



Centurion
UNIVERSITY

*Shaping Lives...
Empowering Communities!*

PRESENTATION ON

SYSTEMIC TOXICOLOGY

FOR THE SUBJECT

CUTM1648 CONCEPT OF TOXICOLOGY

SCHOOL OF FORENSIC SCIENCES
BHUBANESHWAR CAMPUS

Light-curing



Cavity



Enamel



SYSTEMIC TOXICOLOGY

Local Toxicity



Good Form



DEFINITION

- Systemic toxicology deals with adverse effect of chemical on a particular system of organism
- NS, CNS, immune system.
- Toxic effects are generally categorized according to the site of the toxic effect. In some cases, the effect may occur at only one site. This site is termed the specific target organ
- In other cases, toxic effects may occur at multiple sites. This is known as systemic toxicity. A systemic toxin is one that affects the entire body or many organs rather than a specific site.
- For example, potassium cyanide is a systemic toxicant in that it affects virtually every cell and organ in the body by interfering with the cell's ability to utilize oxygen.

TYPES

- Following are types of systemic toxicity:
 - I. Acute Toxicity
 - II. Sub chronic Toxicity
 - III. Chronic Toxicity
 - IV. Carcinogenicity
 - V. Developmental Toxicity
 - VI. Genetic Toxicity (somatic cells)

ACUTE TOXICITY



Figure 1. Faulty gas heaters can emit toxic carbon monoxide

- Acute toxicity occurs almost immediately (hours/days) after an exposure.
- An acute exposure is usually a single dose or a series of doses received within a 24 hour period.
- Death is a major concern in cases of acute exposures.
- Examples are: - In 1989, 5,000 people died and 30,000 were permanently disabled due to exposure to methyl isocyanate from an industrial accident in Bhopal, India. - Many people die each year from inhaling carbon monoxide from faulty heaters.
- Non-lethal acute effects may also occur, e.g., convulsions and respiratory irritation

SUB CHRONIC TOXICITY

- Sub chronic toxicity results from repeated exposure for several weeks or months.
- This is a common human exposure pattern for some pharmaceuticals and environmental agents.
- Examples are: - Ingestion of coumadin tablets (blood thinners) for several weeks as a treatment for venous thrombosis can cause internal bleeding.
- Workplace exposure to lead over a period of several weeks can result in anemia.



Figure 2. Warfarin Tablets (left); old lead pipes (right)

CHRONIC TOXICITY



- Chronic Toxicity Chronic toxicity represents cumulative damage to specific organ systems and takes many months or years to become a recognizable clinical disease.
- Damage due to subclinical individual exposures may go unnoticed. With repeated exposures or long-term continual exposure, the damage from these subclinical exposures slowly builds-up (cumulative damage) until the damage exceeds the threshold for chronic toxicity.
- Ultimately, the damage becomes so severe that the organ can no longer function normally and a variety of chronic toxic effects may result.
- Examples of chronic toxic affects are: - cirrhosis in alcoholics who have ingested ethanol for several years; - chronic kidney disease in workmen with several years exposure to lead; - chronic bronchitis in long-term cigarette smokers; - pulmonary fibrosis in coal miners (black lung disease).

DEVELOPMENTAL TOXICITY

- Developmental Toxicity pertains to adverse toxic effects to the developing embryo or fetus.
- This can result from toxicant exposure to either parent before conception or to the mother and her developing embryo-fetus.
- The three basic types of developmental toxicity are :
 - i. Embryolethality- failure to conceive, spontaneous abortion, or stillbirth.
 - ii. Embryotoxicity — growth retardation or delayed growth of specific organ systems.
 - iii. Teratogenicity — irreversible conditions that leave permanent birth defects in live offspring, such as cleft palate or missing limbs.

Chemicals cause developmental toxicity by two methods.

