Pathophysiology

Unit 1

Cell Pathology, Inflammation, Neoplasia

Cell Review

Disease at the Cellular Level

Pathology at the Cellular Level

- You are what you are (structurally and functionally) because of structure and function of cell interaction
- Most understanding of pathology is based on cellular understanding. Molecular understanding is not as solid (some examples PSA with prostate cancer, produces specific antigen... check this)
  - Ex) prostatic cancer cells produce a certain antigen (basis for PSA test)
- We study disease at the cellular level with some aspects of molecular level
- When we see the signs and symptoms of disease, it is due to altered cell biology

Altered Cell Biology

- When we see altering cell biology, it is the result of one of the following:
  - Cellular adaptation
  - Cellular injury
  - Cellular death
  - Aging
  - Neoplasia

Altered Cell Biology
Cellular Adaptation

Cellular Adaptation

- Cell may not be functioning properly because it is trying to adapt to circumstances.
- The cell has been exposes to some sort of injurious agent
- The cell reacts to try to prevent cellular injury and survive
- The types of adaptation are:
  - Atrophy
  - Hypertrophy
  - Hyperplasia
  - Metaplasia

Cellular Adaptation
Atrophy

- Atrophy denotes a decrease in the size of a cell. This is a change in the components of a cell (it is not a shrinking of the cell due to water loss). The structural components are being reduced.
- Common causes include:
  - Decreased load or workload
  - Decrease blood supply
  - Inadequate nutrition
  - Change in hormonal stimulation
  - Loss of innervation
- Results of atrophy are:
  - Production of autophagic vacuoles
  - Production of unremovable byproducts (lypofusion, myelin figures)

Cellular Adaptation
Atrophy due to Decreased Workload

- Ex) Broken arm
  - Actin and myosin breaks down normally, but are replaced with load on the muscles. When a arm is broken and casted and there is not stress to stimulate production of new actin and myosin, the arm atrophies.

Cellular Adaptation
Atrophy due to Decreased Blood Supply

- In order to survive, cells become smaller
- Ex) When there is atherosclerosis with decreased circulation to legs, the hair on dorsum of toes will disappear and the skin will get thinner. This will progressively affect a greater range (feet, legs, thighs). Eventually the cells will die (decubitus ulcer).
- Other signs and symptoms of

Cellular Adaptation
Atrophy due to Inadequate Nutrition

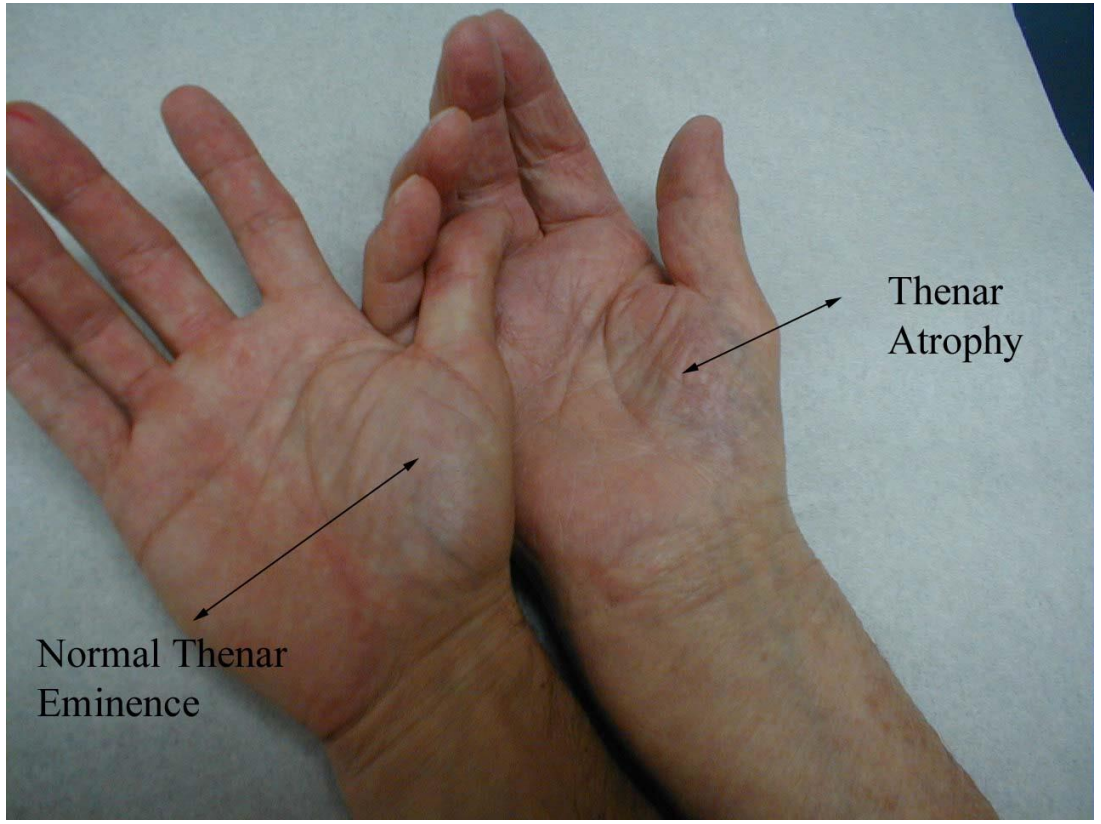
- If cell does not have building blocks, it will become smaller

