



# DRUGS, PREGNANCY & NEWBORN

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# Introduction

- **Drugs are likely to be self administered or prescribed by the physician during pregnancy.**
- **Intelligent use of drugs during pregnancy requires that the physician understands the interaction between drugs and pregnancy.**

# Pharmacokinetics during Pregnancy

- **Drug absorption**: High circulating levels of progesterone slow the gastric emptying as well as gut motility, thus increasing the intestinal transit time.
- **Drug distribution**: Pregnancy is accompanied by an increase in total body water by upto 8 liters and a 30% increase in plasma volume, with consequent decrease(0.5-1.0 g%) in plasma albumin due to hemodilution.

## Contd...

- **Drug metabolism**: Hepatic drug metabolizing enzymes are induced during pregnancy, probably by the high concentrations of circulating progesterone.
- **Drug excretion**: During pregnancy, the renal plasma flow increases by 100% and the glomerular filtration rate by 70%.
- Ex: Ampicillin, gentamicin, cephalixin, digoxin.

# Drugs & the Fetus

- **Placental transfer of drugs**: Placenta acts as an intravenous portal for entry of drugs into the fetus.
- As pregnancy progresses and the placenta develops, the surface available for transfer between the maternal and fetal circulations increases, at the same time the placento-fetal barrier becomes progressively thinner.

# Fetal-neonatal pharmacokinetics

- The fetal liver & the adrenals are capable of metabolizing many substrates by oxidation.
- Because of low renal plasma flow & GFR (30-40% of adult values) and the more acidic urine, drugs such as aminoglycosides, digoxin, penicillin, salicylic acid, paracetamol & several sulfonamides are cleared very slowly by the neonate.

# Fetal-neonatal pharmacodynamics

- For a given plasma concentration the response of the fetal tissues to most drugs is equal to or less than that of maternal tissues.
- Tetracycline get deposited in fetal teeth & bones and retard their growth.  
Salicylates can cause neonatal hemorrhage.

# Contd...

- Antithyroid drugs can inhibit fetal thyroxine synthesis and can cause goitre.
- Phenothiazines given to the mother can produce cerebral depression in the neonate, and extrapyramidal signs which may persist for several months.

# Teratogenicity

- Means congenital malformations grossly visible at birth and caused by exposure to exogenous agents (*teratogens*) in the first trimester.
- Any birth defect (morphological, biochemical, or behavioral) induced at any stage of pregnancy and detected at birth or later.

## Drug with proven teratogenic effects in humans

<b>Drug</b>	<b>Teratogenic effect</b>
<b>Tetracycline</b>	<b>Anomalies of teeth &amp; bones.</b>
<b>Thalidomide</b>	<b>Limb-shortening, internal organ defects.</b>
<b>Methotrexate</b>	<b>CNS and limb malformations</b>
<b>ACE inhibitors</b>	<b>Prolonged renal failure in the neonate, decreased skull ossification.</b>
<b>Phenytoin</b>	<b>Growth retardation, CNS defects</b>
<b>Warfarin</b>	<b>Skeletal &amp; CNS defects</b>

# Contd...

<b>Valporic acid, Carbamazepine</b>	<b>Neural tube defects</b>
<b>Antithyroid drugs</b>	<b>Fetal &amp; neonatal goiter and hypothyroidism.</b>
<b>Cyclophosphamide</b>	<b>CNS malformations</b>
<b>Stilbestrol</b>	<b>Vaginal carcinoma in teenage female offspring</b>
<b>Anticancer drugs (Methotrexate)</b>	<b>Multiple defects, fetal death</b>

# Drugs prescribing during pregnancy

- Nausea & vomiting: Antihistaminic antiemetic is prescribed. Metaclopramide is safe.
- Heartburn: Non-systemic antacids & metaclopramide. Anticholinergics usually worsen the heartburn by relaxing the lower esophageal sphincter.
- Peptic ulcer: Non-systemic antacids, sucralfate is safe but carbenoxone sodium and H<sub>2</sub> receptor blockers should be avoided.

# Contd...

- Constipation: Mild laxatives such as milk of magnesia, bisacodyl or senna.
- Antimicrobial drugs: Betalactum antibiotics (penicillin, cephalosporin), Ampicillin, Erythromycin base, Nitrofurantoin & methanamine mandelate Gentamicin or tobramycin.
- Tuberculosis: Isoniazid & Ethambutol

# Contd...

- NSAID: Paracetamol
- Hypertension: Methyl-dopa
- Anticoagulants: Heparin
- D.V.T: Heparin
- Allergic rhinitis: glucocorticoids, decongestants, diphenhydramine.
- Cough: diphenhydramine, codeine, dextromethorphan.

# Contd...

- Pruritus: zinc oxide cream, glucocorticoids, calamine lotion
- Bronchial Asthma: Aminophylline, glucocorticoids
- Diabetes mellitus: Insulin
- Epilepsy: Phenobarbitone, phenytoin, carbamazepine
- CNS: Barbiturates, antidepressants

# Contraindicated drugs during pregnancy

- **Aminoglycosides**
- **Tetracycline**
- **Chloramphenicol**
- **Co-trimoxazole**
- **Sulfonamides**
- **Rifampicin**
- **Streptomycin**
- **Primaquine pyrimethamine**
- **Mefloquine**

# Contraindicated drugs during pregnancy

- **NSAID**
- **Aspirin**
- **Beta blockers**
- **ACE inhibitors**
- **Vasopressor agents (nonadrenalin, dopamine & dobutamine)**
- **Anticoagulants: Warfarin, Streptokinase**
- **Salbutamol**
- **Oral hypoglycemic agents**
- **Valproic acid**
- **Benzodiazepines**

# Precautions while prescribing drugs to a pregnant women

- Treat minor ailments without drugs.
- Safe drugs should be prescribed.
- Adjust the dose of the drug to the pregnant state.
- Discourage the patient from self administering over the counter (OTC) drugs.

# Conclusion

- The pregnant women is likely to be exposed to a variety of environmental, nontherapeutic agents which can affect the fetal health.
- If a drug is used therapeutically in the neonatal period, one may use it safely in breast feeding women.

