

Reproductive Toxicity

- Exposure to chemical substances can cause adverse effects on the male and female reproductive systems.

Adverse effects on the Female

- Toxicants that target the female reproductive system can cause changes in: -
 - sexual behavior,
 - onset of puberty,
 - menstrual cycle,
 - fertility,
 - gestation time,
 - lactation
 - premature menopause
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- These can disrupt a woman's ability to successfully reproduce.
- Exposure to lead, can result in menstrual disorders and infertility.
- The toxicants carbon disulfide, mercury, and polychlorinated biphenyls (PBCs) have been shown to cause irregularities in the menstrual cycle

Adverse effects on the Male

- Toxicants that target the male reproductive system can affect sperm count or shape, alter sexual behavior, and/or increase infertility.
- Exposure to lead can affect sperm count
- Carbon disulfide and the pesticides chlordane (kepone), ethylene dibromide (EDB), and dibromochloropropane (DBCP) are examples of chemicals known to disrupt male reproductive health.

Toxic responses of the reproductive system

- The developing gonad is very sensitive to chemical insult.
- Modified by:
 - 1) Barriers in the reproductive system
 - 2) Metabolism in the gonads
 - 3) DNA repair mechanisms

Barriers in the reproductive system

- **Placenta** does not prevent most chemicals from crossing it.
- **NO special barriers prevent chemicals from acting on the ovary.**

Examples of drugs interfering with ovarian function: prednisone, anticancer drugs e.g. cyclophosphamide, methotrexate, vincristine.

- **Blood-testis-barrier:** This is a special barrier present in the male gonad.

Blood-testis-barrier prevents exchange of chemicals between blood and the fluid inside the seminiferous tubules.
Crossed by lipid soluble and non-ionized chemicals.

Effect of metabolism

- There is metabolism in the testes by e.g. cytochrome-P-450.
 - Chemicals or their metabolites may affect spermatogenesis and steroidogenesis e.g.:
 - n-hexane (environmental toxicant) causes peripheral neuropathy + testicular atrophy
 - Dietary zinc deficiency causes decreased spermatogenesis
 - Other drugs include amiodarone, valproic acid or metabolites of cephalosporins.....etc.

DNA REPAIR

- Spermatogenic cells are less able to repair DNA damage resulting from alkylating agents, X-ray ,UV light or lead
 - Lead poisoning can reduce fertility in males and females (causes chromosomal breaks, spermicidal, abortifacient, and can cause stillbirth)
- Like testes, the ovaries can metabolize chemicals, but unlike mature sperms the mature oocyte maintains a DNA repair ability

Some major targets for chemical toxicity on the reproductive system

- Target: hypothalamus/anterior pituitary:
Affected by neuroleptics (e.g. chlorpromazine), methyl-dopa, reserpine –
These can cause hyperprolactinaemia, gynecomastia, galactorrhoea and infertility in both sexes.

-Synthetic steroids decrease gonadotrophins release leading to decreased fertility

- Target: testes:

Alkylating agents may arrest quickly dividing cells (e.g. they block spermatogenesis).

- Target: uterus:

Antioestrogens (e.g. tamoxifen) leads to infertility