Cellular Adaptation
Atrophy due to Changes in Hormonal Stimulation

- Ex) The anterior pituitary gland produces ACTH which stimulates production of adrenal cortex hormones. It causes growth of adrenal cortex. Adrenal cortex produces cortisone. Cortisone feeds back to pituitary which causes it to stop making ACTH. If cortisone is given as a drug (hydrocortisone, prednisone), the pituitary stops producing ACTH and adrenal glands atrophy. Patients who take these drugs need to ween off.
- Image shows a functional tumor involving only one of the two adrenal glands. The tumor secreted glucocorticoids which elevated plasma levels of the hormones, activating the adrenal -pituitary axis negative feedback system which in turn caused the pituitary to decrease its production of ACTH. The lowered levels of ACTH then caused the contralateral adrenal gland to atrophy due to lack of stimulation by ACTH.

Cellular Adaptation
Atrophy due to Loss of Innervation

- This image show a patient with carpal tunnel syndrome affecting the right hand. The reduced innervation has led to an atrophy of the thenar muscle on the right hand.



Cellular Adaptation
Results of Atrophy

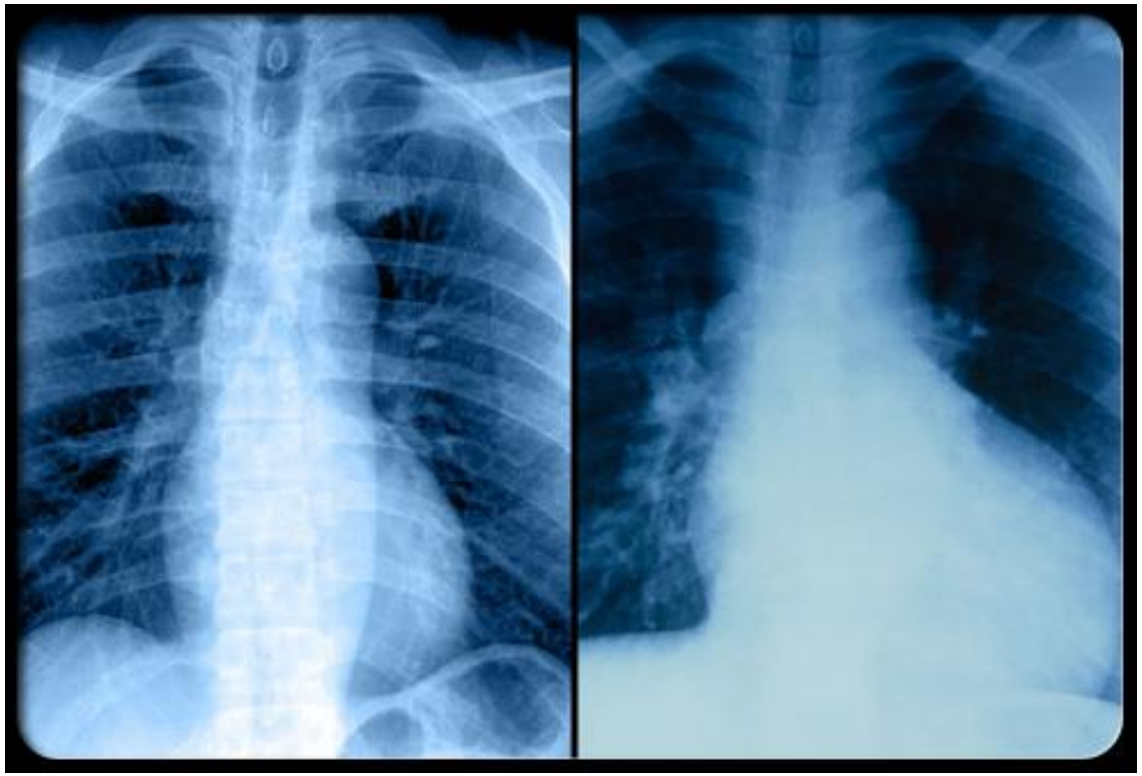
- Production of autophagic vacules
  - Normal cells have lysosomes
  - If cell is atrophying, the number and size of lysomes will increase
- Production of unremovable byproducts (lypofusion, myelin figures)

