

Types of cell necrosis

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1. **Coagulation (coagulative) necrosis.**
2. **Liquefaction (liquefactive) necrosis.**
3. **Fat necrosis.**
4. **Caseation (caseous) necrosis.**
5. **Gangrenous necrosis.**

Coagulation necrosis

- Results from sudden severe ischemia in such organs as the heart, kidney etc.
- **Microscopically** the fine structural details of the affected tissue (and cells) are lost but their outlines are maintained.
- The nucleus is lost.
- The cytoplasm is converted into homogeneous deeply eosinophilic and structureless material.
- The outlines of the affected cells are still discernible.

Liquefaction necrosis

Seen in two situations:

1. Brain infarcts i.e. ischemic destruction of brain tissue.
2. Abscesses i.e. suppurative bacterial infections.

Liquefaction necrosis is characterized by complete digestion of dead cells by enzymes and thus the necrotic area is eventually liquefied i.e. converted into a cyst filled with debris and fluid.

Fat necrosis

This is a specific pattern of cell death seen in adipose tissue due to action of lipases.

It is most commonly seen in **acute pancreatitis**. The released fatty acids from necrotic cells, complex with calcium to create calcium soaps.

These are seen grossly as chalky white deposits.

Fat necrosis can also be induced by mechanical trauma as in female breast (**traumatic fat necrosis**).

Caseous necrosis (caseation)

This combines the features of coagulative and liquefactive necrosis. It is encountered principally in the center of tuberculous granulomas.

The body response to tuberculous infection is a specific form of chronic inflammation referred to as granulomatous inflammation. The morphologic unit of this is called granuloma.

Grossly the caseous material is soft, friable, and tan to whitish-gray cheesy material.

Microscopically the area is surrounded by granulomatous inflammation. It has distinctive amorphous granular pinkish debris.

Gangrenous necrosis

This does not represent a distinctive pattern of cell death, but is still in use as a term in surgical practice. It describes a limb (usually the lower) that has lost its blood supply and has subsequently attacked by bacteria. So it is a combination of coagulative necrosis modified by liquefactive action of enzymes derived from bacteria and inflammatory cells. When the coagulative pattern is dominant the affected parts shrink and appear contracted (dry); the process is termed **dry** gangrene. Conversely, when the liquefactive action is more prominent, the affected parts are swollen (edematous); the term **wet** gangrene is used.

Apoptosis

(Programmed cell death)

This distinctive pattern of cell death differs from necrosis in that it is an internally controlled process through which cells are disassembled and removed with minimal damage, if any, to the tissue containing them. If necrosis is considered as a morphological

expression of cellular "homicide", then apoptosis, if the same philosophy is used, is a cellular "suicide". In essence, apoptosis is an energy-dependent process for deletion of unwanted individual cells. In every human, 10 billion cells must die every day (e.g. from the skin, mucosa of GIT, cellular elements of the blood, etc) to balance the 10 billion produced through mitosis.

Examples where apoptosis occurs include:-

1. During embryogenesis i.e. it is responsible for shaping various organs and structures (morphogenesis); normal cells undergo apoptosis when they end up outside the places they should be in body tissues.

2. Hormone-dependant involution

a. Physiological e.g. of the endometrium during the menstrual cycle and of lactating breast after weaning.

b. Pathological e.g. atrophy of the prostate after castration

3. Deletion in proliferating cells e.g.

a. Physiological e.g. of intestinal epithelium, skin and blood cells.

b. Pathological e.g. in tumors.

4. Apoptosis induced by cytotoxic lymphocytes seen in two situations:

A. Virally infected cells attacked by cytotoxic T-lymphocytes
typical example is acute viral hepatitis.

B. Some immature B and T lymphocytes within the body can not discriminate between self and nonself-antigens. If such cells persist after get activated, they may destroy healthy body cells (autoimmune diseases).

5. Injurious agents that cause irreparable DNA damage

that triggers apoptotic pathway of cell death e.g. irradiation and anti-cancerous chemotherapeutic drugs that are used in the treatment of malignant tumors, can induce apoptosis in some types of cancer cells.

From the above listed examples, it is conceivable that failure of

cells to undergo apoptosis may result in undesirable effects that include:-

- a. Anomalous development of various organs and tissues (birth defects).
- b. Progressive acceleration of tumor growth.
- c. Autoimmune diseases e.g. systemic lupus erythematosus and rheumatoid arthritis.

Morphology of apoptosis

Apoptosis usually involves single cells or clusters of cells (falling leaves). The apoptotic cell appears as rounded or oval with intensely eosinophilic (red) cytoplasm. The nuclear chromatin is aggregated under the nuclear membrane with nuclear shrinkage (pyknosis). This is followed by nuclear fragmentation (karyorrhexis). Then cytoplasmic budding (or blebbing) occur and each nuclear fragment will be contained within one bud. The resulting structures are called apoptotic bodies. These bodies are quickly phagocytosed or degraded. Apoptosis does not trigger an inflammatory response.

Intracellular accumulations

Under certain situations, cells may accumulate abnormal amounts of various substances.

The accumulated substance falls into one of three categories

1. A normal cellular constituent accumulated in excess e.g. lipid, protein, and CHO.
2. An abnormal substance that is a product of abnormal metabolic pathway.
3. A pigment i.e. a colored substance.

The accumulated substance may be harmless or severely toxic to the cell. The site of accumulation is either nuclear or cytoplasmic. Within the cytoplasm, the accumulated substance is most frequently within the lysosomes.

The mechanisms of abnormal intracellular accumulations are many but can be divided into four general types:

1. **Abnormal metabolism:** a normal substance is produced at a normal rate, but the rate of its removal is inadequate e.g. fatty change of the liver and occurrence of protein droplets in the epithelial cells of proximal convoluted tubules in cases of proteinuria due to leaky glomeruli.

2. **Genetic mutations producing changes in protein folding and transport.** A protein is composed of amino acids linked in specific sequences by peptide bonds and coiled and folded into complex globular or fibrous structures. A change in this configuration may result in interference with its transport so that it gets accumulated at the site of production.

3. A normal or abnormal substance is produced but cannot be metabolized. This is most commonly due to lack of an enzyme, which is genetically determined (inborn error of metabolism). Such a deficiency of enzymes blocks a specific metabolic pathway resulting in the accumulations of unused metabolite (s) proximal to the block. The resulting diseases are referred to as storage diseases.

4. An abnormally exogenous substance is deposited and accumulates because the cell is incapable to get rid of it (through enzymatic degradation or to transport it to the outside) e.g. carbon particles in anthracosis and silica particles in silicosis.

Features of Necrosis and Apoptosis

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome-size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic, means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA damage