SCBM341 - Cellular Adaptation

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Objectives

1. Definition and classification of cellular adaptation.

2. Compare and contrast the terms atrophy, hypertrophy, hyperplasia, metaplasia and dysplasia.

3. Definition and classification of pigment materials in tissues

4. Recognize exogenous and endogenous pigments that may be found in human tissues

5. Describe the simple tests to identify the major pigments
Morphology of Cellular Adaptation

1. Atrophy
2. Hypertrophy
3. Hyperplasia
4. Metaplasia
5. Dysplasia  Neoplasia

Intracellular storage  Accumulation or Pigmentation

1. Physiological – usually in response to a normal stimulation, ex: hormonal
2. Pathological – a response to a stress in the cells environment
Atrophy

- Greek, “Lack of food”
- Atrophy normally does not involve cell death.
- It is mostly decreased in a size and function of cell

82 y/o male

25 y/o male

Brain Atrophy
An aging process
Atrophy is found in the following condition: Decreased workload, Loss of innervation, Diminished blood supply, Inadequate nutrition, Loss of endocrine stimulation, Aging: Brown atrophy

Normal Muscle

Anorexia

Denervated Muscle

Brown atrophy

Splint for fractured bone
Atrophy

Mechanisms:

- Cell shrinkage (accelerated normal catabolic functions)
- Degradation of cellular components by lysosomal enzymes
Hypertrophy

- Increase in cell size accompanied with increased functional capacity.
- Mostly seen in tissues composed of cells which are unable to divide (skeletal and cardiac muscle)
- Also can be seen in cells that have the capacity to divide.
- 3 Types of cell
  - 1. Labile (continuously dividing) cells
  - 2. Stable cells
  - 3. Permanent (non-dividing) cells
Hypertrophy

1. Physiological (hormonal) hypertrophy:

* Pregnant uterus
* Hypertrophy of juvenile sex organs and organs associated with secondary sex characteristics
* Muscle hypertrophy in athletes by anabolic hormones

Myometrium during pregnancy
Hypertrophy

Skeletal Muscle - Normal vs. Hypertrophy

Normal

Hypertrophy
Hypertrophy

2. Pathological Hypertrophy

Hypertrophic heart in hypertension

Normal cardiac muscle

Hypertrophic cardiac muscle. Cells enlarged and irregular shape (same magnification as left)
Hyperplasia

1. Physiological Hyperplasia (hormonal)
   - Endometrium in the early phase of menstrual cycle (estrogen stimulation)
   - Hormonal Stimulation – normal increase in estrogen during puberty or pregnancy leading to glandular breast epithelial cell proliferation
   - Hyperplasia of red blood cell precursors in residence at high attitude (2° polycythemia)

Endometrial hyperplasia in response to estrogen
Hyperplasia

2. Pathological Hyperplasia

- Gynecomastia – enlargement of male breast during treatment of prostate carcinoma with estrogen therapy
- Skin warts caused by papilloma virus

Nodular hyperplasia of the prostate gland
The Cell Cycle

Possible Site of Block Leading to Cell Hypertrophy

Possible Site of Block Leading to Cell Hyperplasia

Stimulated by Subtotal Hepatectomy Renal Tubular Necrosis Nephrectomy

Liver Kidney

Permanently Non-dividing Cells

Neurons, Normoblasts, Polymorphonuclear Leucocytes, Adult Myocardial Cells
Metaplasia

- Conversion of one differentiated cell type to another.
- Most common is replacement of glandular epithelium by a squamous one, *e.g.*, atrophic gastric gland in chronic irritation, and columnar epithelium of bronchus in chronic smoking.
- Metaplasia is fully reversible if the stimulus is removed *e.g.*, when one stops smoking the metaplastic epithelium returns to normal.
Metaplasia

Metaplasia -- reversible change in which one adult cell is *replaced* by another adult type

LARYNX: squamous metaplasia in a smoker’s bronchus
Squamous Metaplasia and CIS in Bronchus

Squamous Carcinoma *in situ* (arising from squamous metaplasia)

Squamous Metaplasia

Normal Glandular Lining
Dysplasia

Refers to disturbance of the normal appearance of the epithelium by

* Variation in size and shape of cell
* Enlargement, irregularity and hyperchromatism of the nucleus
* Disorderly arrangement of the cells within the epithelium

Dysplasia is strongly implicated as a precursor of cancer
Dysplasia -- abnormality in cell size, appearance, with or without a *disorganized* growth pattern.
Intracellular accumulations

1. Normal endogenous or exogenous substance is produced at normal rate, but *rate of metabolism is inadequate* to remove it e.g., fatty change in liver.
Intracellular accumulations

2. *Abnormal exogenous* substance is deposited and accumulates because the cell has no enzymatic machinery to degrade the substance *e.g.*, accumulations of carbon or silica particles.
Intracellular accumulations

3. Normal or abnormal substance accumulates because it cannot be metabolized due to genetic enzymatic defect in a specific metabolic pathway e.g., storage diseases.
Disorders of mineral and pigment metabolism

1. Accumulation of endogenous pigment
   1.1 Hemoglobin derived endogenous pigment
      - Hemosiderin
      - Hemozoin
   1.2 Non-hemoglobin derived endogenous pigment
      - Lipofuscin

2. Accumulation of exogenous pigment
   - Coal dust
   - Copper
   - Calcium
Hemosiderin

- Hemosiderin, a complex mixture of proteins and ferric ions, is faintly visible as shiny golden granules in unstained tissue sections.

