Pathology

Sheet Slide

number

3

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Subcellular responses to injury

It involves changes that occur on cellular components or organelles;

1. Lysosomal Catabolism: lysosomes have digestive enzymes (hydrolases), once they are released, they form lysosomes and they begin to digest the cell. If the lysosome is released from a cell and it digests its own\same cell this is called **Autophage**, but if it digests foreign material or bodies this is called **Heterophage.**

! Not all materials that fuse with lysosome will be completely dissolved, there are some residual particles, and this residue can last forever. In addition, this residue can show that there was an injury and lyses in that region.

Ex. 1. Lipid Digestion; Lysosome begins to break lipid but not completely, it makes an internal pigment in the lipid called **Lipofuscin,** which can remain inside the cell for many years.

2. Carbon particles; Inhalation of carbon particles then these particles go to the lungs so alveolar macrophages engulf these particles for dissolution, but not completely, there is some indigestible material which can remain for years.

! Sometimes the residual particles don't affect the cell function they are just present without any effects.

2. Hypertrophy of SER:

Once the cell is exposed to injury, the SER undergoes hypertrophy, it increases in size, therefore its function will increase.

One of the most important functions of the SER is the release of P450 oxidase, this enzyme is responsible for converting active drugs to metabolites to reach therapeutic effect.

SER injury -> Hypertrophy -> P450 high -> so if I take a drug it will be broken-down rapidly, so its half-life would be very short -> I should take a larger dose.

3. Mitochondrial Alteration:

Mitochondria after injury becomes larger in size (mega) or smaller (micro).

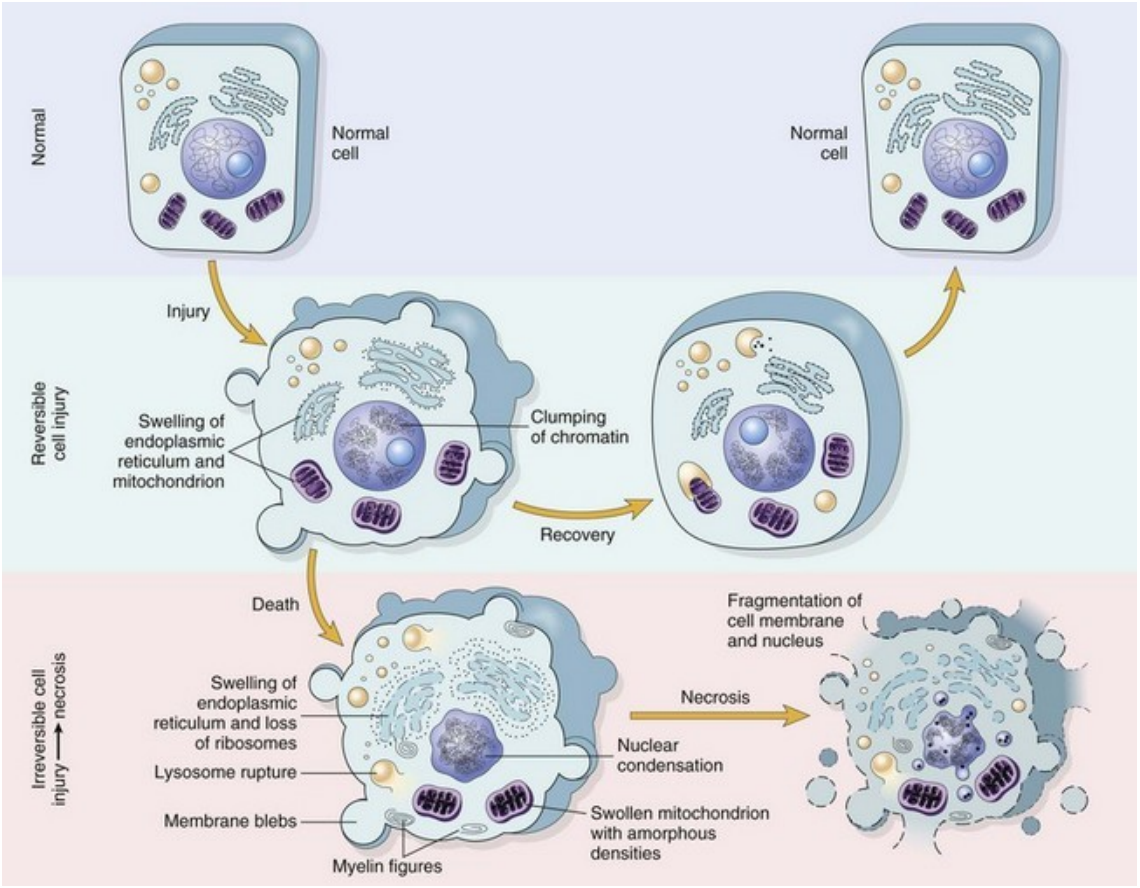
4. Cytoskeletal Abnormality:

When the protease enzyme damages proteins, the cytoskeleton is also damaged so microtubules (cilia and flagella) will be damaged which means that function will be inhibited.

Heat Shock Proteins:

Their function is to repair damaged proteins (misfolded proteins), if they fail to repair the damaged ones then Ubiquitin will repair them.

Reversible vs. Irreversible



Irreversible: leads to necrosis.

Reversible: if we neutralize the cause of injury the cell can go back to normal, or at least it rests in adaptation.

Morphological changes in <u>reversible</u>;

1. Cellular Swelling: ex. Liver's color is dark red; if H2O influxes then swelling occurs and its color will be light red, **Pallor of the organ.**
2. Fatty Change: in cells that deal with fat metabolism like liver and cardiac

Low protein synthesis -> High protein degradation -> Smaller amount of protein -> No transport outside the cell -> Accumulation of fats inside the cell

- High level of (Ca++) activates many enzymes, so Ca is a very essential and important factor in cell injury whether it was reversible or irreversible, but it's more essential in **irreversible.**

- Lipids have a negative charge, and Ca+ has a positive charge so there will be an attraction between the lipid from dead or dying cells and Ca, this process is called **dystrophic calcification, the presence of calcification in the cell indicates that there is a dying or dead cell.**

Necrosis

To observe the morphologic changes of a dead cell, the dead part of cell must be surrounded by living tissue, if it was surrounded by dead tissue then I won't observe any change.

Ex: if a patient died from myocardial infarction, within one hour we won't be able to find any changes in cardiac muscle; because morphologic changes in necrosis require hours to develop to see the change.

Types of Necrosis are determined by two factors:

- **Lysosomal enzymes:** if there is a large amount in the cell, they will damage the tissue and then the tissue will become liquid or semi liquid.
- **Protein Denaturation** which restricts the activity of enzymatic digestive.

In Lysosomal damage, some proteins will be released into blood vessels causing its level in the blood to be higher, this higher level is a signal that indicates that there is a tissue which is exposed to necrosis.

Changes in Nucleus and Cytoplasm: Cytoplasm becomes more pink, acidophilia\eosinophilia.

Nucleus undergoes 3 stages;

1- **Pyknosis:** The nucleus size will be decreased due to condensation of chromatids in one region.
2- **Karyorrhexis:** Activation of digestive enzyme due to increase in calcium level, fragmentation in nucleus by nuclease.
3- **Karyolysis:** Fragments will disappear by the DNase.

Types of Necrosis

Lysosomal Enzyme: 1 **Protein Denaturation: 2**

Necrosis is determined by those 2 factors according to which one overcomes the other.

"The number which I write after the type of necrosis will be the predominant one"

*** Coagulative necrosis:** 2, Ischemia in all organs except brain.

*** Liquefactive necrosis:** 1, and it can be: - Ischemia in the brain or –any type of ischemia + infection.

*** Caseous necrosis:** 1, this type is specific to Tuberculosis by mycobacterium TB, called caseous because tissue isn't liquid but a creasy-like metal.

*** Fatty necrosis:** 2, like coagulative but it occurs in adipose tissue (such as: subcutaneous tissue, breast, pancreas...)

*** Gangrenous necrosis:** 2, in extremities or intestines. Gangrene without infection -> Dry gangrene, Gangrene + Infection -> Wet gangrene

*** Fibrinoid necrosis:** 2, in blood vessel wall.