3.4: Organ Specific Toxic Effects

Organ Specific Toxic Effects

Toxic effects that pertain to specific organs and organ systems include:

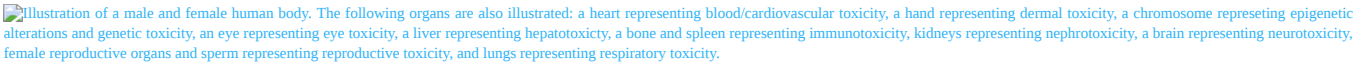

Figure 3.4.1. Organ-specific toxic effects pertain to specific organs and organ systems
(Image Source: Adapted from iStock Photos, ©)

Blood and Cardiovascular/Cardiac Toxicity

Blood and Cardiovascular/Cardiac Toxicity results from xenobiotics acting directly on cells in circulating blood, bone marrow, and the heart. Examples of blood and cardiovascular/cardiac toxicity are:

- Hypoxia due to carbon monoxide binding of hemoglobin preventing transport of oxygen.
- Decrease in circulating leukocytes due to chloramphenicol damage to bone marrow cells.
- Leukemia due to benzene damage of bone marrow cells.
- Arteriosclerosis due to cholesterol accumulation in arteries and veins.
- Death of normal cells in and around the heart as a result of exposure to **drugs used to treat cancer**.

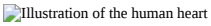

Figure 3.4.2. Heart cells can be damaged by exposure to certain drugs (Image Source: iStock Photos, ©)

Dermal Toxicity

Dermal Toxicity can occur when a toxicant comes into direct contact with the skin or is distributed to it internally. Effects range from mild irritation to severe changes, such as irreversible damage, hypersensitivity, and skin cancer. Examples of dermal toxicity include:

- Dermal irritation from skin exposure to gasoline.
- Dermal corrosion from skin exposure to sodium hydroxide (lye).
- Dermal itching, irritation, and sometimes painful **rash** from poison ivy, caused by **urushiol**.
- Skin cancer due to ingestion of arsenic or skin exposure to UV light.

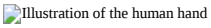

Figure 3.4.3. Hand (Image Source: iStock Photos, ©)

Epigenetic Alterations

Epigenetics is an emerging area in toxicology. In the field of genetics, epigenetics involves studying how external or environmental factors can switch genes on and off and change the programming of cells.

More specifically, epigenetics refers to stable changes in the programming of gene expression which can alter the phenotype without changing the DNA sequence (genotype). Epigenetic modifications include DNA methylation, covalent modifications of histone tails, and regulation by non-coding RNAs, among others.

Toxicants are examples of factors that can alter genetic programming.

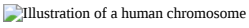

Figure 3.4.4. Chromosome, which contains DNA (Image Source: iStock Photos, ©)

In the past, toxicology studies have assessed toxicity without measuring its impact at the level where gene expression occurs. Exogenous agents could cause long-term toxicity that continues after the initial exposure has disappeared, and such toxicities remain undetected by current screening methods. Thus, a current challenge in toxicology is to **develop screening methods that would detect epigenetic alterations** caused by toxicants.

Research is being done to assess epigenetic changes caused by toxicants. For example, the **National Institutes of Health (NIH) National Institute of Environmental Health Sciences (NIEHS) Environmental Epigenetics program** provides funding for a variety of research projects that use state-of-the-art technologies to analyze epigenetic changes caused by environmental exposures. NIEHS-supported researchers use animals, cell cultures, and human tissue samples to pinpoint how epigenetic changes can lead to harmful health effects and can potentially be passed down to the next generation.

Eye Toxicity

Eye Toxicity results from direct contact with or internal distribution to the eye. Because the cornea and conjunctiva are directly exposed to toxicants, conjunctivitis and corneal erosion may be observed following occupational exposure to chemicals. Many household items can cause conjunctivitis. Chemicals in the circulatory system can distribute to the eye and cause corneal opacity, cataracts, and retinal and optic nerve damage. For example:

- Acids and strong alkalis may cause severe corneal corrosion.
- Corticosteroids may cause cataracts.
- Methanol (wood alcohol) may damage the optic nerve.

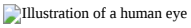

Figure 3.4.5. *Eye (Image Source: iStock Photos, ©)*

Hepatotoxicity

Hepatotoxicity is toxicity to the liver, bile duct, and gall bladder. Because of its extensive blood supply and significant role in metabolism, the liver is particularly susceptible to xenobiotics Thus, it is exposed to high doses of the toxicant or its toxic metabolites. The primary forms of hepatotoxicity are:

- **Steatosis** — lipid accumulation in the hepatocytes.
- **Chemical hepatitis** — inflammation of the liver.
- **Hepatic necrosis** — death of the hepatocytes.
- **Intrahepatic cholestasis** — backup of bile salts into the liver cells.
- **Hepatic cancer** — cancer of the liver.
- **Cirrhosis** — chronic fibrosis, often due to alcohol.
- **Hypersensitivity** — immune reaction resulting in hepatic necrosis.

