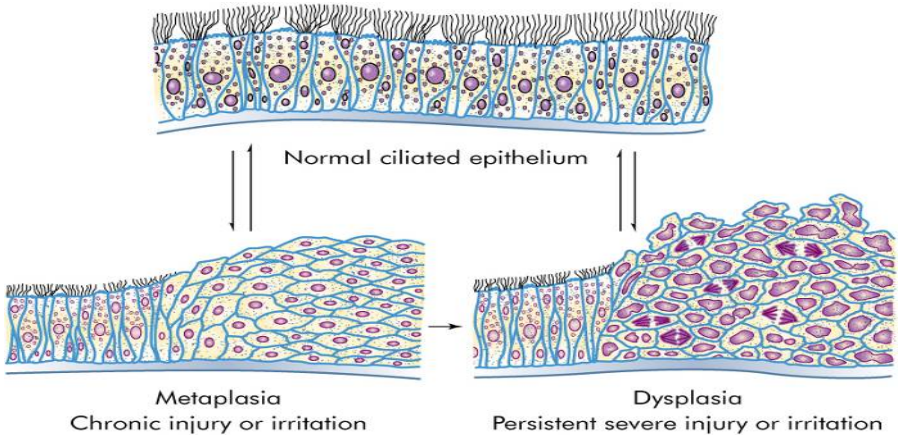
- Compensatory hyperplasia is when organs regenerate (spleen and liver)
- Hormonal hyperplasia occurs as a result of estrogen
- Pathologic hyperplasia is usually caused by hormonal or growth factors

Metaplasia is a reversible of a mature cell to a less differentiated cell

- Smoking and Epithelial cells

Dysplasia is abnormal changes in the size and shape of cells

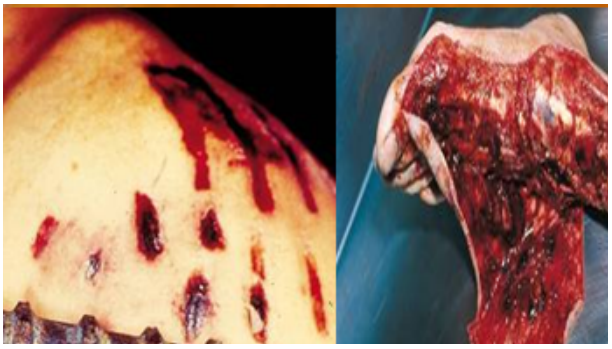
- Not a true adaptive process but is like hyperplasia and is often called atypical hyperplasia
- Seen often in breast cancer development



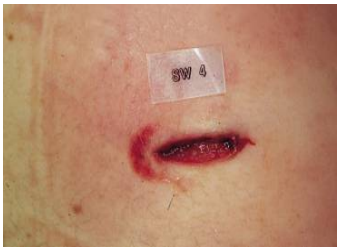
Causes of Cellular Injury Deficiency

- Deficiency- Lack of substance(s) necessary for cell's "health"
    - Primary Nutrient Deficiency- Cell doesn't get needed materials
    - Secondary Nutrient Deficiency- Nutrients are present in diet, but cannot be absorbed
    - May also be caused by…
        - Genetic Errors
        - Infections
        - Lack of adequate precursors of needed materials
- Intoxication- Cell is exposed to a substance that interferes with normal function (a "toxin") a.k.a. "poisoning"
    - Exogenous Toxin- Comes from outside source
        - Pathogenic Microbes
        - Physical or Chemical Means (e.g. radiation, toxic chemicals, etc.)
    - Endogenous Toxin- Cell is producing something toxic to itself and/or other cells
        - Defective Genes
        - Examples of defective genes:
            - Huntington's- neurological dysfunction due to toxic substances
            - PKU- phenylketones build up due to malfunctioning enzyme

Unintentional and Intentional Injuries



- Blunt force injuries
  - Application of mechanical energy to the body resulting in the tearing, shearing, or crushing of tissues
  - Contusion vs. hematoma
  - Abrasion
  - Laceration
  - Fractures
- Sharp injuries
  - Incised wounds
  - Stab wounds
  - Puncture wounds
  - Chopping wounds



