Pathology

Second Year - First Semester Course

Lecture 2

Sarah Al Sharie

Underlined sentences refer to anything that was mentioned in the record but not in the slides.

Cellular Responses and Adaptations to Stress

- Cells undergo certain changes to survive and that's the meaning of adaptation

Cellular Response to Stress

- Normal cell needs special conditions "environment" to function properly.
- Cells try to adapt to surrounding stimuli or changes → so it can survive.
- The normal condition or the standard environment that the cell looks to live in is called: (Homeo-stasis).
  - Homeo: home or environment.
  - Stasis: stable or standing still or fixed.
- The cell may undergo a lot of changes (stimulus) that may affect the homeostasis and that may lead:
  - the cell to adapt to the new environment (stress) and function properly
  - cell injury then cell death if the cell was unable to adapt to the change

  If the stimulus was injurious it can be reversible or irreversible:
  - the cell gets back to the normal state after the injurious stimulus is removed if the injury was reversible
  - cell injury then cell death if the injury was irreversible ***notice figure (2-1)***
- Things that might change around the cell: PH, Temp., Electrolytes level, Glucose.

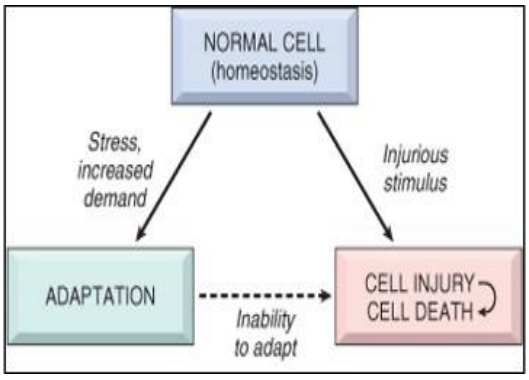

Figure (2-1)

Cellular Responses

1. Adaptation: the changes that cells undergo to survive and they are: hypertrophy, hyperplasia, atrophy, metaplasia.
2. Injury: reversible and irreversible (cell death).
3. Intracellular accumulation, calcification.
4. Cellular aging: during normal environment and normal conditions.

❖ Cellular adaptation:

- **Reversible** changes in size, number, phenotype, metabolic activity or function in response to changes in their environment.
- Adaptation can be both **physiologic (we want to happen/**under normal conditions**)** and/or pathologic **(disease** that led to adaptation**)**.

i. **Hypertrophy**: ***Notice figures (2-2) to (2-5) for examples of hypertrophy***

- **Hypertrophy** is an increase in **cell size** resulting in increase in the size of the organ
- Alone in non-dividing cells (e.g. cardiac myocytes or skeletal muscles).
- Coexisting with hyperplasia in dividing cells (skin or GI tract cells).
- Hypertrophy may be physiologic or pathologic.
- The increase in the cell size is caused by increased functional demand (workload) or stimulation by hormones or growth factors.
- Mechanism: increased production of cellular structural proteins and organelles.
- There is a limit for hypertrophy, if a cell exceeds the limit of hypertrophy it begins the phase of ischemia and necrosis.
- The most common stimulus for hypertrophy of muscle is increase workload (Bodybuilders)
- Subcellular organelle may undergo selective hypertrophy. (drugs causing smooth ER hypertrophy).

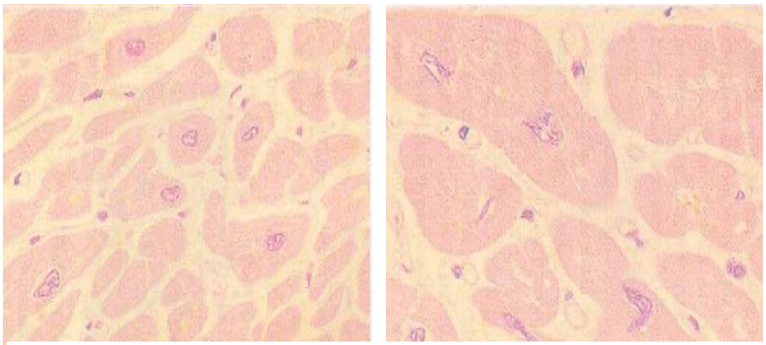

Figure (2-2), the left photo shows a standard muscle tissue, but the one on the right show a hypertrophic muscle tissue

Figure (2-3), Heart: left ventricle hypertrophy (Pathological increase in the thickness of the left ventricle).