1. They can act directly on cells of the embryo causing cell death or cell damage, leading to abnormal organ development.
2. A chemical might also induce a mutation in a parent's germ cell which is transmitted to the fertilized ovum. Some mutated fertilized ova develop into abnormal embryos.



GENETIC TOXICITY

- Genetic Toxicity results from damage to DNA and altered genetic expression. This process is known as mutagenesis.
- The genetic change is referred to as a mutation and the agent causing the change as a mutagen.
- There are three types of genetic change :
 1. Gene mutation — change in DNA sequence within a gene.
 2. Chromosome aberration — changes in the chromosome structure.
 3. Aneuploidy or polyploidy — increase or decrease in number of chromosomes.
- If the mutation occurs in a germ cell the effect is heritable. There is no effect on the exposed person; rather the effect is passed on to future generations.
- If the mutation occurs in a somatic cell, it can cause altered cell growth (e.g. cancer) or cell death (e.g. teratogenesis) in the exposed p

CARCINOGENICITY

Carcinogenicity is a complex multistage process of abnormal cell growth and differentiation that can lead to cancer. The two stages of carcinogenicity are:

1. Initiation — a normal cell undergoes irreversible changes.
2. Promotion — initiated cells are stimulated to progress to cancer.

Chemicals can act as initiators or promoters.

The initial transformation that causes normal cells to undergo irreversible changes results from the mutation of the cellular genes that control normal cell functions. The mutation may lead to abnormal cell growth. It may involve a loss of suppresser genes that usually restrict abnormal cell growth. Many other factors are involved, such as growth factors, immune suppression, and hormones.

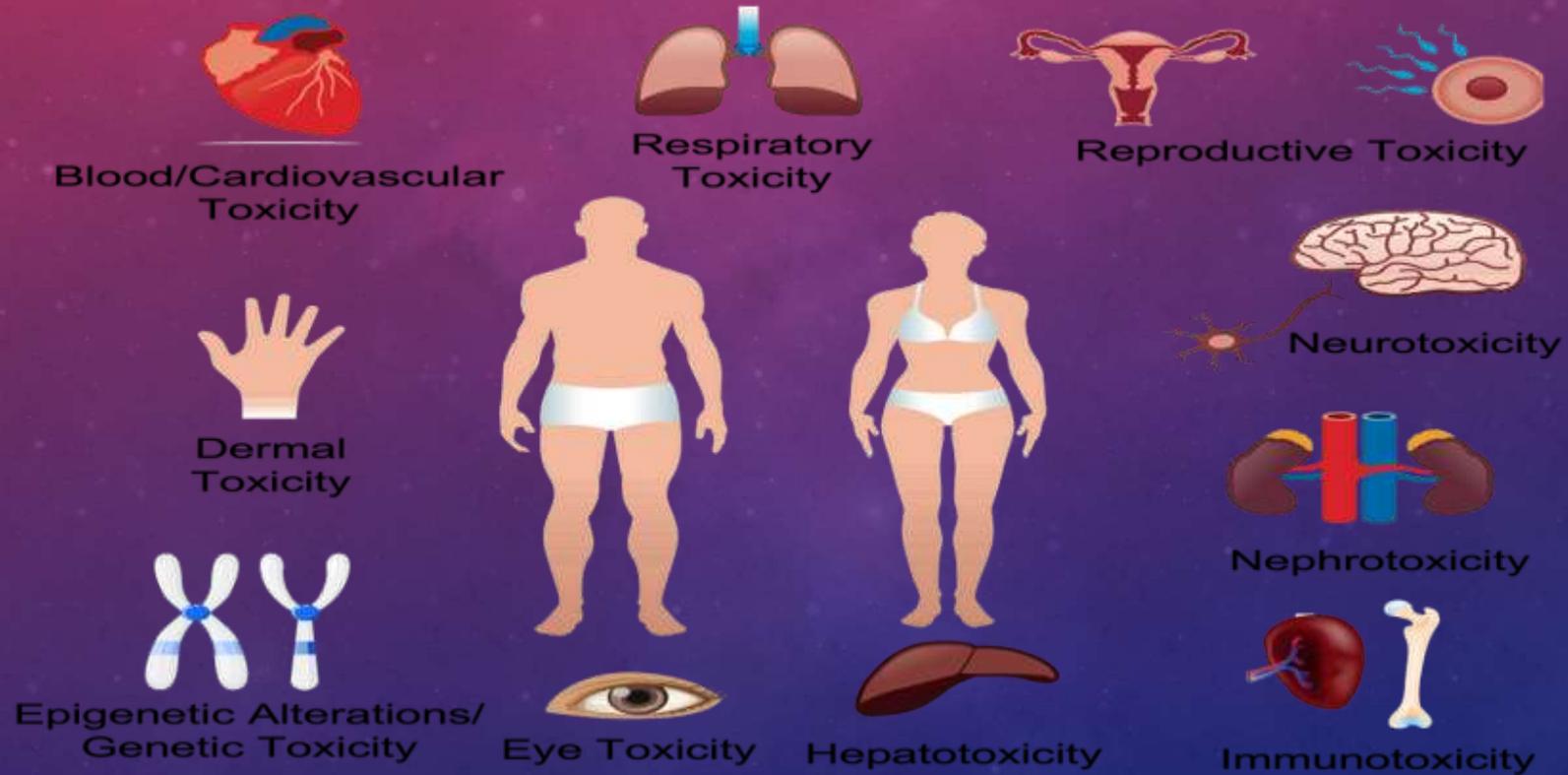
A tumor (neoplasm) is simply an uncontrolled growth of cells:

