Pathology is a science dealing with the study of diseases.

Four important components of pathology are

Etiology (causative factors).

Pathogenesis (mechanism or process by which disease develops).

Morphology (appearance of cells, tissues or organs).

**Clinical features.**

Adaptations   
Cell Injury & Cell Death

Adaptations

**Cellular responses to stress and noxious stimuli**

**Adaptive responses are**

Hypertrophy.

Hyperplasia.

Atrophy.

Metaplasia.

**Cell injury develops**

Adaptive capability is exceeded.

External stress is inherently harmful.

**Cell death**

Itis one of the most crucial events in the evolution of disease in any tissue or organ.

**pathological Causes of cell death**

Ischemia (lack of blood flow).

Infections, toxins, and immune reactions.

**Physiological Cell death**

Embryogenesis.

The development of organs.

The maintenance of homeostasis.

**The relationship among normal, adapted, reversibly injured, and dead myocardial cells.**

**Myocardial hypertrophy** Myocardium shows functional effects without any gross or light microscopic changes

**Reversible changes** like cellular swelling and fatty change.

**The irreversible injury** is ischemic coagulative necrosis.

The transmural acute myocardial infarction.

**Physiologic adaptations**

usually represent responses of cells to normal stimulation

by hormones or endogenous chemical mediators (e.g., the hormone-induced enlargement of the breast and uterus during pregnancy).

**Pathologic adaptations are**

responses to stress that allow cells to modulate their structure and function and thus escape injury.

**Hyperplasia**

Tissue contains cell populations capable of replication; it may occur concurrently with hypertrophy and often in response to the same stimuli.

Can be physiologic or pathologic.

In both situations, cellular proliferation is stimulated by growth factors that are produced by a variety of cell types.

**physiologic hyperplasia are**

(1) hormonal hyperplasia, exemplified by the proliferation of the glandular epithelium of the female breast at puberty and during pregnancy.

(2) compensatory hyperplasia, in which residual tissue grows after removal or loss of part of an organ. For example, when part of a liver is resected, mitotic activity in the remaining cells begins as early as 12 hours later, eventually restoring the liver to its normal weight.

**Atrophy:** Shrinkage in the size of the cell by the loss of cell substance

**Causes of atrophy**

1. Decreased workload (e.g.,immobilization of a limb to permit healing of a fracture),
2. Loss of innervation
3. Diminished blood supply.
4. Inadequate nutrition.
5. Loss of endocrine stimulation.
6. Aging (senile atrophy).

• Protein synthesis decreases because of reduced metabolic activity.

• The degradation of cellular proteins occurs mainly by the *ubiquitin-proteasome pathway.*

Nutrient deficiency and disuse may activate ubiquitin ligases, which attach multiple copies of the small peptide ubiquitin to cellular proteins and target them for degradation in proteasomes.

**Autophagy** (“self-eating”)

Resulting increases in the number of *autophagic vacuoles.*

The starved cell eats its own components in an attempt to survive.

**Metaplasia** is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.

Metaplasia is thought to arise by reprogramming of stem cells to differentiate along a new pathway rather than a phenotypic change (transdifferentiation) of already differentiated cells.

Cell injury

Disease occurs due to alteration of the functions of tissues or cells at the microscopic level.

**Causes of cell injury include**

**1. Hypoxia:**

It is the most common cause of cell injury.

It results due to decrease in oxygen supply to the cells.

**Hypoxia may be caused by**

**a. Ischemia (most common cause):** Results due to decrease in blood supply.

It is the most common cause of hypoxia

b. **Anemia:** Results due to decrease in oxygen carrying capacity of blood

c. **Cardio-respiratory disease:** Results from decreased oxygenation of blood due to car-diac or respiratory disease.

2. **Physical Agents:** Cell injury may occur due to radiation exposure, pressure, burns, frost bite etc.

3. **Chemical Agents:** Many drugs, poisons and chemicals can result in cell injury.

4. **Infections:** Various infectious agents like bacteria, virus, fungus and parasites etc can cause cell injury.

5. **Immunological reactions:** These include hypersensitivity reactions and autoimmune diseases.

6. **Genetic causes:** Cell injury can also result due to derangement of the genes.

7. **Nutritional imbalance:** Cell injury can result due to deficiency of vitamins, minerals etc.

**Sub cellular changes in cell injury**

● Swelling of organelles like endoplasmic reticulum results in decreased protein synthesis.

• Bleb formation results due to outpouching from the cell membrane to accommodate more water.

• Loss of microvilli.

• Formation of myelin figures due to breakdown of membranes of cellular organelles like endoplasmic reticulum.

These are composed of phospholipids.

Myelin figures are intracellular whorls of laminated lipid material (resembling myelin of nerves). When these are present in membrane bound structures containing lysosomal enzymes, these are known as myeloid bodies or myelinoid bodies.

**Reversible cell injury**

In early stages or mild forms of injury the functional and morphologic changes are reversible if the damaging stimulus is removed.

In this type of injury, although there may be significant structural and functional abnormalities, the injury has typically not progressed to severe membrane damage and nuclear dissolution.

**Mitochondria** is the *earliest organelle* affected in cell injury.

**Hydropic change** or swelling of the cell due to increased water entry is the *earliest change* seen in reversible cell injury.

Reversible cell injury

There are two types of Irreversible cell injury/cell death

(necrosis and apoptosis) which differ in their mechanisms, morphology, and roles in disease and physiology.

Necrosis is always a pathologic process.

Apoptosis serves many normal functions and is not necessarily associated with pathologic cell injury.

Apoptosis does not elicit an inflammatory response.

**IRREVERSIBLE CELL INJURY:**

Features of irreversible cell injury include

1. **Damage to cell membrane:**

It results due to continued influx of water, loss of membrane phospholipids and loss of protective amino acids (like glycine). Damage to cell membranes result in massive influx of calcium.

**2. Calcium influx:**

Massive influx of Ca2+ results in the formation of large flocculent mitochondrial densities and activation of enzymes.

3. **Nuclear changes:**

These are the most specific microscopic features of irreversible cell injury.

These include:

**Pyknosis** is nuclear condensation

**Karyorrhexis** is fragmentation of the nucleus.

**Karyolysis** is nuclear dissolution

**Inability to reverse mitochondrial dysfunction** and development of profound **disturbances in the membrane function** characterize irreversibility.

**Increased calcium, reactive oxygen species and oxygen deprivation** causes damage of **mitochondria.**