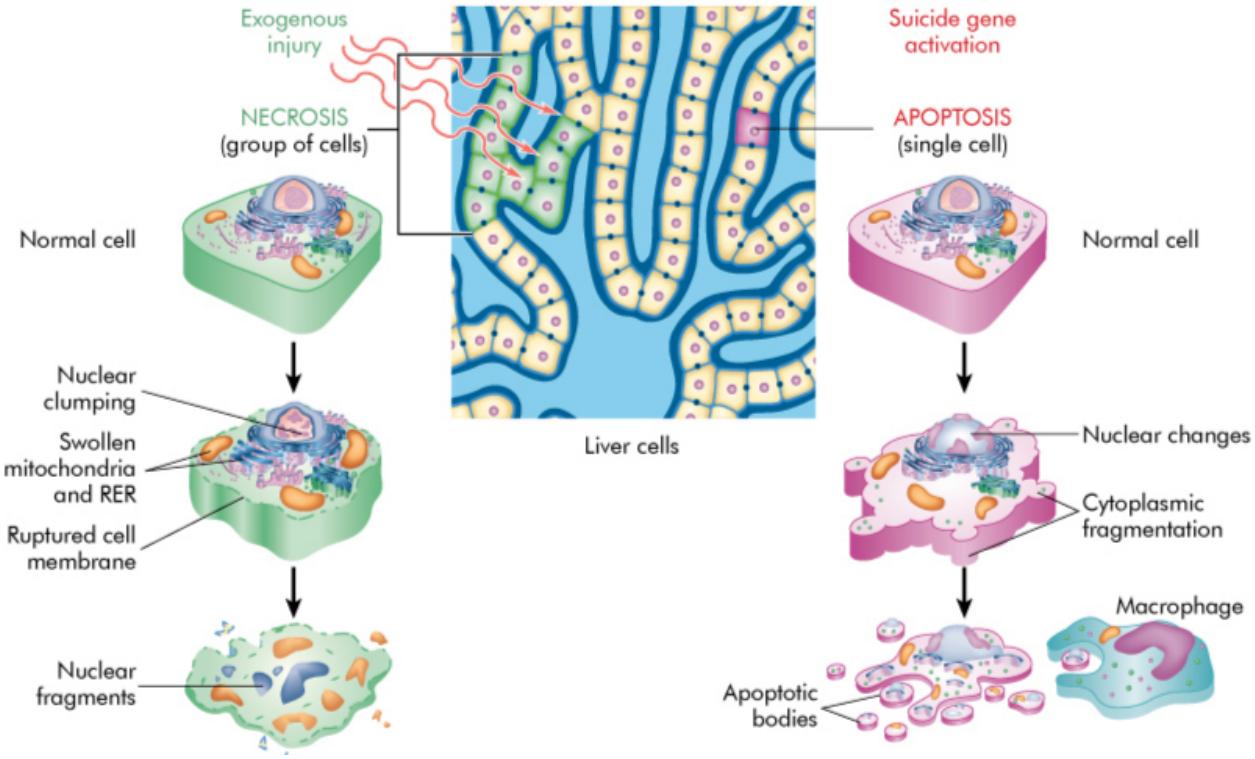
- Gunshot wounds
  - Entrance wounds
    - Contact range entrance wound
      - Blow-back and muzzle imprint
    - Intermediate range entrance wound
      - Tattooing and stippling
    - Indeterminate range entrance wound
  - Exit wounds
    - Shored exit wound
- Asphyxial injuries
  - Caused by a failure of cells to receive or use oxygen
    - Suffocation - Choking asphyxiation
    - Strangulation - Hanging, ligature, and manual strangulation
    - Chemical asphyxiants - Cyanide and hydrogen sulfide
    - Drowning

Effects of Cellular Injury

- Effects may be **reversible or irreversible**
- Usually affect cell's…
  - Function
  - Structure
- Effects of and response to injury determined by:
  - Nature of causing agent
  - Intensity of causing agent
  - Duration of causing agent
  - Number of exposures to causing agent

Reversible Changes: Functional

- Adaptive Responses
  - Alternative Metabolism
    - Allow cell to adjust to conditions
    - i.e. aerobic → anaerobic cellular respiration
  - **Apoptosis-** Programmed cell death
    - Programmed cellular death
    - Every day we can produce 10 billion new cells and kill off the same number
    - Physiologic - Is important in body tissue development
    - Pathologic - The result of intracellular events or exogenous stimuli
  - Absence of apoptosis can cause pathologic change and gene mutation



Cell Stress Proteins

- Formed when cell exposed to adverse conditions
  - Trauma, temp/pH changes, toxins, nutrient depletion
- Prevent damaged proteins from clumping and forming insoluble tangles
- Cell stress proteins - help in 3 ways:
  - Bind to damaged proteins- easier to destroy
  - Stabilize and enable to refold damaged proteins
  - Easier to pass through cell membrane and be expelled

