CELL INJURY AND CELL DEATH

Part 2

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CELLULAR ADAPTATIONS

ADAPTATION

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

PHYSIOLOGIC ADAPTATION

usually represent responses of cells to normal stimulation by hormones or endogenous chemical mediators (e.g., hormone-induced enlargement of the breast and uterus during pregnancy).

PATHOLOGIC ADAPTATION

responses to stress that allow cells to modulate their structure and function and thus escape injury.
CELLULAR ADAPTATIONS

• Hypertrophy
• Hyperplasia
• Atrophy
• Metaplasia
HYPERTROPHY

• Increased cell and organ size
• Often in response to increased workload
• Induced by growth factors produced in response to mechanical stress or other stimuli
• Occurs in tissues incapable of cell division
• Can either be a physiologic or pathologic adaptation
HYPERTROPHY: Physiologic

*The massive physiologic enlargement of the uterus during pregnancy occurs as a consequence of estrogen stimulated smooth muscle hypertrophy and smooth muscle hyperplasia.
HYPERTROPHY: Pathologic*

*Hypertrophy: caused by hypertension or aortic valve disease
HYPERPLASIA

• Increased cell numbers in response to hormones and other growth factors
• Occurs in tissues whose cells are able to divide or contain abundant tissue stem cells
• Can be physiologic or pathologic
HYPERPLASIA

- Increased cell numbers in response to hormones and other growth factors
- Occurs in tissues whose cells are able to divide or contain abundant tissue stem cells
- Can be physiologic or pathologic
- The hyperplastic process remains controlled; if the signals that initiate it abates, the hyperplasia disappears
PHYSIOLOGIC HYPERPLASIA

• **Hormonal Hyperplasia**
  • Occurs mainly in organs that depend on estrogen

  • e.g Exemplified by the proliferation of the glandular epithelium of the female breast at puberty and during pregnancy
PHYSIOLOGIC HYPERPLASIA

• **Compensatory Hyperplasia**
  • Residual tissue grows after removal or loss of part of an organ
  • e.g Compensatory Liver Hyperplasia*

*The liver undergoes cellular division after acute injury, resulting in new cells that restore liver function back to baseline. Approximately 75% of the liver can be acutely damaged or resected with seemingly full regeneration through hepatocyte division
PATHOLOGIC HYPERPLASIA

• An abnormal increase in cell division caused by excessive hormonal or growth factor stimulation
e.g Endometrial Hyperplasia*

• *Caused by the disturbed balance between estrogen and progesterone. After a normal menstrual period, there is a burst of uterine epithelial proliferation that is normally tightly regulated by stimulation through pituitary hormones and ovarian estrogen and by inhibition through progesterone.

• *Hyper-proliferation of the endometrium, usually in response to unopposed estrogen stimulation in the setting of polycystic ovary syndrome or exogenous administration of hormones. A typical endometrial hyperplasia may represent an early neoplastic process which can lead to endometrial adenocarcinoma.
ATROPHY

• Shrinkage in the size of the cell by the loss of cell substance
• Decreased cell and organ size
• As a result of decreased nutrient supply or disuse
• Associated with decreased synthesis of cellular building blocks and increased breakdown of cellular organelles
• Characterized by the combination of decreased activity of protein synthesis and increased protein degradation in cells
ATROPHY

- **Causes**
  - Decreased workload (e.g., immobilization of a limb to permit healing of a fracture)
  - Loss of innervation
  - Diminished blood supply
  - Inadequate nutrition
  - Loss of endocrine stimulation
  - Aging (senile atrophy)
Figure 1–4 Atrophy as seen in the brain. A, Normal brain of a young adult. B, Atrophy of the brain in an 82-year-old man 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 bottom half of each specimen to reveal the surface of the brain.
METAPLASIA

• Reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.
• Change in phenotype of differentiated cells, often in response to chronic irritation, that makes cells better able to withstand the stress
• Usually induced by altered differentiation pathway of tissue stem cells
• May result in reduced functions or increased propensity for malignant transformation
METAPLASIA: Epithelial Metaplasia

• Exemplified by the squamous change that occurs in the respiratory epithelium of habitual cigarette smokers
• The normal ciliated columnar epithelial cells of the trachea and bronchi are focally or widely replaced by stratified squamous epithelial cells. The rugged stratified squamous epithelium may be able to survive the noxious chemicals in cigarette smoke that the more fragile specialized epithelium would not tolerate. Although the metaplastic squamous epithelium has survival advantages, important protective mechanisms are lost, such as mucus secretion and ciliary clearance of particulate matter. Moreover, the influences that induce metaplastic change, if persistent, may predispose to malignant transformation of the epithelium.
Figure 1–5 Metaplasia of normal columnar (left) to squamous epithelium (right) in a bronchus, shown schematically (A) and histologically (B).
NECROSIS
Necrosis