Cellular Adaptation
Hypertrophy

- Hypertrophy is an increase in functional components of cell.
  - Does not mean cell is swelling with water
  - It is an increase in the size of the cell
- This is normally a result of normal physiology and not pathophysiology (e.g., lifting weights increases mass)
- Occasionally it is a result of disease (e.g.. brain pathology causing increased muscle tone)

Cellular Adaptation Hypertrophy

- Pure hypertrophy occurs in cardiac and skeletal muscle, and nerves as these cells are not able to divide.
- Ex) Cardiac Hypertrophy
  - Often occurs as an adaptation of the heart to workload. It is a typical complication of hypertension and affects the left ventricle. The myocardium has to pump harder and the cardiac muscle fibers enlarge.

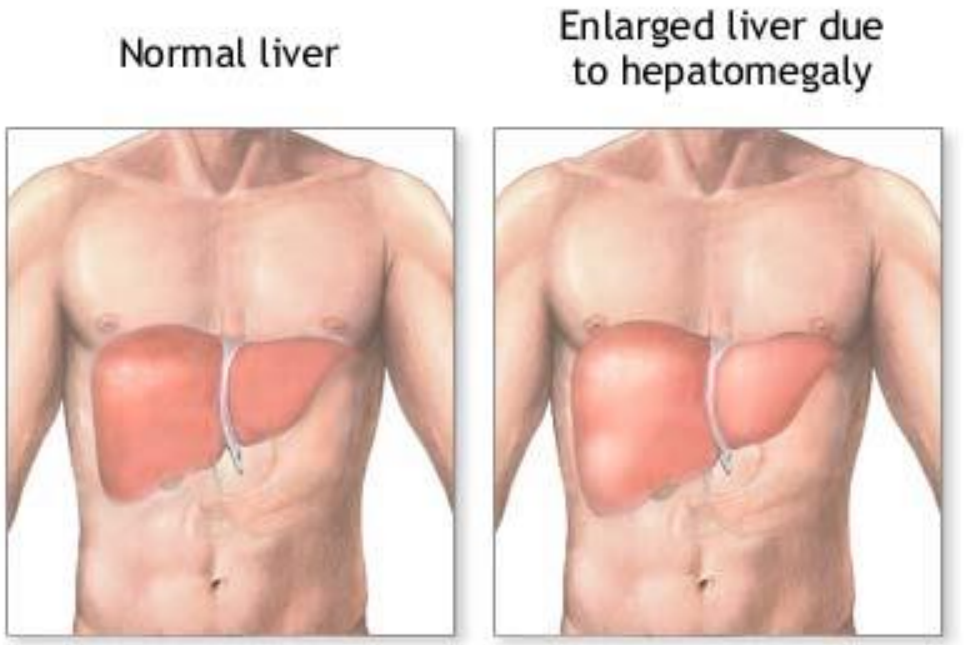


Cellular Adaptation
Hyperplasia

- Hyperplasia involves an increase in cellular number . The cells divide faster than they are dying.
- Classifications of hyperplasia include:
  - Compensatory hyperplasia
  - Hormonal hyperplasia
  - Pathological hyperplasia
  - Atypical hyperplasia (dysplasia)

Cellular Adaptation
Hyperplasia – Compensatory Hyperplasia

- Might be due to regeneration
  - Ex) Alcoholism - Alcohol broken down in the liver. Liver will make more cells and become enlarged.
- Might be mechanical
  - Ex) Callusing