Reversible Changes: Functional

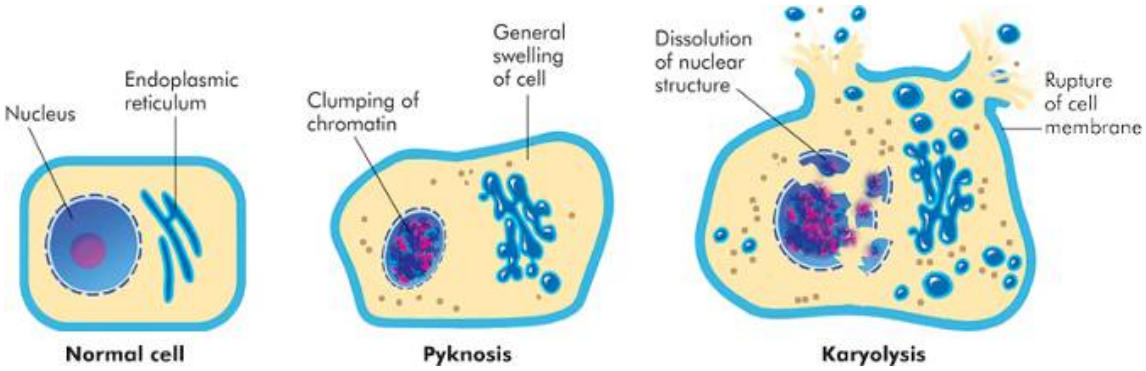
- Other Adaptive Changes
    - Organelle Changes - Make or destroy organelles depending on demand
- Cell and Tissue Accumulations
    - Hydropic Changes
        - Reduced ATP production decreases ion pump activity
        - Affect cell's ability to keep osmotic balance
        - Water accumulation in vacuoles of cells- becomes pale
- Fatty Changes
    - Injury causes fats to accumulate in cells
        - Most often in kidneys, heart, liver
    - FFAs (free fatty acids) accumulate in vacuoles of cells
    - Can be caused by toxin damage or anoxia
    - May cause cells to rupture
    - Fatty changes occur in cells that metabolize a large amount of fat
- Cell and Tissue Accumulations
    - Residual Body Accumulation
        - Happens when materials (bacteria, damaged organelles) are not properly digested by the cell
        - Lipofuscin Granules – Residual bodies that contain undigested cell membrane lipids - Most often in neurons, liver, and myocardium
    - Hyaline Changes
        - a.k.a. "hyalinization"
        - Deposition of hyaline around cells
        - Usually a good indication of cell damage elsewhere

Reversible Changes: Structural

- Plasma membrane changes
    - Blebs- Cells develop cytoplasmic bulges at the plasma membrane
    - Will also disrupt integrity of many organelles
    - Nuclear structure appears unchanged

Irreversible Changes: Structural

- More extreme structural changes
    - Plasma membrane distortion and increased permeability
    - Mitochondrial and ER breakdown
    - Fewer lysosome- released into cytoplasm
    - Altered nucleus most significant indicator of irreversible cell injury
- Altered nucleus
    - **Karyolysis**- Nucleus fragments and disintegrates
    - **Pyknosis-** Nucleus shrinks, condenses, or
    - **Karyorrhexis-** Nucleus breaks up into densely staining fragments that disperse into cytoplasm



Irreversible Changes: Mechanism

- Organelle and plasma membrane damage leads to compromised permeability and cytoplasm- organizing functions
    - Sodium influx and cell swelling
    - Protein denaturation by high calcium concentrations
    - Activate damage causing enzymes
    - Decreased ATP production → anaerobic
        - Lower pH
    - Flawed protein synthesis
    - Disruption of cytoskeleton- form blebs