Benign tumors grow at the site of origin; do not invade adjacent tissues or metastasize; and generally are treatable.

Malignant tumors (cancer) invade adjacent tissues or migrate to distant sites (metastasis). They are more difficult to treat and often cause death.

ORGAN-SPECIFIC TOXIC EFFECTS

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



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.

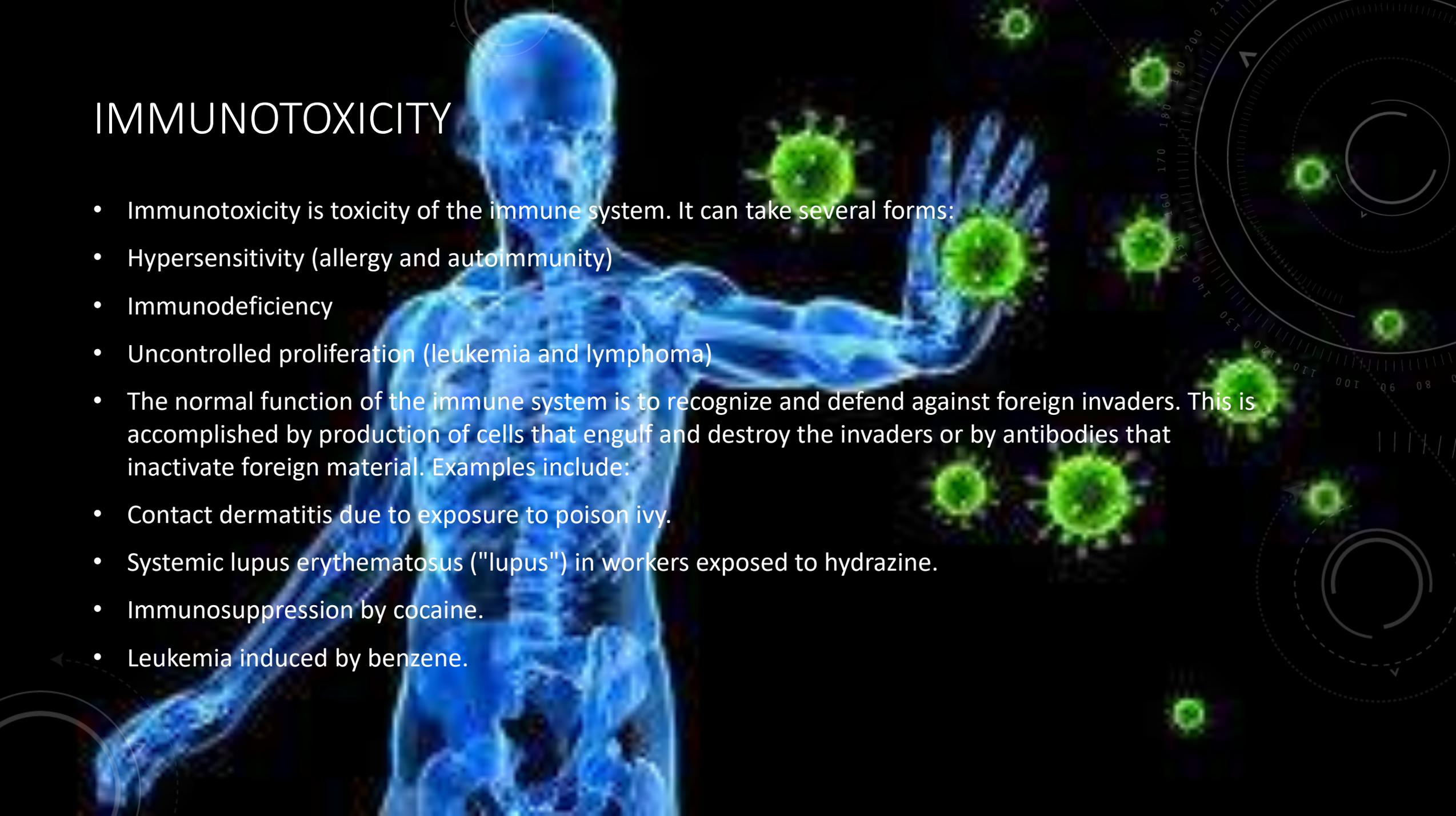
DERMAL TOXICITY

- 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.

HEPATOTOXICITY

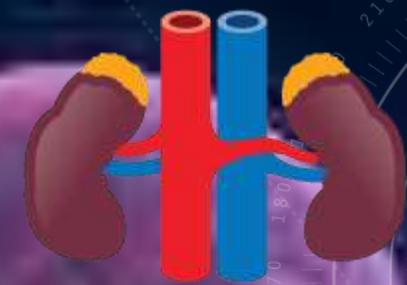
- Hepatotoxicity is toxicity to the liver, bile duct, and gall bladder. Because of its extensive blood supply and significant role in metabolism, the liver is particularly susceptible to xenobiotics. Thus, it is exposed to high doses of the toxicant or its toxic metabolites. The primary forms of hepatotoxicity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

IMMUNOTOXICITY

The background features a blue-tinted human silhouette with glowing green virus-like particles scattered around. On the right side, there are circular data graphics with numerical scales and arrows, suggesting a scientific or medical context.

- 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.

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).