Cellular Adaptation
Hyperplasia – Hormonal Hyperplasia

- Cell stimulation due to hormonal changes
- Ex) Breast and uterine growth during pregnancy

Cellular Adaptation
Hyperplasia – Pathological Hyperplasia

- Abnormal proliferation of normal cells (differentiated from tumor growth which are abnormal cells)
- Ex) Hemangioma (overgrowth of capillaries)

Cellular Adaptation
Hyperplasia – Atypical Hyperplasia

- Abnormal size, shape, and/or orginazation of mature cells (again, differentiated from cancer cells which tend to look like embryonic cells)
- This tends not to be adaptive, but happens for various other reasons
- Generally occurs in the cervix and respiratory region
- Tends to be associated with cancer (precancerous)
  - Ex) Cervical dysplasia - caused by infection with the human papillomavirus (HPV), but other factors also play a role.

Cellular Adaptation
Metaplasia

- Reversible replacement of a normal tissue type by another normal tissue type

Cellular Adaptation
Metaplasia

- Ex) Replacement of ciliated columnar epithelium with stratified squamous epithelium in the respiratory tract.
  - This is a result of smoking
  - It is reversible and takes about two weeks to reverse which is the time it takes for smokers cough to go away.

Cellular Adaptation
Metaplasia

- Ex) Barett's esophagus

Altered Cell Biology
Cellular Injury

Cellular Injury

- Cell may not be functioning properly because it has been exposed to an injurious agent
- The cell tries to adapt. If it fails to adapt, it is injured. This is marked when it is no longer able to maintain balance.
  - Ex) Tissue is not getting enough oxygen. Cell will make itself smaller to get by without oxygen. When it can no longer maintain balance and functions abnormally, it is injured.

- Injurious agents include:
  - Hypoxia
  - Chemicals/Toxins
  - Infectious agents
  - Immune response
  - Nutritional imbalances
  - Physical agents
- Results of injurious agents include:
  - Accumulations - things build up in the cell (water, lipids, calcium, hyaline change)

Cellular Injury
Hypoxia

- A decreased oxygen availability causes cellular injury. Without oxygen, the cellular mechanisms can not run.
- This especially affects the protein-ion pumps. Hypoxia will lead to a decreased functioning of the Na-K pumps. *Note: 70% of energy is used to pump ions.*
- When ion pumps fail, ions accumulate inside the cell, changing osmotic pressure. This pulls water into the cell and the cell swells.

Cellular Injury
Toxins

- Toxins block cellular mechanisms
- They fit into the metabolic scheme of the cell and block the machinery.
- This is like sand vs pingpong balls in a cars transmission.

Cellular Injury
Infectious agents

- These injure cells in several ways:
  - They cause a direct destruction of cells
    - Ex) Malaria - protist which gets into RBC, reproduce until they pack RBCs and then the RBC bursts
  - They secrete toxins
  - The body mounts an immune defense and there could be a hypersensitivity reaction. The immune system gets carried away and destroys your tissue.
    - Ex) Microbacterium tuberculosis (TB) which is not very strong or invasive. However, immune system is aggressive and attacks it (and damages lungs).

Cellular Injury
Immune Response, Nutritional Imbalances

- The immune system reacts to things other than pathogens. It will be discussed later.
- Nutritional deficiencies can injure cells. Specific nutritional deficiencies will be discuss in clinical nutrition.

Cellular Injury
Physical Agents

- These include:
  - Temperature extremes (burns, frostbite, fever)
  - Pressure
  - Ionizing Radiation
  - Mechanical factors (trauma) causes
    - Interruption of blood supply
    - Inflammatory response (swelling)

Cellular Injury
Results of injurious agents

- In the presence of injurious agent, cell will try to adapt (probably atrophy to get by on less oxygen or nutrients), if it can't adapt it will then begin to fail (it can't do what cells need to do) and we would say it is injured.
- Accumulations are observed within the cell, including:
  - Water
  - Lipids
  - Calcium
  - Hyaline change

Cellular Injury
Results of injurious agents

- Water accumulation
  - If cell swells, reactions slow down as chemicals are farther apart
  - This will progress to hydropic degeneration
    - Definition
    - If pathologist looks at swollen cells, there will be big clear vacules in cytoplasm
    - Vacoules are organelles distended with water
- Water accumulation is reversible

Cellular Injury
Results of injurious agents

- Lipids accumulate when the cell is injured. Causes of lipid accumulation include:
  - Starvation - causes abnormal enzyme compliments (building blocks of enzymes, coenzymes, etc.), Liver cells accumulate fat as they can't process raw materials
  - Genetic disease – abnormal enzymes are produced
  - Toxic compounds – alcohol is a common cause of fatty change of liver. Liver will be enlarged and greyish yellow. It will also be greasy.

