DEGENERATION NECROSIS AND INFILTRATION

Cellular Degenerations and Infiltrations

1. **Cloudy swelling and hydopic degeneration**
   Cloudy swelling and hydopic degeneration occur when the regulatory mechanisms which control the normal ionic balance of a cell fail, and sodium and water enter the cell. The mitochondria swell giving the cytoplasm a cloudy or granular appearance and, with continued accumulation of fluid, a clear appearance. Cloudy swelling and hydropic degeneration may be reversible.

   **Causes of cloudy swelling and hydropic degeneration include:**
   
   a) bacterial toxins  
   b) chemical toxins  
   c) hypoxia

2. **Fatty degeneration**
   Fatty degeneration is the accumulation of excessive quantities of neutral fat in cells of parenchymatous organs and muscle fibres. The fat accumulates in the cytoplasm as small droplets. These coalesce to form large globules of lipid which may push the nucleus to one side. Fatty degeneration may be reversible.

   **Causes of fatty degeneration**
   
   a) infectious disease: eg bacterial toxins and in diphtheria and typhoid fever.  
   b) chemical toxins: eg phosphorus and halogenated hydrocarbons.  
   c) hypoxia: eg severe anaemia  
   d) metabolic disturbances: eg diabetes mellitus  
   e) dietary deficiencies: eg protein malnutrition.

3. **Necrosis**
   Severe or continuing noxious influences on cells may result in cell death. This is known as necrosis and is an irreversible state. Necrotic cells appear shrunken and may show one of the following features:-

   a) pyknosis - nucleus small and darkly staining  
   b) karyorrhexis - nucleus fragmented  
   c) karyolysis - nucleus disappeared

Degeneration of Connective Tissue and Vascular Tissues

1. **Mucoid Degeneration**
   Mucoid degeneration is the accumulation of muco-proteins within the ground substance of connective tissue. Ganglion of wrist is an example of mucoid degeneration. The cause is unknown.
2. **Fibrinoid Degeneration**
   
a) **Connective tissue fibrinoid.** This is formed by the breakdown of collagen fibres and of the mucopolysaccharide ground substance between the fibres resulting in the formation of material that has similar staining properties to fibrin. Connective tissue fibrinoid occurs in patients with rheumatoid arthritis.

   b) **Vascular fibrinoid.** This occurs in conditions in which there is damage to blood vessel walls with extravasation of fibrin into the tissues of the wall.

3. **Hyaline Degeneration**
   
Substances that have a homogenous glassy appearance in tissue sections are described as hyaline. Hyaline degeneration may occur in fibrous tissue in scars and some tumours due to the deposition of glycoproteins between collagen bundles. It may also occur in the walls of blood vessels.

4. **Amyloidosis**
   
Amyloid is a group of eosinophilic fibrillary materials, deposited along basement membranes and in walls of blood vessels. It probably enters the tissues from the blood. It is often associated with conditions of chronic antigenic stimulation and plasma cell proliferation eg chronic infections, rheumatoid disease and myelomatosis.

Amyloidosis most frequently affects the liver, kidneys, spleen and endocrine glands. The organs have a firm waxy consistency and are enlarged. They stain mahogany brown with iodine solution (starch-like reaction).

Amyloid also has an affinity for Congo red.

Amyloid deposits interfere with diffusion from blood vessels and may lead to atrophy of the cells in the organ.

5. **Pathological Calcification**
   
a) **Dystrophic Calcification** is the deposition of calcium salts in association with normal blood levels of calcium and phosphate. It may occur in old scars, old tuberculous lesions, dead parasites, atheromatous plaques, areas of fat necrosis, old infarcts, some neoplasms, etc.

   b) **Metastatic Calcification** is the deposition of calcium salts, especially in blood vessels and kidney, in patients with raised blood calcium levels.
ABNORMALITIES OF CELL GROWTH AND DEVELOPMENT

Abnormal growth can be due to excessive or reduced growth rate. Excessive growth rate leads to the conditions of hyperplasia and hypertrophy. Reduced growth rate leads to hypoplasia if development is still occurring, and atrophy if development has fully occurred. Abnormalities of cell development lead to metaplasia and dysplasia.

EXCESSIVE GROWTH RATE

The stimulus for excessive growth rate of cells is usually an increased demand for function, and may be mechanical, chemical or hormonal.

