

Unit II – Problem 1 – Pharmacology: Drug Use In Pregnancy and Lactation



- Thalidomide Crisis:

- Thalidomide is a sedative-hypnotic مهدئ-منوم which causes PHOCOMELIA تشوه الأطراف if given to pregnant women.

- The placenta:

- It is a semi-permeable mother/fetus barrier which has transporters such as P-glycoprotein (a multidrug resistance protein: pumping drugs back from fetus to mother) and enzymes which are going to metabolize drugs and prevent them from exerting their harmful effects.

- Umbilical vein:

- Maternal drugs enter umbilical arteries then cross the placenta and enter fetal blood via the umbilical vein (in fetoplacental circulation: umbilical vein carries oxygenated blood from mother to fetus). 40-60% of the drug will be metabolized in the fetal liver. The remainder bypasses the liver and enters the general circulation.

- Effects of drugs on the fetus depend on three factors:

Stage of fetal development (harmful in organogenesis period)	Duration of exposure to the drug	Distribution of the drug in the fetus
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- Drug properties:

Lipid/water solubility	Molecular weight	Protein binding
Lipophilic drugs diffuse readily	Large drugs cross poorly	High protein binding don't cross placenta easily

- Teratogenic drugs: a teratogen should:

- Causes set of malformations (تشوهات خلقية) in certain target organs.
- Exerts effects at particular stage of fetal development (organogenesis).
- Shows a dose-dependent incidence: increasing the dose will increase the risk.
- Causes not only major malformation, but also:
 - ✓ Intrauterine growth restriction (smoking).
 - ✓ Miscarriage- abortion (alcohol).
 - ✓ Stillbirth- ولادة جنين ميت (smoking)
 - ✓ Neurocognitive delay (alcohol).

- Teratogens may interfere with the passage of oxygen and nutrients through the placenta and therefore causing anomalies (Vitamin A which is used for acne is a strong teratogen). Administering folic acid before & during pregnancy reduces risk of neural tube defects.

- Important teratogenic drugs:

Carbamazepine & mthotrexate	Neural tube defects.
Ethanol	Fetal alcohol syndrome.
Iodine	Congenital hypothyroidism.
Tetracycline	Teeth discoloration.



Drugs are present in milk but in low-concentrations. If a drug is safe, a nursing mother must take it 30-60 min after nursing & 3-4 hours before the next feeding.



FETAL THERAPEUTICS

- Drug administration to a pregnant woman with the fetus as the target of the drug. Examples:
- **CORTICOSTEROIDS:** administered to pregnant women to stimulate fetal lung maturation when preterm birth is expected to accelerate lung maturation and prevent respiratory distress.
- **PHENOBARBITAL:** administration to pregnant women to induce fetal hepatic enzymes for bilirubin metabolism to prevent newborn jaundice.
- **ZIDOVUDINE:** is an anti-HIV drug that decreases transmission of HIV from the mother to the fetus when given to a pregnant mother.