

Cellular injury and adaptation

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Each cell in the body is devoted to carry specific function, which are dependent on the machinery and metabolic pathways present within the cell.

This functional specificity is genetically determined.

Normally the cells of the body are in equilibrium with the external environment.

They maintain their internal machinery in a dynamically stable and steady state; this is called **homeostasis** i.e. the supply of raw material (substrates) and O₂ are well coordinated with the production of the materials or jobs required.

In the presence of external disturbances that tend to upset the aforementioned fine equilibrium, changes within the cell occur through internal regulatory mechanisms that counteract the external changes.

In other words the cells are able to handle normal (physiological) and sometimes , abnormal (pathological) demands without get injured; to achieve this, a number of changes inside the cells occur that eventually lead to a new but altered steady state.

These induced changes are referred to as **adaptations.**

The aim of adaptations is to preserve cell viability i.e. prevent cell injury.

the increase in muscle mass (as in athletes or heavy mechanical workers) is a reflection of an increase in the size of individual muscle fibers so that when the muscle is subjected to excess workload, this will be shared by the thick and strong muscle fibers and thus each fiber is spared excess work; in other words escape injury.

This protective adaptation is referred to as **hypertrophy**.

Hypertrophy may be **physiological** as that of the uterus in pregnancy or **pathological** as that of the left ventricle in systemic hypertension.

Lt. ventricular hypertrophy



This is cardiac hypertrophy. The number of myocardial fibers never increases, but their size can increase in response to an increased workload, leading to the marked thickening of the left ventricle in this patient with hypertension. Note: normal Lt. ventricular wall thickness is 1.2 cm. to 1.5 cm

Uterine hypertrophy in pregnancy

On the left is a normal uterus showing the normal mass of smooth muscle in its wall. On the right is a uterus from a pregnant woman, in which the striking increase in mass of smooth muscle is evident. At cellular level this is due to both hyperplasia and hypertrophy of uterine smooth muscle.



Opposite to the above is the adaptive response

atrophy in which there is a decrease in the size and function of cells and consequently the size of the organ or tissue containing them.

Brain atrophy



A, Normal brain of a young adult. B, Atrophy of the brain in an 82-year-old male with atherosclerotic disease. Atrophy of the brain is due to aging and reduced blood supply. Note that loss of brain substance narrows the gyri and widens the sulci. The meninges have been stripped from the right half of each specimen to reveal the surface of the brain.

Cell injury occurs in two situations in respect to the adaptive responses:

1- The limits of the adaptive capacity are exceeded, as occurs with the persistence of the injurious agent.

Or

2- When there is not enough time for the adaptive responses to take place, as occurs with sudden attack by a severe injurious agent.

With the failure of the adaptive responses to counteract the effects of injurious agent, a sequence of events follows that are collectively known as cell injury.

Cell injury is divided into

1-Reversible

2-Irreversible

Reversible cell injury indicates that the cellular changes will regress and disappear when the injurious agent is removed ; the cells will return to normal, both morphologically and functionally.

Irreversible cell injury occurs when the injury persists or when it is severe from the outset.

Here the cell alterations reach the point of no return and progression to cell death is inevitable.

Let us take an example:

If the blood supply to a portion of the heart musculature is cut off for few minutes and then restored; the muscle cells will sustain reversible injury **i.e. *after restoration of blood it will recover and function normally (as in angina pectoris).***

But if cessation of blood continues for a longer period of time (for e.g. 60 minutes) and then restored , the myocardial cells in this instance sustain irreversible injury that terminate invariably to death.

So there is a spectrum of cellular changes in response to injurious agents ranging from adaptation to cell death.

Categorization of injurious agents (causes of cell injury)

Injurious agent can be categorized as follows

1. oxygen deprivation (hypoxia).
2. physical agents.
3. chemical agents.
4. infectious agents.
5. immunological reactions.
6. genetic derangement.
7. nutritional imbalances. 16

Hypoxia

This refers to a decrease in oxygen supply to the cells. It acts through interference with oxidative (aerobic) respiration of the cells.

Hypoxia results from

- 1-Loss of blood supply (ischemia), which is the **most** common cause & occurs when arterial flow is interfered with by e.g. narrowing of the lumen of an artery by atherosclerosis , thrombi or emboli.
- 2-Inadequate blood oxygenation due to for e.g. cardiac failure and/or respiratory failure.

3-Decrease in the oxygen-carrying capacity of blood e.g. anemia and carbon mono-oxide poisoning.

Depending on the severity and duration of the hypoxia, the cells may show one of the following changes.

I. Adaptive atrophy.

II. Injury.

III. Necrosis (the morphological expression of cell death).

For e.g. if the femoral artery is narrowed, the muscles of the leg shrink in size (atrophy).

This adaptive response continues till there is a balance between the metabolic needs of the cells (low in this instance) and the available oxygen supply.

More severe hypoxia (for e.g. when there is more severe narrowing or complete occlusion of the artery) will induce injury (reversible then irreversible that progresses to cell death).

Physical agents that include:

- Mechanical trauma
- Extreme heat
- Deep cold
- Radiation

Chemical agents that include :

- Simple chemicals such as glucose and salts in hypertonic concentration.
- Oxygen in high concentration.
- Poisons such as arsenic or cyanide.
- Air pollutants.
- Insecticides.
- Occupational exposure e.g. to asbestos.

- Social poisons such as alcohol, smoking, and narcotic drugs.

Infectious agents; these include :

Viruses, bacteria, fungi, and parasites.

Immunological reactions; these are primarily protective defense mechanisms against for e.g. infectious agents.

However, sometimes they are harmful and injurious; this occurs in two situations:-

1. Hypersensitivity reactions that are triggered for e.g. by drugs.
2. The immunological attack is directed to the person own antigens (self-antigens) leading to a group of diseases known as autoimmune diseases.

Genetic derangements are exemplified by the wide variety of hereditary diseases that ranges from those with gross chromosomal defects leading to severe congenital malformation e.g.

Down's syndrome, to those that are caused by a single amino acid substitution in the structure of hemoglobin leading to the synthesis of an abnormal one e.g. HbS in sickle cell anemia.

Nutritional imbalances

Deficiency: as of proteins-caloric malnutrition or vitamins deficiency etc.

Excess: as of lipids that leads to obesity with all its consequences including fatty change in cells and predisposition to atherosclerosis.

THANK YOU