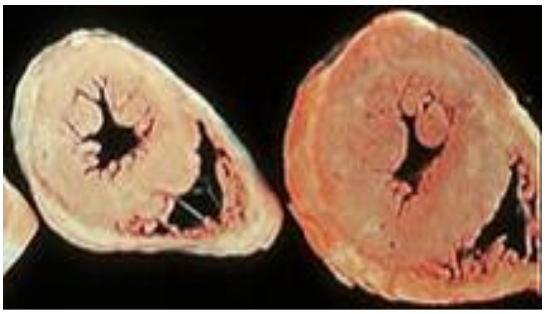

Figure (2-4), a normal heart on the left vs a hypertrophic heart on the right

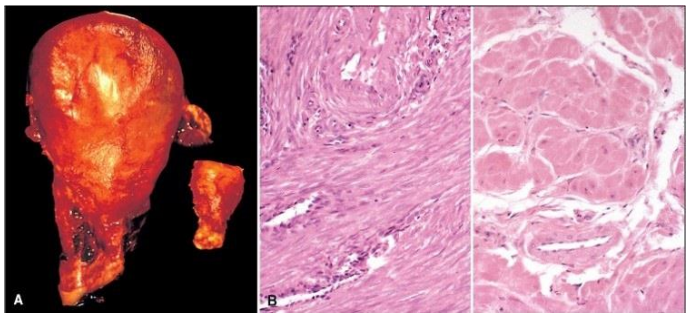

Figure (2-5), Hypertrophy in the uterus of pregnant women (physiological)

ii. **Hyperplasia**:

- Increased **number** of cells resulting in increased mass of the organ or tissue. (e.g. smooth muscles in the uterus)
- **Takes place in cells capable of dividing.**
- Mechanism:
  - it is the result of growth factor-driven proliferation of mature cells.
  - In some cases, by increased output of new cells from tissue stem cells (progenitor cells that are able to divide and differentiate to different types of cells like the bone marrow that provides all types of blood cells).

- Sometimes some tissues have both adaptation element going on at the same time like the uterus of pregnant women that undergo both hypertrophy and hypeplasia.

- There are both physiological and pathological hyperplasia.

- Physiological Hyperplasia (hormonally induced or compensatory), Examples:
  - Female breast in puberty & lactation (Hormonal).
  - Compensatory hyperplasia in partial liver resection.
  - In addition to the female uterus previous example.

- Pathological Hyperplasia
  - Hyperplasia of the endometrium (excessive hormone stimulation) and prostate hyperplasia, mostly happens during menopause and leads to endometrial cancer.
  - Prostate hyperplasia that leads to urinary symptoms. ***Notice figue (2-6)***
  - Infection by papillomavirus (skin warts).
  - Pathologic hyperplasia can be a fertile soil for development of malignancy.

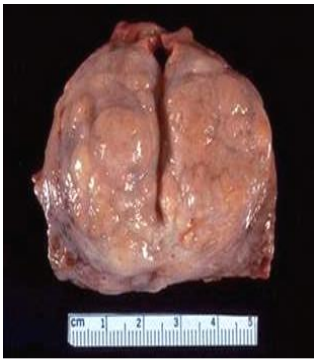

Figure (2-6), the normal size of prostate is 3 to 4Cm but in this photo its size is more than 5Cm