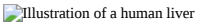

Figure 3.4.6. *Liver (Image Source: iStock Photos, ©)*

Related Resource: LiverTox®

Immunotoxicity

Immunotoxicity is toxicity of the immune system. It can take several forms:

- Hypersensitivity (allergy and autoimmunity)
- Immunodeficiency
- Uncontrolled proliferation (leukemia and lymphoma)

The normal function of the immune system is to recognize and defend against foreign invaders. This is accomplished by production of cells that engulf and destroy the invaders or by antibodies that inactivate foreign material. Examples include:

- Contact dermatitis due to exposure to poison ivy.
- Systemic lupus erythematosus ("lupus") in workers exposed to hydrazine.
- Immunosuppression by cocaine.
- Leukemia induced by benzene.

Figure 3.4.7. *Bone (which contains bone marrow) and spleen, both components of the immune system, which recognizes and defends against foreign invaders*
(Image Source: iStock Photos, ©)

Nephrotoxicity

The kidney is highly susceptible to toxicants because a high volume of blood flows through the organ and it filters large amounts of toxins which can concentrate in the kidney tubules.

Nephrotoxicity is toxicity to the kidneys. It can result in systemic toxicity causing:

- Decreased ability to excrete body wastes.
- Inability to maintain body fluid and electrolyte balance.

- Decreased synthesis of essential hormones (for example, erythropoietin, which increases the rate of blood cell production).

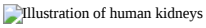

Figure 3.4.8. *Kidneys (Image Source: iStock Photos, ©)*

Neurotoxicity

Neurotoxicity represents toxicant damage to cells of the central nervous system (brain and spinal cord) and the peripheral nervous system (nerves outside the CNS). The primary types of neurotoxicity are:

- Neuronopathies (neuron injury)
- Axonopathies (axon injury)
- Demyelination (loss of axon insulation)
- Interference with neurotransmission

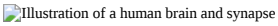

Figure 3.4.9. *Brain and synapse are susceptible to toxicant damage (Image Source: iStock Photos, ©)*

Reproductive Toxicity

Reproductive Toxicity involves toxicant damage to either the male or female reproductive system. Toxic effects may cause:

- Decreased libido and impotence.
- Infertility.
- Interrupted pregnancy (abortion, fetal death, or premature delivery).
- Infant death or childhood morbidity.
- Altered sex ratio and multiple births.
- Chromosome abnormalities and birth defects.
- Childhood cancer.

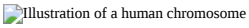

Figure 3.4.10. *Female reproductive organs (left); male and female germ cells (right) (Image Source: iStock Photos, ©)*

Respiratory Toxicity

Respiratory Toxicity relates to effects on the upper respiratory system (nose, pharynx, larynx, and trachea) and the lower respiratory system (bronchi, bronchioles, and lung alveoli). The primary types of respiratory toxicity are:

- Pulmonary irritation
- Asthma/bronchitis
- Reactive airway disease
- Emphysema
- Allergic alveolitis
- Fibrotic lung disease
- Pneumoconiosis
- Lung cancer

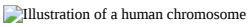

Figure 3.4.11. *Lungs (Image Source: iStock Photos, ©)*

Knowledge Check

Knowledge Check

1. Toxic effects are primarily categorized into two general types:

- ◯ Systemic or organ-specific effects
- ◯ Carcinogenic or teratogenic effects
- ◯ Hepatic or nephrotoxic effects

Answer

Systemic or organ-specific effects - **This is the correct answer.**
Toxic effects are broadly categorized as either systemic or organ- specific effects.

2. What is the main difference between acute and chronic toxicity?

- ◯ Different organs are involved
- ◯ Acute toxicity occurs only after a single dose, whereas chronic toxicity occurs with multiple doses
- ◯ Acute toxicity appears within hours or days of an exposure, whereas chronic toxicity takes many months or years to become a recognizable clinical disease
- ◯ Acute toxicity is less likely to lead to death than is chronic toxicity

Answer

Acute toxicity appears within hours or days of an exposure, whereas chronic toxicity takes many months or years to become a recognizable clinical disease - **This is the correct answer.**

3. Police respond to a 911 call in which two people are found dead in an enclosed bedroom heated by an unvented kerosene stove. There was no sign of trauma or violence. A likely cause of death is:

- ◯ Excess oxygen generated by the combustion of kerosene
- ◯ Acute toxicity due to uncombusted kerosene fumes
- ◯ Acute toxicity due to carbon monoxide poisoning

Answer

Acute toxicity due to carbon monoxide poisoning - **This is the correct answer.**
The victims most likely died as a result of acute toxicity from exposure to carbon monoxide.

4. Genetic toxicity can result in:

- ◯ Gene mutation
- ◯ Changes in the structure and/or number of chromosomes
- ◯ Epigenetic alterations
- ◯ All of the above

Answer

All of the above - **This is the correct answer.**
Genetic toxicity can cause gene mutations, changes in chromosome structure (aberration), increases or decreases in the number of chromosomes (aneuploidy or polyploidy), and changes to genetic programming (epigenetic alterations).