Pathology

3rd Stage
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Lecture 1

Cellular adaptation, cell injury and cell death

Cellular responses to stress and noxious stimuli

Cells actively interact with their environment, constantly adjusting their structure and function to accommodate changing demands and stresses.

The intracellular environment of cells is normally regulated such that it remains fairly constant, a steady state known as homeostasis (the ability of the cell to maintain a dynamically stable internal state).

When cells are exposed to stress or pathological stimuli, cells may adapt, or become injured reversibly and recover, or irreversibly damaged and die.

1.Adaptation: Aims to achieve a new steady state preserving viability and function.

2.Cell injury: Develops if the adaptive capability of the cell is exceeded or the external stress is inherently harmful. If the stress is mild or transient, injury is reversible, and cells return to their stable baseline; however, if the stress is severe, persistent and rapid in onset, it results in irreversible injury and cell death.

Cellular adaptations to stress

Adaptations are reversible changes in the number, size, phenotype, metabolic activity, or functions of cells in response to changes in their environment.

1.Physiologic adaptations (responses of cells to normal stimulation by hormones or endogenous chemical mediators or the demands of mechanical stress).

2.Pathologic adaptations (responses to stress that allow cells to modulate their structure and function and thus escape injury, but at the expense of normal function)

***Physiologic and pathologic adaptations can take several distinct forms:**

(Hypertrophy, atrophy, hyperplasia and metaplasia)

1.Hypertrophy: is an increase in the size of cells resulting in an increase in the size of the organ. In pure hypertrophy there are no new cells, only larger cells with increased amounts of structural proteins and organelles.

Hypertrophy can be physiologic or pathologic and is caused by increased functional demand or growth factor or hormonal stimulation.

***Physiologic hypertrophy E.g. Enlargement of the uterus during pregnancy due to estrogen stimulated smooth muscle hypertrophy and hyperplasia.**

E.g. Enlarged size of skeletal muscles in athletes in response to increased workload.

***Pathologic hypertrophy E.g. Left ventricular hypertrophy in systemic hypertension or aortic stenosis (to generate the required higher contractile force as a result of persistently increased workload)**

2. Hyperplasia: is an increase in the number of cells in an organ that results from increased proliferation, either of differentiated cells or progenitor cells. It occurs in tissues that contain cell populations capable of replication. In both physiologic and pathologic hyperplasia, cellular proliferation is stimulated by hormones or growth factors.

***Physiologic hyperplasia: E.g. Hormonal hyperplasia of the female breast at puberty and pregnancy. E.g. compensatory hyperplasia (residual tissue grows after removal or loss of part of organ), e.g. if part of liver resected, it can return to normal size.**

***Pathologic hyperplasia: E.g. Endometrial hyperplasia due to increased estrogenic stimulation (common cause of abnormal menstrual bleeding). E.g. Benign prostatic hyperplasia**

3. Atrophy: is shrinkage in the size of cells by the loss of cell substance. When a sufficient number of cells are involved, the entire tissue or organ is reduced in size. It results from decreased protein synthesis and increased protein degradation

Causes of atrophy:

1. Decreased workload (e.g., immobilization of a limb to permit healing of a fracture)

2. Loss of innervation (e.g. poliomyelitis and spinal cord injury)

3. Diminished blood supply (e.g. arterial obstruction by atherosclerosis)

4. Inadequate nutrition (e.g. starvation)

5. Loss of endocrine stimulation (e.g. postmenopausal endometrial atrophy)

6. Aging (senile atrophy)

4. Metaplasia: is a change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type (better able to withstand the adverse environment). It is thought to arise by the reprogramming of stem cells.

***Epithelial metaplasia: E.g. that occurs in respiratory epithelium of habitual cigarette smokers (normal ciliated columnar epithelial cells of the trachea and bronchi often are replaced by stratified squamous epithelium that may be able to survive chemicals in cigarette smoke). E.g. Bilharzial infection of urinary bladder can cause metaplasia of transitional epithelium into squamous epithelium.**

E.g. Metaplasia of stratified squamous epithelium of the lower esophagus to gastric or intestinal-type columnar epithelium, in case of chronic gastric reflux.

***Mesenchymal metaplasia: e.g. bone is occasionally formed in soft tissues, particularly in foci of injury.**

Stimuli that induce epithelial metaplastic changes, if persistent, may predispose to malignant transformation.

Cell injury

Causes of cell injury

1. Hypoxia and ischemia: Hypoxia (oxygen deficiency) and ischemia (reduced blood supply) , are among the most common causes of cell injury. Hypoxia affects aerobic oxidative respiration and the generation of ATP.

Causes of hypoxia:

a. The most common cause of hypoxia is ischemia due to arterial obstruction.

b. Inadequate oxygenation of the blood, as diseases of the lung

c. Reduction in oxygen-carrying capacity of blood (e.g. anemia, carbon monoxide poisoning).

2. Chemical agents: **E.g. air pollutants, insecticides, CO, cigarette smoke, ethanol, glucose, salt, water, oxygen and drugs. Many drugs in therapeutic doses can cause injury in a susceptible patient or if used excessively or inappropriately.**

3. Infectious agents: **All infectious pathogens (viruses, bacteria, fungi and parasites) can injure cells by e.g. producing toxins or stimulating harmful immune response.**

4. Immunologic reactions: **E.g. autoimmune reactions against individual's own tissues and allergic reactions against environmental substances.**

5. Genetic abnormalities: **Such as chromosomal abnormalities and specific gene mutations. E.g. *congenital malformations in Down syndrome or *single amino acid substitution of hemoglobin in sickle cell anemia, *deficiency of functional proteins, such as enzymes in inborn errors of metabolism.**

6. Nutritional imbalances: **Excess or deficiency e.g. *Protein–calorie insufficiency, *specific vitamin deficiencies, *excessive dietary fat intake (may result in obesity and e.g. type 2 diabetes mellitus and atherosclerosis).**

7. Physical agents: **Trauma, extremes of temperature, radiation, electric shock and sudden changes in atmospheric pressure.**

8. Aging: **Aging results in impairment of replicative and repair abilities of individual cells that will diminish ability to respond to damage and end in cell death.**

THANK YOU