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| **An-Najah National University College of Medicine and**  **Health Sciences** |  | **جامعة النجاح الوطنية**  **كلية الطب وعلوم الصحة** |

**Toxicology**

**Teratogens**

**Teratology:** The study of structural birth defect.

Examples of chemicals that cause teratogens:

1. Thalidomide (1960): newborns with rare limb malformations in West Germany
   * Amelia: babies with no limbs
   * Phocomelia: truncated lims

1940-1959: no cases.

1959: 1 case.

1960: 30 cases.ormation

1961: 154 cases

When the medicine was taken out: 0 cases

OUTCOME: all regulatory agencies began to develop animal testing requirement for evaluating effects of pregnancy.

Mechanism:

* + Inhibits angiogenesis; inhibits blood vessels formation which is correlated to limb length.
  + Increases tumor susceptibility to apoptosis.
  + Stimulation of immune-mediated response.

The drug is used now to treat leprosy, solid tumors, and multiple myeloma.

1. DES (used between1940’s and1970’s) It was used for miscarriage.
2. Fetal Alcohol Syndrome (FAS)
3. Retinoids (excess vitamin A): Hoxgene is affected, motor skills, low IQ.
4. Methylmercury: Minimata disease.

**Critical periods of susceptibility:**

1. **Toxicity during pre-implementation -blastocysts** 
   1. Lethality
   2. Rapid cell division
   3. Tubulin formation
2. **Toxicity during gastrulation- process of forming the three primary germ layers-ectoderm, mesoderm, and endoderm.** 
   1. Lethality or,
   2. Defect in critical organs such as heart and brain.
3. **Organogenesis :**
   1. period of heightened susceptibility
   2. Morphological defect
4. **Fetal period: starts at the end of organogenesis:** Differentiation of growth and physiological maturation at that period.
   1. Functional changes
   2. Motor skills behavior
   3. Metal capacity growth

**Mechanism of teratogens:**

1. Mutations
2. Altered mitosis, cell cycle, apoptosis
3. Nucleic acid function: inhibit the synthesis of nucleic acids or tubulin

**Factors that influence toxicity:**

1. Genetics:
   1. tumor suppressor genes are mutated.
   2. Decreased in DNA repair enzymes.
   3. Changes in detoxification enzymes
2. Nutrition:
   1. Fat and calories changes
   2. Change in vitamins
   3. Folic acid
3. Disease:
   1. Rubella viruses
4. Placental toxicity:
   1. Lipophilic compounds that are capable of crossing the placenta
   2. Metals such as Cd induce a protein called metalothionin (MT), high induction of MT leads to sequestering of Cu and Zn in fetus.