CHAPTER OVERVIEW

Section 14: Cellular Toxicology

Learning Objectives

After completing this lesson, you will be able to:

- Explain cellular adaptation.
- Identify four possible endpoints to toxic damage to cells and tissues.
- Define commonly used cancer terms.
- Describe the phases of and genetic activity associated with carcinogenesis.
- Identify mechanisms and potential outcomes of neurotoxicity.

In this section...

Topics include:

Section 14: Key Points

What We've Covered

This section made the following main points:

- To maintain homeostasis, cells and tissues undergo:
  - Physiological adaptation, which is beneficial in nature — for example, increased skeletal muscle cells in athletes.
  - Pathological adaptation, which is detrimental — for example, cellular changes in people who smoke cigarettes.
- Specific types of adaptation include:
  - Atrophy — a decrease in the size of cells.
  - Hypertrophy — an increase in the size of individual cells.
  - Hyperplasia — an increase in the number of cells in a tissue.
  - Metaplasia — the conversion from one type of mature cell to another type.
  - Dysplasia — abnormal cell changes or deranged cell growth.
  - Anaplasia — cells that are undifferentiated.
  - Neoplasia — new growth of tissue.
- Most toxic effects, especially due to xenobiotics, are due to specific biochemical interactions without causing recognizable damage to a cell or its organelles. Cellular or biochemical toxicity leads to:
  - The tissue being completely repaired and returned to normal.
  - The tissue being incompletely repaired but capable of functioning with reduced capacity.
  - Death of the organism or complete loss of a tissue or organ.
  - Neoplasm or cancers.
- Tumors are either:

- Benign — similar to the cell of origin, slow-growing, and usually without systemic effects.
- Malignant — dissimilar from the cell of origin, rapid-growing, and commonly with systemic effects and life-threatening. Most malignant tumors are either:
  - Carcinomas — arising in epithelium, the most common form of cancer, usually spread in the lymphatic system.
  - Sarcomas — arising in connective or muscle tissue, usually spread by the blood stream.

- Carcinogenesis is a multi-step, multi-factorial genetic disease consisting of at least three main phases:
  1. Initiation — irreversible alteration of the DNA (mutation) of a normal cell.
  2. Promotion/Conversion — promoters enhance further development of the initiated cells, often influencing further expression of the mutated DNA such that the initiated cell proliferates and progresses further.
  3. Progression — development of the initiated cell into a biologically malignant cell population, often with metastasis to other areas of the body.
- Regulatory genes control the activity of structural genes and direct the proliferation process of the cell. Regulatory genes that play roles in carcinogenesis include:
  - Proto-oncogenes — normal cellular genes that encode and instruct the production of regulatory proteins and growth factors within a cell or its membrane.
  - Oncogenes — altered or misdirected proto-oncogenes with the ability to direct the production of proteins within the cell that change or transform the normal cell into a neoplastic cell.
  - Tumor suppressor genes (anti-oncogenes) — present in normal cells and counteract and change the proto-oncogenes and altered proteins, preventing a cell with damaged DNA from proliferating and evolving into an uncontrolled growth.
    - The p53 gene normally halts cell division, stimulates repair enzymes, and if necessary, commands the mutated cell to self-destruct
    - p53 is the most frequently altered in human tumors and is incapable of its defense mechanisms
- Toxic damage to the nervous system is divided into three categories:
  1. Damage to sensory receptors and sensory neurons impacting the sensory functions.
  2. Damage to motor neurons causing muscular weakness and paralysis.
  3. Interneuronal damage causing learning deficiencies, memory loss, incoordination, and emotional conditions.
