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PATHOLOGY OF GROWTH DISTURBANCES

The disturbances in growth cover a broader spectrum of changes from no growth to uncontrolled growth. While uncontrolled growth (neoplasm) is dealt separately, the other forms of growth disturbances are considered in this chapter.

Cells may fail to develop or adapt to changing environment or physiological or pathological stimuli.

- Aplasia
- Agenesis
- Hypoplasia
- Hyperplasia
- Hypertrophy
- Atrophy
- Metaplasia
- Dysplasia

The cells respond to altered physiological or pathological stimuli by adapting themselves. These changes are reflected as atrophy, hyperplasia, hypertrophy, metaplasia and dysplasia besides aplasia and hypoplasia. Following an injurious stimulus or to stress, the normal cell's homeostatic state may respond with cellular injury resulting in either death or adaption. Hence, the cellular adaptation to the increased demand is a state in between normal and stressed.

Aplasia

Aplasia *(* **A** : *Without; not)* *(* **Plasia***: Development or formation)* :- is the complete failure of an organ to develop. This developmental disturbance occurs in

the embryo or fetus in utero. In the place of the organ, rudimentary tissue of fat and connective tissue are present. The condition is incompatible with life when it involves vital organs like heart, brain etc.

Hypoplasia

It is the failure of an organ or tissue to attain its full normal adult size.

Causes

Any injury occurring in late stages of development of fetus or neonates. e.g. Genetic mutation affects proper differentiation and migration of cells in embryo, virus causes hypoplastic changes; drug induced hypoplasia occurs through degeneration and necrotic changes.

Pathological changes: Organ will be smaller than adult size. The cells show alterations in lysosomes and inspissated protein in cytoplasm. The phagolysosomes increase in size with lipofuscin pigment.

Atrophy

Atrophy is the decrease in the size (quantitative) or amount (numerical) of cells/tissues/organ after attaining full normal growth. Atrophy is representing adaptation to deficient nutrient supply, lack of stimulation and decreased work load. This may affect any organ or part of an organ.

Atrophy can be broadly classified into physiological atrophy and pathological atrophy.

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***Physiological atrophy*:-**

Involution of the organs can be observed as the age is advanced. Involution is the decrease in the size of the organ due to decrease in the number of cells, caused by apoptosis. e.g. Involution of thymus on attaining puberty, uterine involution after parturition (decrease in smooth muscle size and number)

***Senile atrophy*:-**

Atrophy of the organs occurs with ageing and reproductive organs like testis and ovaries are the first to show such changes. It is associated with loss of cells.

Pathological atrophy

***Nutritional atrophy*:-**

This is due to starvation. Starvation of the tissue is caused by malnutrition, malabsorption, chronic infection, parasitism, neoplasia etc. Mismothering is also quoted in starvation atrophy in neonates. In starvation following depletion of glycogen and fat reserves, protein of the musculature and vital organs is lost, resulting in muscular wasting.

Atrophied muscles appear smaller than normal. Lack of physical activity due to an injury or illness, poor nutrition, genetics, and certain medical conditions can all contribute to muscle atrophy. Also this type may causes a muscle atrophy, which can occur after long periods of inactivity.

Angiotrophic atrophy: -

Abnormalities that diminished blood supply (ischaemia, chronic passive congestion, anaemia) may lead to atrophic changes of skin, hair, nails,

subcutaneous tissues, and bone, caused by peripheral nerve lesions.

e.g. Parasitic ischaemia caused by Strongylus larvae by the occlusion of femoral artery leads to atrophy of hind limb in horses. Also, hepatic atrophy can occur due to decreased portal venous blood flow. Chronic venous congestion results in centrilobular necrosis of liver due to inadequate oxygen and nutrition supplied to the hepatocytes.

Disuse atrophy:-

It is a type of muscle atrophy, or muscle wasting, which refer to a decrease in the size of muscles in the body. Disuse atrophy occurs when a muscle is no longer as active as usual. Decreased work load, causes decrease in the size of the body musculature due to inactivity as in the case of race horses, so, when muscles are no longer in use, they slowly become weaker. Eventually, they begin to shrink.

Immobilization *causes skeletal muscle atrophic changes can occur in plaster casted animals (like in Dogs or Cats), especially in fracture, there will be decrease in the size of the myocytes.*

Neurotrophic atrophy:

Decrease in the size of muscle fibres occurs if a nerve is severed or injured. *e.g. In horses*, laryngeal muscle atrophy occurs due to the injury to left recurrent laryngeal nerve and shoulder muscle atrophy (sweening) occurs due to suprascapular nerve injury.