- Comparison between cell hypertrophy and hyperplasia. ***Notice figure (2-7)***

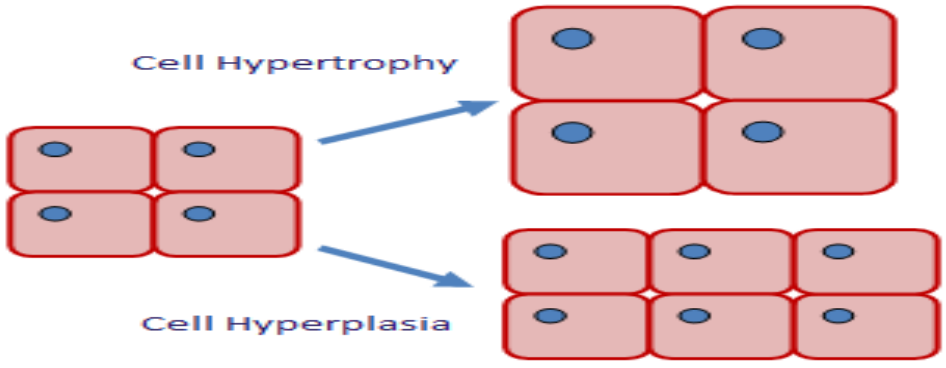

Figure (2-7)

iii. **Atrophy:** the opposite of hypertrophy and hyperplasia.

- Reduced size of cell, tissue or organ due to loss of cell substance (size and number). ***Notice figures (2-8) to (2-11)***
- Two types of atrophy physiologic and pathologic:
- Physiologic:
  - During normal development (Thyroglossal duct).
  - Involuting gravid uterus, after pregnancy when the uterus goes back to its normal size.

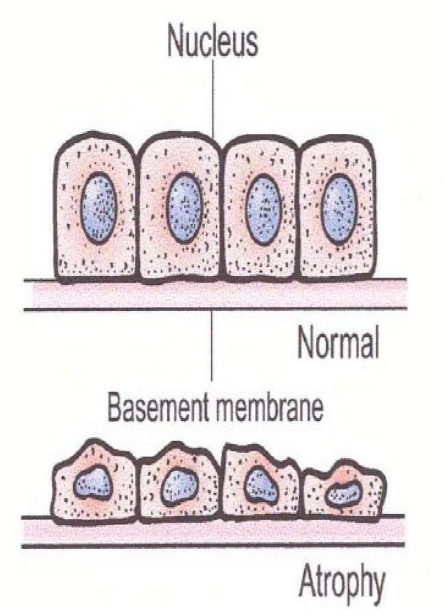

Figure (2-8)

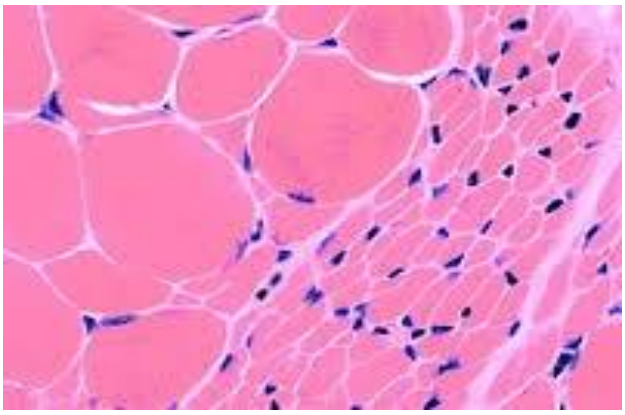

Figure (2-9), at the right side the figure shows the normal size of muscle cell and at the right side it shows the atrophic size of a muscle cell

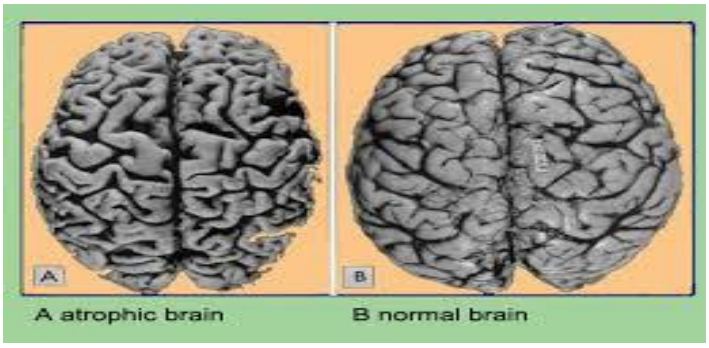

Figure (2-10), brain atrophy that happens with people who suffer from Alzheimer's disease