- Type of cell death that is associated with loss of membrane integrity and leakage of cellular contents culminating in dissolution of cells
- A result from the degradative action of enzymes on lethally injured cells

Characterized by:
- Increased eosinophilia
- Nuclear shrinkage
- Fragmentation and dissolution
- Breakdown of plasma membrane and organellar membranes
- Abundant myelin figures
- Leakage and enzymatic digestion of cellular contents
Necrosis

- Coagulative Necrosis
- Liquefactive Necrosis
- Gangrenous Necrosis
- Caseous Necrosis
- Fat Necrosis
- Fibrinoid Necrosis
COAGULATIVE NECROSIS

• a form of necrosis in which the underlying tissue architecture is preserved for at least several days
• affected tissues take on a firm texture
• characteristic of infarcts (areas of ischemic necrosis) in all of the solid organs
• Characterized by the presence of eosinophilic, anucleate cells
COAGULATIVE NECROSIS

Figure 1–9 Coagulative necrosis. A, A wedge-shaped kidney infarct (yellow) with preservation of the outlines. B, Microscopic view of the edge of the infarct, with normal kidney (N) and necrotic cells in the infarct (I). The necrotic cells show preserved outlines with loss of nuclei, and an inflammatory infiltrate is present (difficult to discern at this magnification).
LIQUEFACTIVE NECROSIS

• seen in focal bacterial or, occasionally, fungal infections, because microbes stimulate the accumulation of inflammatory cells and the enzymes of leukocytes digest (“liquefy”) the tissue

• dead cells are completely digested, transforming the tissue into a liquid viscous mass

BACTERIA-CAUSED

• the material is frequently creamy yellow and is called pus
LIQUEFACTIVE NECROSIS

Figure 1–10 Liquefactive necrosis. An infarct in the brain showing dissolution of the tissue.
GANGRENOUS NECROSIS

• a distinctive pattern of cell death, the term is still commonly used in clinical practice
• refers to the condition of a limb, generally the lower leg, that has lost its blood supply and has undergone coagulative necrosis involving multiple tissue layers
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BACTERIA-CAUSED

coagulative necrosis is modified by the liquefactive action of the bacteria and the attracted leukocytes (resulting in so-called wet gangrene).
CASEOUS NECROSIS

• Caseous means “cheese-like,” referring to the friable yellow-white appearance of the area of necrosis
• Encountered most often in foci of tuberculous infection
• The area of caseous necrosis is often enclosed within a distinctive inflammatory border; this appearance is characteristic of a focus of inflammation known as a **granuloma**
CASEOUS NECROSIS

Figure 1-11 Caseous necrosis. Tuberculosis of the lung, with a large area of caseous necrosis containing yellow-white (cheesy) debris.
FAT NECROSIS

• refers to focal areas of fat destruction, typically resulting from release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity

• Released fatty acids combine with Calcium to produce grossly visible chalky white areas (fat saponification)
Figure 1–12 Fat necrosis in acute pancreatitis. The areas of white chalky deposits represent foci of fat necrosis with calcium soap formation (saponification) at sites of lipid breakdown in the mesentery.
FIBRINOID NECROSIS

• a special form of necrosis, visible by light microscopy, usually in immune reactions in which complexes of antigens and antibodies are deposited in the walls of arteries

• These deposited immune complexes together with fibrin that has leaked out of vessels, produce a bright pink and amorphous appearance on H&E preparations called fibrinoid
FIBRINOID NECROSIS

Figure 1–13 Fibrinoid necrosis in an artery in a patient with polyarteritis nodosa. The wall of the artery shows a circumferential bright pink area of necrosis with protein deposition and inflammation.
INTRACELLULAR ACCUMULATIONS
INTRACELLULAR ACCUMULATIONS

• Inadequate removal of a normal substance secondary to defects in mechanisms of packaging and transport
INTRACELLULAR ACCUMULATIONS

• Accumulation of an abnormal endogenous substance as a result of genetic or acquired defects in its folding, packaging, transport, or secretion
INTRACELLULAR ACCUMULATIONS

• Failure to degrade a metabolite due to inherited enzyme deficiencies.

Lysosomal storage disease: accumulation of endogenous materials
INTRACELLULAR ACCUMULATIONS

• Deposition and accumulation of an abnormal exogenous substance when the cell has neither the enzymatic machinery to degrade the substance nor the ability to transport it to other sites
END