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

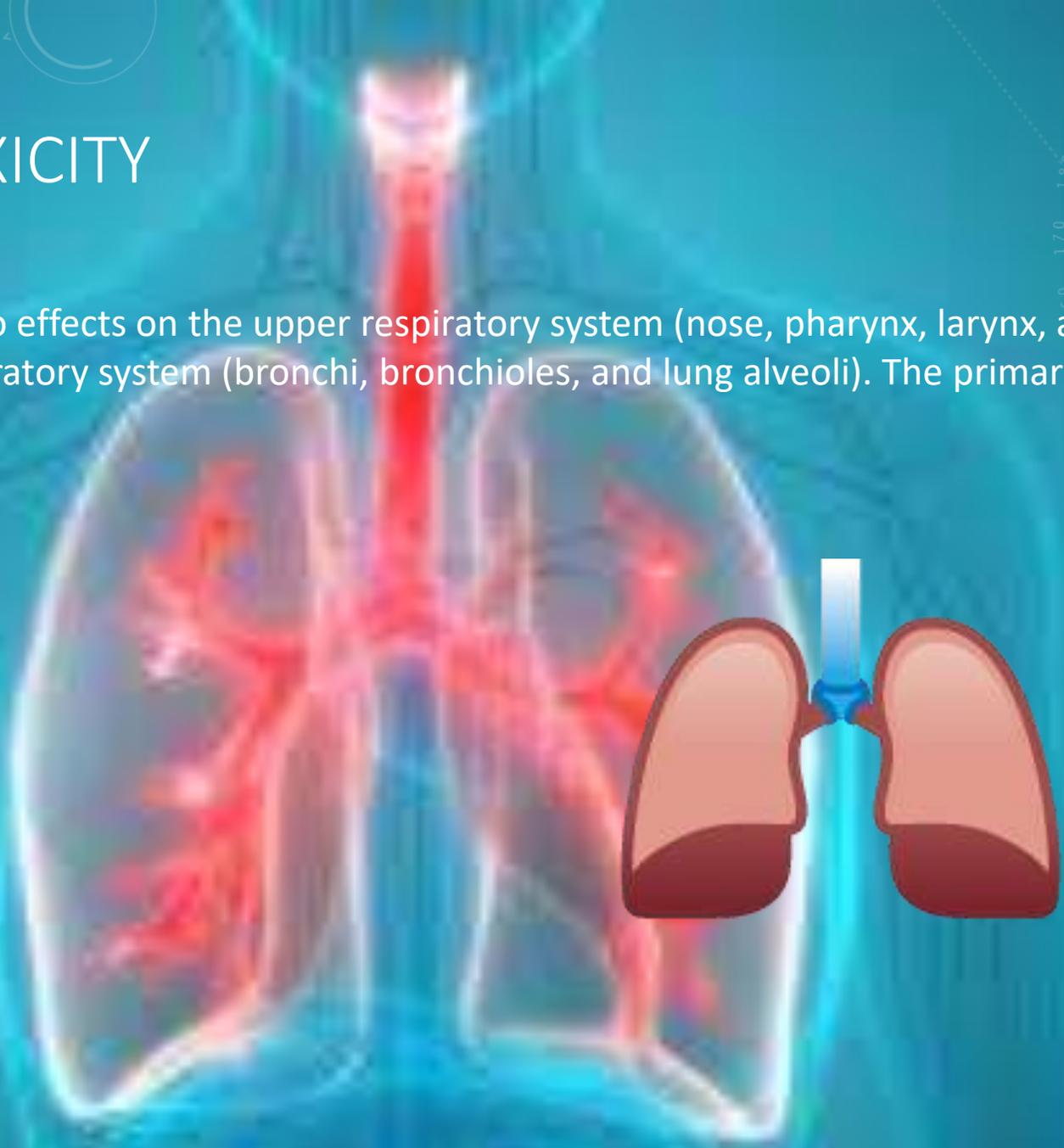
REPRODUCTIVE TOXICITY

- 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.



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



FORENSIC IMPORTANCE

- Forensic toxicology is the analysis of sample including toxins.
- The key significance is the systematic toxicology will help us to know how the toxins will affect the organs and different systems in the body.

REFERENCE

- https://ec.europa.eu/health/ph_projects/2003/action3/docs/2003_3_09_a21_en.pdf
- <https://www.toxmsdt.com/33-systemic-toxic-effects.html>

A row of colorful pens in shades of blue, pink, red, orange, and yellow. Each pen has a diamond-shaped logo on its barrel. The logos include a stylized figure, a tree, a globe, and a scale of justice. The background is a light gray with a digital overlay of white circles, dashed lines, and numbers (40, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260).

THANK YOU