Cellular Injury
Results of injurious agents

- Calcium accumulation is due to failure of calcium pumps, calcium builds up inside cell and crystalizes.
- This can be seen when there is dead or dying tissue and is common in atherosclerosis (referred to as dystrophic calcification)
- This can also be seen systemically (throughout the body) due to hypercalcemia which can be cause by hormonal or renal abnormalities.

Cellular Injury
Results of injurious agents

- Hyaline change is an accumulation of glassy translucent crystals which are denatured proteins. This might be degenerate proteins, antigen-antibody complexes, extracellular proteins, and it might be due to environmental changes (pH, for instance).

Altered Cell Biology
Cellular Death

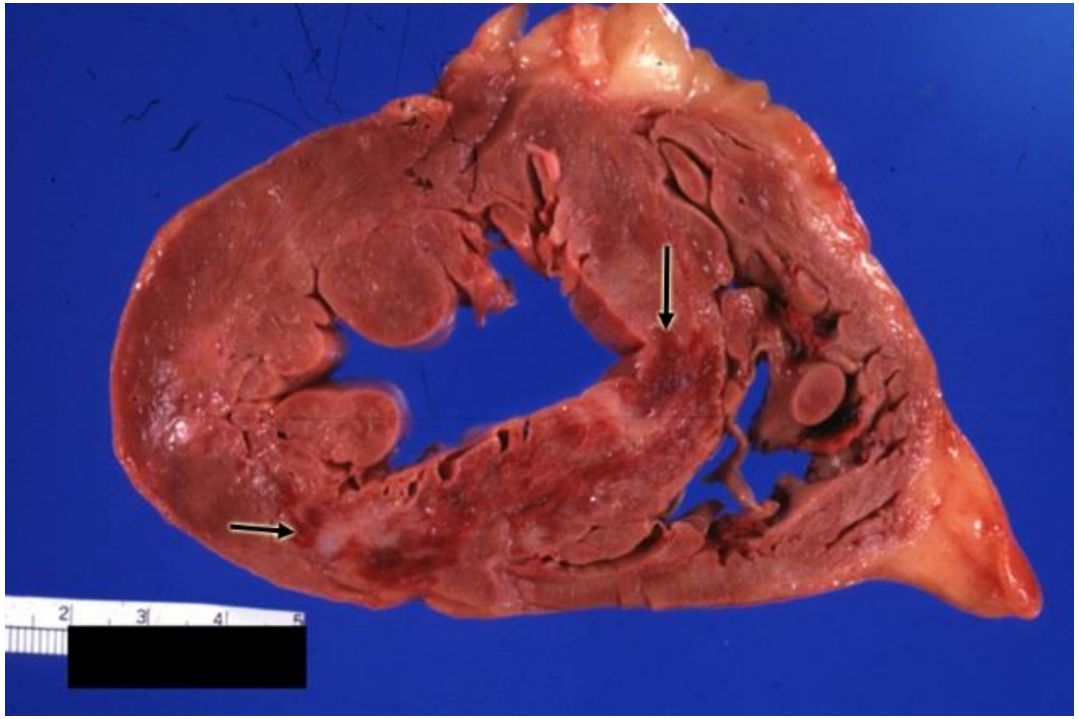
Cellular Death

- Cell may not be functioning because it is dead
- This is referred to as necrosis - localized cell death
  - Ex) Myocardial Infarction
- Autolysis will occur due to dissolution of lysosomes
- Immune response will occur to remove dead cells

- Types of necrosis include:
  - Coagulative necrosis
  - Liquifactive necrosis
  - Caseous necrosis
  - Fat necrosis