Pressure atrophy:-

Indicated to damage and wasting of hard or soft tissue resulting from excessive pressure applied to tissue by a denture base. In space occupying lesions like tumors,

abscesses …*etc*., the neighboring tissues undergo atrophic changes mainly due to lack of nutrition from pressure ischemia.

Endocrine atrophy:-

Atrophic lesion affecting the pituitary gland with loss of hormones leads to atrophy of the thyroid gland, adrenal glands, and gonads and in turn brings atrophic changes to their target organs and the viscera, the decrease in size of the endocrine glands may be extreme ; e.g. prolonged steroid therapy leads to atrophy of *Zona fasciculata* layer, *Castration* leads to atrophy of prostate. *Hyperestrogenism associated with sertoli cell tumour* results in seminiferous cell atrophy. *Ovariectomy* leads to uterine atrophy.

HYPERPLASIA

Hyperplasia is the increase in the size of the tissue or an organ or a part of an organ due to quantitative increase in the number of cells.

Hyperplasia is classified into [physiological hyperplasia and pathological hyperplasia].

- **Physiological hyperplasia:-**

Physiological hyperplasia may be the result of hormonal influence as in the case of increase in the size of mammary gland due to glandular epithelial cell proliferation in puberty and pregnancy. Also there is another type of physiological hyperplasia, called " *Compensatory hyperplasia* " that mostly happen in skin=[in which basal layer proliferates to form the superficial layers], and in liver = [Hepatic regeneration occurs following partial hepatectomy by the proliferation of surviving cells].

❖ **Pathological hyperplasia:-**

This is most commonly caused by excessive hormonal stimulation. e.g. endometrial hyperplasia or effects of growth factors on target cells;for example:-

- In canine uterus, cystic endometrial hyperplasia occurs in prolonged progesterone secretion;
- In wound healing, hyperplasia of connective tissue (e.g. fibroblast and blood vessels) occurs under the influence of growth factors;
- hyperplasia also occurs in viral infections involving the epithelium i.e. epidermis or mucosal epithelium. e.g. papilloma virus infections. Pathological hyperplasia may also lead to cancerous growth.

Pathological hyperplasia may be (*localized*) - e.g. Nodular hyperplasia in liver, spleen of aged dogs. And/or (*generalized/diffused*)- e.g. diffuse enlargement of an organ, prostatic hyperplasia in dogs and thyroid hyperplasia in case of Goitre.

Hyperplasia ability depends on different adult cell types. Accordingly three cell populations are identified:

1. ***Labile cells***: These cells can proliferate normally. e.g. Epidermis, bone marrow cells.

2. ***Stable cells***: These cells proliferate when need arises. e.g. Liver, bone, cartilage, smooth muscle.

3. ***Permanent cells***: These cells have lost their ability to regenerate/ become hyperplastic. e.g. Neurons, cardiac and skeletal myocytes.

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HYPERTROPHY

It is increase in the size of the cells or the organ. The number of the cells does not increase. The hypertrophic changes are seen in the permanent/stable cells, e.g. Striated muscles are most commonly affected.

Types of hypertrophy:-

Physiologic hypertrophy :- It occurs following work or exercise/specific hormonal stimulus, example:

- Muscles in race and draft horses
- In pregnancy with increased estrogen stimulation hypertrophy of uterus occurs and in lactation mammary gland development occurs under the influence of prolactin and estrogen.

Compensatory hypertrophy:- It occurs due to the loss of a part of the organ or loss of one of the paired organs, With the continued haemodynamic overload, the compensatory mechanisms fail, resulting in the decompensation, then organ failure, example:

- One kidney undergoes hypertrophy with the loss of the other.
- Due to the obstruction of the lumen in hollow muscular organ (Right ventricular hypertrophy in pulmonary stenosis.

In microscopic view, the organ will be normal but the cells are bigger. The number and the size of the organelles will be increased due to the increase in the functional demand. e.g. smooth endoplasmic reticulum in hepatocytes are enlarged in chronic alcoholism and increase in the size of the Rough Endoplasmic Reticulum RER and

Golgi apparatus as a need for increased synthesis of proteins (e.g. collagen and immunoglobulin); the mitochondrial number varies with ATP requirements.

METAPLASIA

Metaplasia is the reversible change in which one adult cell type is replaced by another adult cell type of the same germinal layer. *It is also defined* as the transformation of one cell type to another cell type within the embryological limits.

Metaplasia may involve epithelial or mesenchyme tissue. In metaplasia, one type of epithelium may be converted into another, usually less special type or one type of mesenchyme tissue into another type.