Tissues which consist of continuously dividing cells, or cells with a slow turnover rate, respond to increased demand for function with increased rate of division and they may also respond with an increase in cell size. Cells which do not normally divide can only respond with an increase in cell size.

Hyperplasia is the enlargement of an organ or tissue due to an increase in the number of cells present.

The stimulus is usually chemical or hormonal.

1.  **Hyperplasia in endocrine glands**
   a)  Parathyroid - due to fall in serum Ca$^{++}$ ion
   b)  Thyroid - due to increased TSH or LATS in primary thyrotoxicosis
   c)  Adrenal cortex - due to increased ACTH secretion.

2.  **Hyperplasia of endocrine target organs**
   a)  Breast ducts and acini - occurs in pregnancy and lactation due to oestrogens and progesterone.
   b)  Prostate - in hyperplasia due to hormonal imbalance
   c)  Endometrium - in response to oestrogens.

3.  **Epithelium**  Covering epithelium of the skin, mouth, alimentary and respiratory tracts undergo hyperplasia if there is a persistent traumatising agent.

4.  **Lymphoid tissue**  Hyperplasia occurs in chronic infections

5.  **Bone Marrow**  Bone marrow cells proliferate following haemorrhage and in conditions of anaemia.

Hypertrophy is the enlargement of an organ due to an increase in the size of cells. Hypertrophy without accompanying hyperplasia occurs in muscle and the stimulus is usually mechanical.

1.  **Smooth muscle**
   a)  Bladder - hypertrophy occurs if there is obstruction to outflow
b) Alimentary tract - proximal to obstruction
c) Arteries - hypertrophy of media occurs in hypertension.

2. **Cardiac muscle** - hypertrophy occurs when there is a demand for increased work.
   a) Left ventricle - hypertrophy occurs in hypertension, aortic valve disease and ischaemic heart disease.
   b) Right ventricle - hypertrophy occurs in chronic lung disease such as emphysema, pulmonary fibrosis, congenital heart lesions where there is a left to right shunt, pulmonary and mitral valve lesions, and secondary to left ventricular hypertrophy.

**REDUCED GROWTH RATE**

**Hypoplasia** is not the opposite of hyperplasia but refers to an organ which has never attained adult size - therefore it is a developmental abnormality. **Aplasia** means complete failure of development of an organ.

**Atrophy** is the diminution in size of an organ due to a decrease in the size or number of the constituent cells. It can be generalised or localised.

1. **Endocrine atrophy** - follows withdrawal of endocrine stimulus to gland or target tissue. There is atrophy of thyroid, adrenals and gonads in hypopituitarism.

2. **Osteoporosis** - is a metabolic bone disease in which the bone matrix is reduced, it can occur in a variety of conditions such as recumbency, hormonal disturbances and ageing.

**Local atrophy**

1. **Ischaemia** - gradual vascular obstruction to an organ results in atrophy eg cerebral arterial atherosclerosis.

2. **Disuse** - atrophy occurs in bones, ligaments and muscles due to disuse eg poliomyelitis. Loss of innervation also causes local muscle atrophy.
ABNORMALITIES OF CELL DEVELOPMENT

Metaplasia is a form of abnormal regeneration in which is produced a differentiated type of cell or tissue different from that normally found in a given location. It occurs in epithelia and connective tissues.

1. Epithelial metaplasia - occurs when one type of epithelium changes to another. There can be squamous and columnar metaplasia.

   a) Squamous metaplasia often appears to be the result of persistent trauma. It is found in:
      bronchus - in chronic bronchitis, bronchiectasis, abscess cavities
      cervix - in the glands
      gall bladder - in chronic cholecystitis
      renal tract - in association with stones
      prostate - in association with necrosis

   b) Columnar metaplasia is found in:
      Stomach - in chronic gastritis where the normal epithelium is replaced by intestinal epithelium
      breast - in fibroepithelial hyperplasia, where cysts become lined by pink cells resembling apocrine epithelium.

2. Connective tissue metaplasia

   a) Osteoid tissue - areas of ossification in scars, goitres, neoplasms etc. Arise from metaplasia of fibroblasts.
   b) Neoplasms - metaplasia may result in bony areas in neoplasms.

Dysplasia has several meanings. For instance, it is used to mean a disorder which can be congenital, or structure or function, due to perverted nutrition.

   eg pernicious anaemia due to deficiency of vitamin B12

It is also used to mean an abnormal proliferation of cells, particularly epithelium which is not malignant but may be pre-malignant eg in the cervix.