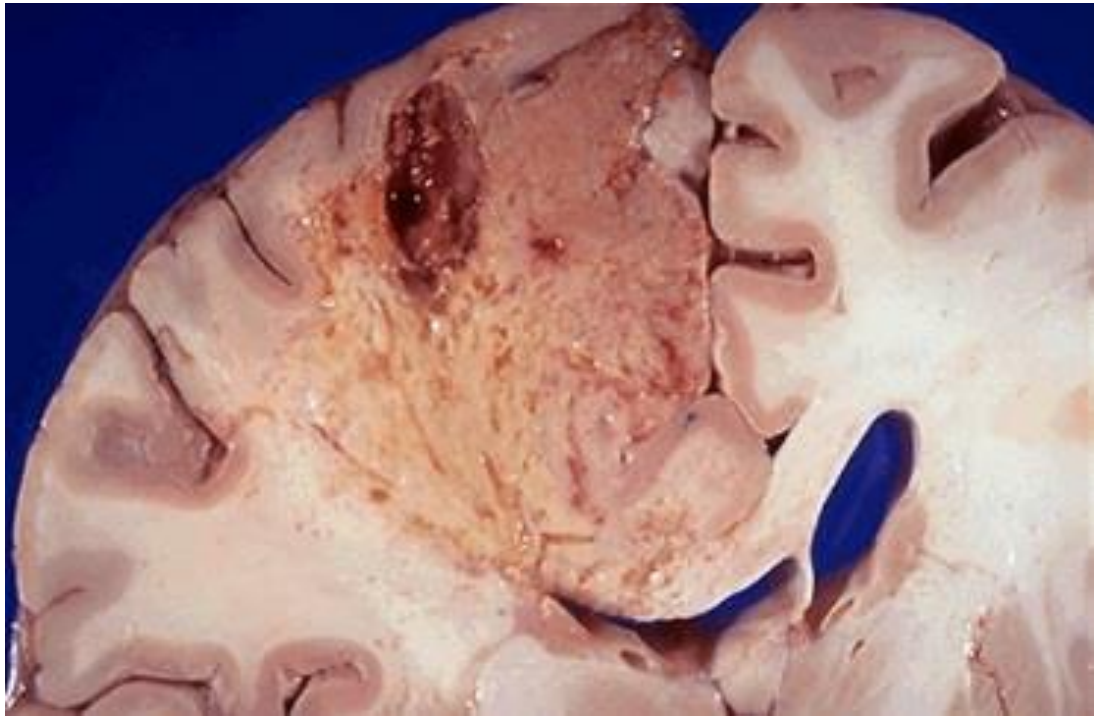
Cellular Death
Coagulative Necrosis

- Intracellular and extracellular proteins coagulate
- Maintains the structure of the tissue (at least for a while)
- Eventually this tissue will degenerate and be replaced with scar tissue
- Depends on the type of tissue, environment and cause of cellular death (most common place is heart due to hypoxia)
  - Ex) Myocardial infarction