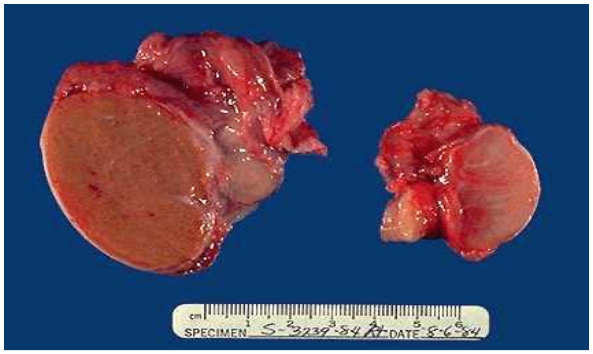

Figure (2-11), atrophy in the undescended testis (because it stays above its normal location so it becomes atrophic)

- Pathologic:
  - Decreased workload (Disuse atrophy), e.g paralysis in certain part of the body like the paralysis of one leg in the body because a muscle becomes atrophic if it weren't used
  - Loss of innervation (Denervation atrophy), e.g cut of nerves at a certain point
  - Diminished blood supply
  - Inadequate nutrition
  - Loss of endocrine stimulation (Loss of estrogen), e.g. in the post-menopausal women.

- Mechanisms of atrophy:
  - Decreased protein synthesis and increased protein degradation.
  - Degradation of cellular protein caused by Ubiquitin-proteasome pathway to control proteins and binds to unwanted proteins and degrade it: Ubiquitin ligases activated → attach small peptide ubiquitin to cellular protein → target these proteins for degradation in Proteasomes.
  - Increased Autophagy (self-eating): The starved cell eats its own component in an attempt to find nutrients and survive, mostly in ischemia cases.

iv. **Metaplasia:** change in the type of cells ***Notice figure (2-12) and (2-13) for examples***

- Metaplasia is a "**reversible**" change in which one differentiated cell type (epithelial or mesenchymal) is **replaced** by another cell type.
- New epithelium is better in dealing with the current stress or irritation.
  But at the same time:
- Persistence of factors causing metaplasia may lead to progression into malignant transformation (e.g. squamous lung cell carcinoma in smokers).
- Most common epithelial metaplasia is columnar to squamous (Respiratory tract).
- **Mechanism**: **reprogramming** of stem cells to differentiate along new pathway

- Signals generated by cytokines, growth factors and extracellular matrix ⟶ promote expression of genes toward a new differentiation.

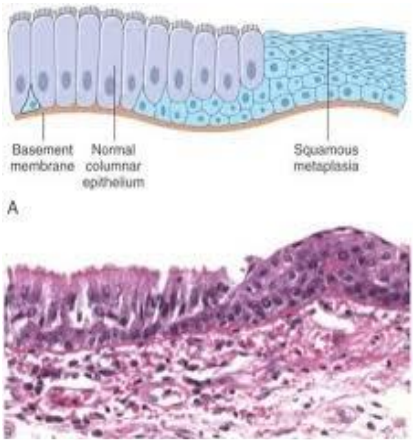

Figure (2-12), Replacement of ciliated columnar epithelium at the left side by stratified squamous epithelium (more resistant to the new condition) at the right side in the respiratory tract of a smoker.

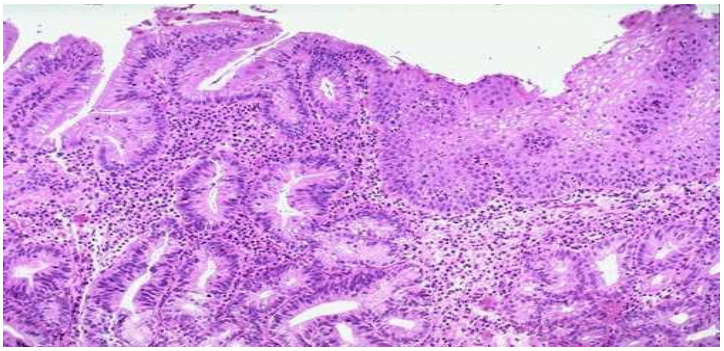

Figure (2-13), replacement of Squamous to Columnar epithelium in esophagus that can stand the type of acidity reflux (Barrett esophagus) and it's the source of especial adenocarcinoma.

Lecture 2 done.