- Using acid ferrocyanide, which forms a blue complex with stainable ferric ion ("Prussian blue").

- Excess hemosiderin eventually causes organ injury by generating free oxygen radicals. This leads to organ failure, which is called "hemochromatosis".
Hemosiderin

1. Localized hemosiderosis
   - Longstanding congestion (lungs, leg veins)
   - Repeated minor injury (shrapnel fragments, sports, etc.)

2. Generalized hemosiderosis
   - Many red cell transfusions without blood loss
   - Too much iron being absorbed by the gut
   - Longstanding hemolysis
   - Heavy drinking, Wine
   - Gross excess of ferrous iron in the diet "iron supplements"
   - Vitamin C abuse (extreme)
Hemosiderin: the brown coarsely granular material in macrophages in this alveolus as a result of the breakdown of RBC's and release of the iron in heme. The macrophages clear up this debris, which is eventually recycled.
Prussian blue - Liver: Hemosiderin in hepatocytes and Kupffer cells
Symptoms and signs of hemochromatosis

- Vertigo
- Hair loss
- Memory loss
- Heart degeneration (arrhythmias, cardiomyopathy)
- Bronze skin
- Hepatomegaly
- Elevated Liver Enzymes
- Cirrhosis
- Diabetes mellitus
- Testicular atrophy (decrease FSH/LH secretion)
- Arthritis
Hemoglobin

- This is a ferric iron pigment that looks like hemosiderin when unstained, but which does not exhibit the Prussian Blue reaction because the iron is sequestered by protein.
- It consists of polymerized heme with each iron atom joined to a carboxyl group on the next porphyrin unit.
- It is seen in RE cells in malaria; the plasmodia protect themselves from free iron-heme complex by converting it into this substance.
A fatal case of *P. falciparum* malaria (liver): malarial pigment within Kupffer cells (H&E x 400)
Lipofuscin (Lipochrome, “Fuscus” is Latin For Brown)

• Brown pigment (un-digestible residue of subcellular membranes) whose unsaturated lipids have been scrambled by free radicals.

• Lipofuscin is the "wear-and-tear pigment".

• Lipofuscin's an important component of the cores of extracellular Alzheimer's lesions.
Lipofuscin
Carbon dust

• Carbon particles enter our bodies in smoke and soot or as the pigment in tattoos.

• Carbon settles in macrophages, where it remains indefinitely.

• Carbon in the lungs and nearby lymph nodes is called "anthracosis".
• The black streaks seen between lobules of lung beneath the pleural surface are due to anthracotic pigment. This anthracosis of the lung is not harmful and comes from the carbonaceous material breathed in from dirty air typical of industrialized regions of the planet.
- Anthracotic pigment in macrophages in a hilar lymph node. It is nothing more than accumulation of carbon pigment from breathing dirty air. Smokers have the most pronounced anthracosis. The anthracotic pigment looks bad, but it causes no major organ dysfunction.
Carbon dust

Healthy Tissue

Healthy Tissue 90-year-old schoolteacher

Progressive massive fibrosis 40-year-old-miner
Wilson Disease in Copper Accumulation

- Copper builds up in the liver and injures liver tissue.
- Damage causes the liver to release the copper directly into the bloodstream.
- Copper buildup leads to damage in the kidneys, brain, and eyes.
- Neurological symptoms, liver failure, and death.

Samuel Alexander Kinnier Wilson
British Physician (1878-1937)
Loss of coordination and ability to move in WD patient
Wilson’s Disease

• Kayser-Fleischer ring (Grey-green or brownish-pigmented ring in the deep epithelial layers at the outer border of the cornea

Bernhard Kayser
German ophthalmologist
1869-1954

Bruno Fleischer
German ophthalmologist
1874-1965
WD

Liver
- Hepatomegaly
- Jaundice
- Acute hepatitis
- Fulminant hepatic failure
- Portal hypertension: bleeding varices
- Cirrhosis

Bone
- Arthritis
- Rickets

Haem
- Hemolysis

CNS
- Deterioration in school performance
- Behavioral changes
- Inco-ordination (handwriting deteriorates)
- Resting and intention tremors
- Dystonia
- Dysarthria
- Excessive salivation
- Mask-like facies
- Dysphagia

Renal
- Proximal renal tubular dysfunction

Cardiac

Eye
- Kayser Fleischer rings
Calcification

• Calcium salts are deposited (dark blue in H&E, special stains - Von Kossa)

• 1. Dystrophic Calcification = calcification that takes place locally, in the presence of normal overall calcium-phosphorus metabolism.

• While a necrotic cell whose mitochondria calcified may provide a nidus for stone-building, some texts suggest that only dead things calcify.
Dystrophic calcification in the wall of the stomach.

At the far left is an artery with calcification in its wall. There are also irregular bluish-purple deposits of calcium in the submucosa. Calcium is more likely to be deposited in tissues that are damaged.
Dystrophic calcification complicating atherosclerosis.

It is seen as well demarcated yellow areas in the centre of elevated atherosclerotic plaques (arrows).
Calcification

2. Metastatic Calcification "Metastatic" means "another place"

Here the serum calcium and/or phosphate ion concentration is already elevated for some reason

Healthy tissues calcify
White deposits of metastatic calcification in the heart.

White dots represent foci of calcification which is quite common in chronic pancreatitis.
REFERENCES