

### O3- Teratogens and drugs of abuse in pregnancy

#### Major Teratogenesis (during the first trimester)

<i>Thalidomide</i>	Phocomelia.
<i>Alcohol</i>	Foetal Alcohol Syndrome (FAS).
<i>Phenytoin</i>	Foetal Hydanotin Syndrome.
<i>Corticosteroids</i>	Cleft lip & palate.
<i>Tetracyclines</i>	Permanent Teeth staining, enamel hypoplasia Altered growth of teeth & bone.
<i>Warfarin</i>	Hypoplasia of nasal bridge and CNS malformation.
<i>Finasteride</i>	Abnormal development of genitalia of male fetuses.
<i>Valproic acid</i>	Spina bifida and Impaired folate absorption
<i>Hormones</i>	Serious genital malformation, testicular atrophy in male -Fetal masculinization in female -Vaginal carcinoma of female offspring
<i>Lithium</i>	Cardiovascular anomalies mainly valvular heart defect involving tricuspid valve <b>Ebstein's anomaly</b>
<i>ACE inhibitors: captopril, enalapril</i>	Fetal & neonatal anuria, Renal damage, Fetal hypotension, growth retardation

#### Major Teratogenesis (during the second & third trimesters)

<i>Tetracyclines</i>	Impaired teeth & bone development, yellow-brown discoloration of teeth
<i>Aminoglycosides</i>	e.g. <i>Streptomycin, kanamycin</i> causes: Ototoxicity = 8 <sup>th</sup> Cranial nerve damage
<i>Cloramphenicol</i>	<b>Gray baby syndrome</b> (also contraindicated in children less than 4 yrs old)
<i>Corticosteroids</i>	Adrenal atrophy – <b>growth retardation</b>
<i>Propranolol (beta blocker)</i>	Bradycardia, neonatal hypoglycemia, placental insufficiency, reduced uterine blood flow, fetal distress
<i>Antithyroid drugs</i>	Iodide, <b>Methimazole, Carbimazole, propylthiouracil</b> Risk of hypothyroidism and goitre
<i>NSAIDs</i>	e.g. <b>Aspirin-indomethacin</b> - Prostaglandin synthesis inhibitors - Constriction of ductus arteriosus (close prematurely), pulmonary hypertension in newborns.
<i>Benzodiazepines as Diazepam</i>	Chronic use → neonatal dependence and withdrawal symptoms
<i>ACEIs</i>	Renal damage
<i>warfarin</i>	Risk of <b>bleeding</b>

#### ADRs During second and third trimesters

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<i>Adverse effects of drugs prior to labor</i>	
<i>NSAIDs</i>	e.g. <b>Aspirin-indomethacin</b> Prostaglandin synthesis inhibitors Increase in gestation time prolong labor, neonatal bleeding Risk of postpartum hemorrhage
<i>CNS depressants</i>	e.g. <b>diazepam, morphine</b> Interference with suckling Respiratory depression Reduced blood flow, fetal distress
<i>Sulfonamides</i>	Displacement of bilirubin from plasma protein (neonatal hyperbilirubinemia)

## Drugs of Abuse in Pregnancy

<b>Alcohol</b>	<b>Fetal Alcohol Syndrome (FAS)</b>
<b>Cocaine</b>	<ul style="list-style-type: none"> <li>Inhibits re-uptake of sympathomimetics (epinephrine, NE, dopamine), causing vasoconstriction, rapid heart rate, hypertension (Vascular disruption).</li> <li>Abruptio placentae (separation of placenta from uterus wall before delivery)</li> </ul>
<b>Tobacco</b>	<ul style="list-style-type: none"> <li>Decreased blood flow to placenta</li> <li>Fetal hypoxia</li> <li>Retarded fetal growth</li> <li>Low birth weight</li> <li>Increased spontaneous abortion</li> <li>Preterm labor and stillbirth</li> </ul>

## Drugs of choice in pregnancy:

<b>Antihypertensive</b>	$\alpha$ -methyl dopa Labetalol ( $\alpha$ - $\beta$ Blocker) Hydralazine (emergency only)
<b>Antibiotics</b>	penicillin, cephalosporins, erythromycin
<b>Antidiabetics</b>	Insulin, avoids oral antidiabetics
<b>Anticoagulants</b>	Heparin (warfarin is contraindicated)
<b>Analgesics</b>	Acetaminophen
<b>Antithyroid drugs</b>	Propylthiouracil (protein-bound)
<b>Anticonvulsants</b>	<ul style="list-style-type: none"> <li>All antiepileptics have potential to cause malformations</li> <li>avoid valproic acid.</li> <li>Folic acid should be supplied.</li> </ul>

## Summary

- The use of drugs during pregnancy should be avoided unless absolutely necessary.
- Most drugs cross the placenta to some extent.
- Birth defects are of great concern.
- Drugs can harm the embryo or foetus depending upon three points:
  - Physiochemical properties of the drug:

Lipid solubility of the drug	Molecular size of the drug	Protein binding.
-More lipid soluble $\rightarrow$ cross placenta $\rightarrow$ affect fetus -Less lipid soluble $\rightarrow$ less crossing placenta $\rightarrow$ less affect on fetus.	-Low MW $\rightarrow$ easy to diffuse placenta $\rightarrow$ affect fetus. -High MW $\rightarrow$ no diffusion in placenta $\rightarrow$ no affect on fetus.	-more protein binding $\rightarrow$ less diffusion in placenta. -less protein binding $\rightarrow$ more diffusion in placenta.

- The stage of mammalian fetal development: The most critical period of pregnancy is organogenesis (17 days – 8 weeks).
  - Duration of exposure to the drug.
- Alcohol, nicotine and other addicting drugs should be avoided.