Metaplasia is reversible, it is considered as a double edged sword, as it may lead to cancer. Metaplastic changes may be caused by chronic irritation, nutritional deficiency, neoplasm etc.

i. **Epithelial metaplasia**:- it is also recognized (Squamous metaplasia): - It may occur due to many reasons like Chronic irritation, Smoking , Nutritional deficiency etc.
   - ❖ Smoking like: In lung of smokers, ciliated cuboidal and columnar epithelia of airways are converted into stratified squamous epithelium.
   - ❖ Estrogenism like: Stratified squamous metaplasia of prostrate or urinary tract.
   - ❖ Calculi like: Calculi of salivary gland, biliary calculi, pancreas etc.
   - ❖ Nutritional deficiency like: Vitamin A deficiency produces squamous metaplasia of esophageal mucous glands of chicken, transitional epithelium of urinary bladder, cuboid and columnar epithelial cells lining the eye and salivary gland ducts.

ii. **Mesenchymal metaplasia**:- *example*

Osseous metaplasia in injured soft tissue. the metaplastic changes in mesenchymal tissue results in the formation of cartilage and bone in mixed mammary tumour of dogs and myeloid metaplasia leading to extra medullary haematopoesis in adult liver and spleen following injury to bone marrow.

DYSPLASIA

The term *dysplasia* is applied to the tissue malformed during maturation. There will be alteration in size, shape and orientation of tissue.

The condition is mainly affecting the epithelium, and the developmental defect involved complex interactions among three germinal layers, this changes are commonly found in the eye, skin, brain and skeletal system. For example:

Dysplasia when marked and in which all layers of stratified squamous epithelium are involved, it is called ‘preinvasive carcinoma, or ‘carcinoma in situ’.

Microscopic appearance in dysplasia, there will be loss of uniformity of cells and their architecture. It is characterized by pleomorphism (Change in the size and shape of cells), abnormally enlarged hyperchromic nuclei, increased mitosis and disorderly arranged cells. The condition is mild to moderate and reversed if the stimulus is removed.

PHOTOSENSITISATION

Photosensitisation is activation of photodynamic chemicals on the skin by long wave length UV or occasionally by visible light. Necrosis and edema are produced in the exposed areas of skin of animals, occur due to several factor included:-

Factors necessary for photosensitization in animals

- Oxygen
- Sunlight
- Photodynamic chemicals
- Skin devoid of hair or wool and lacking pigments

Photosensitisation divide into three types :-

Type I: Primary photosensitization.

Type II: Abnormal porphyrin metabolism associated photosensitivity.

Type III: Hepatogenous photosensitization.

Type I: Primary photosensitization :-

It is occurs when the photodynamic agent is either ingested, injected, or absorbed through the skin. The agent enters the systemic circulation in its native form, where it results in skin cell membrane damage after the animal is exposed to ultraviolet light.

Type II: **Abnormal porphyrin metabolism associated photosensitivity**.

The acute neurovisceral syndrome disorder of porphyrin metabolism occurs in humans and in cattle, due to accumulation of the neurotoxic [(porphyrin precursors), (delta aminolevulinic acid) , and (porphobilinogen)]. Due to decrease in porphobilinogen deaminase enzyme, resulted in the accumulation of porphyrin precursors in the body. Examples

○ Bovine congenital porphyria

○ Bovine haematopoetic protoporphyria .

Type III: **Hepatogenous photosensitization** :-

Hepatogenous photosensitization is caused by impaired hepatic capacity to excrete phylloerythrin derived from chlorophyll degradation in the alimentary tract, mainly affecting herbivores. This type most frequently seen in ruminants, it has also been reported in horses, pigs, and poultry.

Causes:

- Hepatocellular damage or injury (Toxic hepatitis due to Lantana camara, Tribulus terrestris, plants producing pyrrolizidine alkaloids, sporidesmins)
- Inherited hepatic defects
- Biliary obstruction
- Infection: Leptospirosis
- Chemicals: CCl4 poisoning

It is noted in hairless, non-pigmented skin exposed to sun light, erythema, edema, blisters, exudation, necrosis and sloughing of necrotic tissue.

in **Horses**: at (face, nose, distal extremities) ; in **Cattle**: at (teats, udder, perineum, nose) ; in **Sheep**: at (pinnae, eyelids, face, nose, coronary band, facial eczema or "swollen head").

Under microscopy there is coagulative necrosis of epidermis, sub epidermal vesiculation, swelling of endothelial cells, fibrinoid degeneration and thrombosis of blood vessels leading to edema. Secondary bacterial infection culminate in sloughing of epidermis and adnexae.