Permanent Effects of Cellular Injury

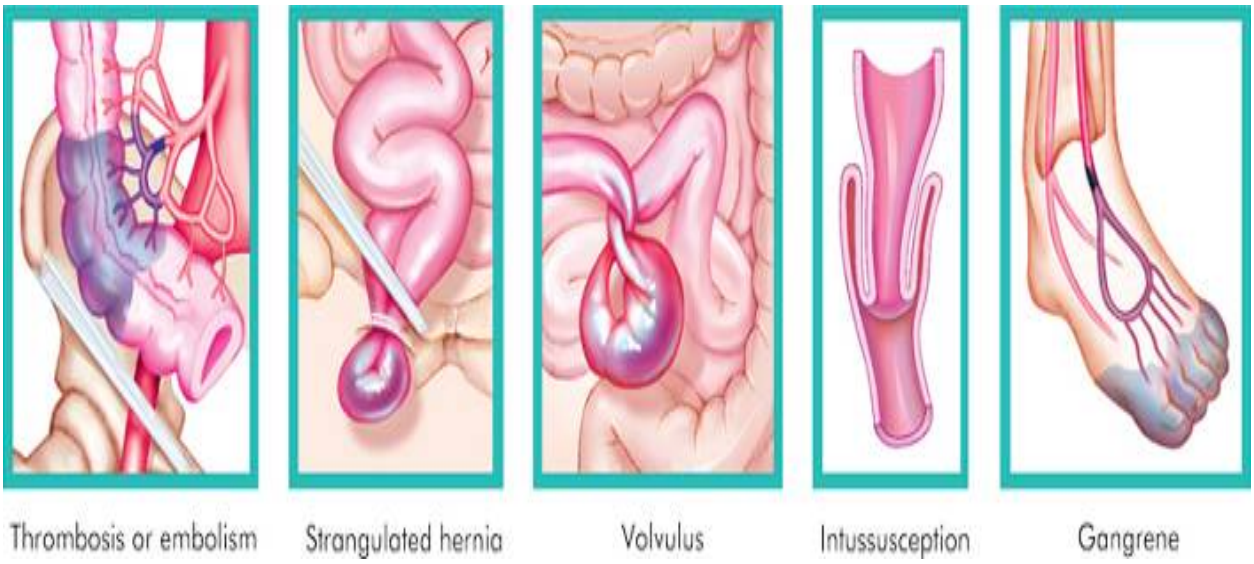
- **Necrosis - Cell death**
    - Lysosomal enzymes released after lethal injury
- **Coagulative Necrosis**
    - Kidneys, heart, and adrenal glands
    - Protein denaturation occurs causing albumin to change from a gel to a firm fibrotic substance

Necrosis

- **Liquefactive necrosis**
    - Neurons and glial cells of the brain - usually from ischemia
    - Hydrolytic enzymes
    - Bacterial infection - Staphylococci, streptococci, and *Escherichia coli*
- **Caseous necrosis**
    - Tuberculous pulmonary infection
    - Combination of coagulative and liquefactive necrosis
    - The dead cells disintegrate but the debris is not completely destroyed leaving granular cheesy clumps behind
- **Fat necrosis**
    - Breast, pancreas, and other abdominal organs
    - Action of very powerful lipases which break down triglycerides and releases fatty acids which combine with calcium, magnesium and sodium and creates soaps (Saponification)

Necrosis

- **Gangrenous necrosis**
    - Characterized by noxious products of anaerobic bacterial metabolism
    - Death of tissue from severe hypoxic injury
        - **Putrefaction-** tissue damage due to reduced blood flow
    - Dry vs. wet gangrene
        - Dry is a result of coagulative necrosis and skin is dry and wrinkled
        - Wet is when massive neutrophils invade the site causing liquefactive necrosis
    - Gas gangrene - Clostridium



Permanent Effects of Cellular Injury

- **Calcification-** may occur in necrotic cells/tissues
    - Calcium deposits form in mitochondria → death
    - **Dystrophic Calcification -** deposits start small and grow which lead to stiff, brittle cells/tissues
    - **Metastatic Calcification**
        - May occur in normal cells (not JUST necrotic cells)
        - Deposition happens because of **hypercalcemia i**n the body

Vulnerability to Injury

- Tissues differ in vulnerability to injury depending on:
    - **Ischemia**- Loss of blood flow (oxygen) to a tissue/organ (e.g. stroke)
        - Some tissues/organs may tolerate ischemia for a period of time better than others
    - **Intoxication -** different toxins may affect and injure different tissue types
    - **Ionizing Radiation**- DNA highly sensitive
        - Tissues with high mitotic rate affected more
    - **Viral Infection** - each virus has specific target cell
        - Disrupt cell from within

Testing for Cellular Injury in a Patient

- **Functional Loss**
  - Test for a physical and/or biochemical defect(s) in the patient
- **Release of Cell Constituents**
  - Certain cell constituents may be released into the bloodstream by damaged cells/tissues/organs (e.g. ions, enzymes, amino acids)
- **Electrical activity**
  - Any change from normal electrical pattern can be interpreted by tests
    - EEG: brain, ECG: heart, EMG: muscle

Testing for Cellular Injury in a Patient

- **Biopsy**
  - Direct microscopic examination of a section of tissue believed to be diseased or damaged
  - Look for evidence of any type of injury or tumor

Somatic Death

- Death of an entire person is somatic death
- **Postmortem changes**
  - Algor mortis – lowered temperature
  - Livor mortis – gravity causes blood to pool in the lowest areas = purple
  - Rigor mortis – muscle stiffening
  - Postmortem autolysis – swelling and bloating of entire body with liquefactive changes