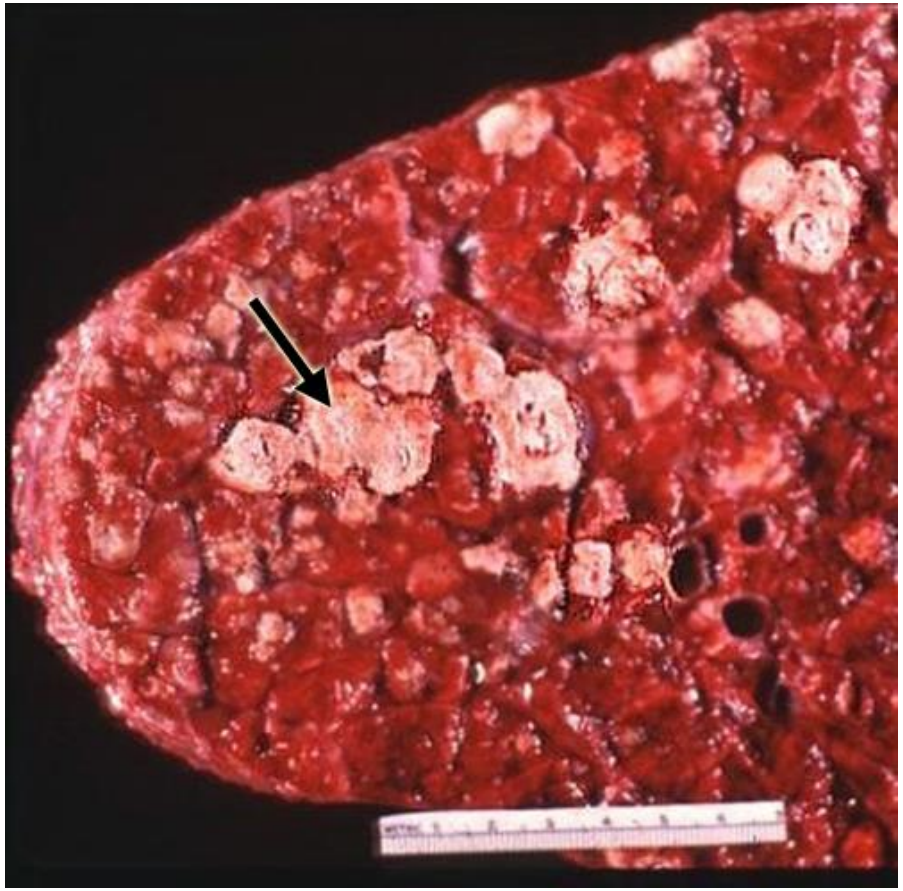
Cellular Death
Liquifactive necrosis

- Occurs where there are many hydrolytic enzymes
- Tissue is liquified, surrounding tissues for a CT capsule
- Most common place is in brain (stroke), area of necrotic tissue will liquify
- Another common place is sebaceous cyst



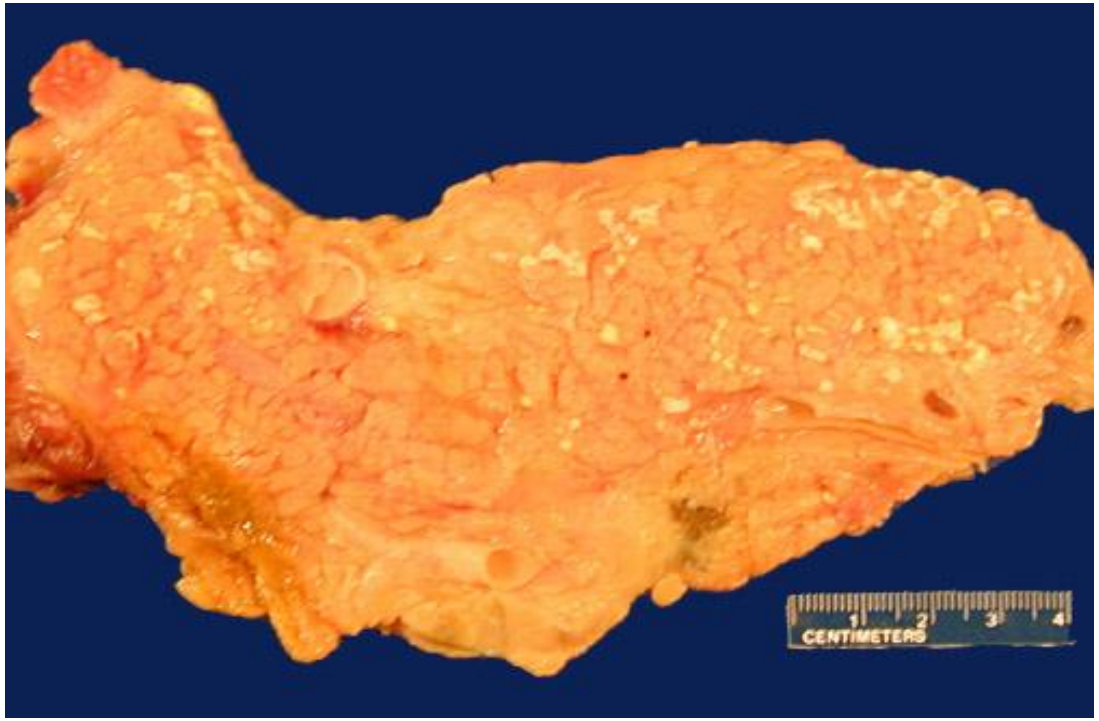
Cellular Death
Caseous Necrosis

- Granular tissue that looks like cottage cheese
- Associated with infection from TB



Cellular Death
Fat Necrosis

- Lipases are spilled due to injury, these come in contact with fat and digest triglycerides.
- Ex) Pancreatic fat necrosis due to traumatic injury



Altered Cell Biology
Aging

Aging

- Cell may not be functioning properly because it is going though and aging process

Altered Cell Biology
Neoplasia

Neoplasia

- Cell may not be functioning properly because it has undergone a neoplastic transformation