

Special situation: Pregnancy, Lactation, Children, Elderly, Renal and Hepatic disease

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Special Situation: Pregnancy

- **Drug use during pregnancy** can have temporary or permanent effects on the fetus.
- Any drug that acts during embryonic or fetal development to produce a permanent alteration of form or function is known as a teratogen.
- More than 50% of pregnant women take prescription or nonprescription (over-the-counter) drugs or use social drugs (such as tobacco and alcohol) or illicit drugs at some time during pregnancy.
- Drugs should not be used during pregnancy unless absolutely necessary because many can harm the fetus.

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Special Situation: Pregnancy

- Sometimes drugs are essential for the health of the pregnant woman and the fetus.
- In such cases, a woman should talk with her doctor or other health care practitioner about the risks and benefits of taking the drug.
- Before taking any drug (including over-the-counter drugs) or dietary supplement (including medicinal herbs), a pregnant woman should consult her health care practitioner.
- A health care practitioner may recommend that a woman take certain vitamins and minerals during pregnancy.

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How drug affect the fetus?

- Act directly on the fetus, causing damage, abnormal development (leading to birth defects), or death.
- Alter the function of the placenta, usually by causing blood vessels to narrow (constrict) and thus reducing the supply of oxygen and nutrients to the fetus from the mother. Sometimes the result is a baby that is underweight and underdeveloped.
- Cause the muscles of the uterus to contract forcefully, indirectly injuring the fetus by reducing its blood supply or triggering preterm labor and delivery.

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Drug can affect the fetus at 3 stages

- **Fertilization and implantation**- conception to 17 days- failure of pregnancy.
- **Organogenesis**- 18-55 days of gestation- most vulnerable period, deformities are produced.
- **Growth and development**- 56 days onwards- development and functional abnormalities can occur.

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Timing and the Effects of Drugs During Pregnancy



Time Frame	Possible Drug* Effects	Status of the Fetus
Within 20 days after fertilization	An all-or-nothing effect (death of the fetus or no effect at all)	The fetus is highly resistant to birth defects.
3-8 weeks after fertilization	Possibly no effect A miscarriage An obvious birth defect A permanent but subtle defect that is noticed only later in life	The fetus's organs are developing, making the fetus particularly vulnerable to birth defects.
2nd and 3rd trimesters	Changes in the growth and function of normally formed organs and tissue Unlikely to cause obvious birth defects Unknown long-term effects	Organ development is complete.

*Only certain drugs are likely to have harmful effects.

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FDA category of Drugs during Pregnancy

Category	Description	Examples
A	No risk in controlled human studies	Inj. Mag sulfate thyroxine
B	no controlled studies conducted in human, No risk in other studies.	amoxicillin Penicillin V
C	Animal studies- risk, but Risk not ruled out in human (No adequate and well controlled studies)	Morphine, Codiene gabapentin
D	Positive evidence of risk on human studies	Aspirin, Phenytoin, lorazepam
X	Contraindicated in Pregnancy (fetal abnormalities shown in animal as well as in human studies)	Estrogen, warfarin Methotrexate

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Teratogenic drug

First Trimester	Second	Third
Analgesic (Aspirin)	ACE inhibitors	Tetracycline
Anticonvulsant (Phenytoin)	Diazepam	ACE inhibitors
Anticoagulant (Warfarin)		Chloramphenicol
Antidepressant (Imipramine)		Aminoglycosides
Aminoglycosides		Sulfamethoxazole/Tri methoprim
Sedatives/hypnotics (Diazepam)		
Lithium		

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Drugs which probably do not harm the fetus

- Paracetamol
- Codiene
- Insulin
- Lactulose
- Methyldopa
- Chloroquine
- Salbutamol
- Penicillin, cephalosporin
- Heparin
- Carbamazepine
- Digoxin

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Guidelines

- Avoid the drugs if possible, especially in the first trimester.
- Administer the drug at lowest dose
- Teratogenic drug should be avoided and substitute if possible.

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Conclusion

- Some drugs are highly toxic and should never be used by pregnant women because they cause severe birth defects. Ex: thalidomide.
- Some drugs cause birth defects in animals, but the same effects have not been seen in people. One example is meclizine, frequently taken for motion sickness, nausea, and vomiting.
- A safer drug can be substituted for one that is likely to cause harm during pregnancy. For prevention of blood clots, the anticoagulant heparin is preferred to warfarin. Several safe antibiotics, such as penicillin, are available to treat infections.

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Drug use during Lactation

- Most drug administered to lactating women are detect in milk.
- When mothers who are breastfeeding have to take a drug, they wonder whether they should stop breastfeeding.
- It depends on the following:
 1. How much of the drug passes into the milk
 2. Whether the drug is absorbed by the baby
 3. How the drug affects the baby
 4. How much milk the baby consumes, which depends on the baby's age and the amount of other foods and liquids in the baby's diet

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Drug that can be used during lactation

- Epinephrine, heparin, and insulin, do not pass into breast milk and are thus safe to take.
- Some drugs pass into breast milk, but the baby usually absorbs so little of them that they do not affect the baby. Examples are the antibiotics gentamicin, kanamycin, streptomycin, and tetracycline.
- Drugs that are considered safe include most nonprescription (over-the-counter) drugs. Exceptions are antihistamines

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Safe drug during lactation

- Antimicrobials- penicillin, ampicillin
- Analgesics- paracetamol, morphine
- Anti- HTN- beta blocker, CCB
- Antimalarial- quinine, chloroquine
- ATT-rifampicin, ethambutol
- Bronchodilator- theophylline, salbutamol
- Antiepileptic- phenobarbitone, valproic acid
- Diuretics- furosemide
- Hypoglycemic agent- insulin

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Harmful drug

- Most antianxiety drugs, antidepressants, and antipsychotic drugs -- stay in the body a long time. For example, the antianxiety drug diazepam (a benzodiazepine) causes lethargy, drowsiness, and weight loss in breastfed babies. Babies eliminate phenobarbital (an anticonvulsant and a barbiturate) slowly, so this drug may cause excessive drowsiness-- they are unlikely to cause significant problems in the baby.
- Some drugs should not be taken by mothers who are breastfeeding. They include amphetamines, chemotherapy drugs (such as doxorubicin and methotrexate), chloramphenicol, ergotamine, lithium, radioactive drugs for diagnostic procedures, and illicit drugs such as cocaine, heroin.

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Harmful drug

- | | |
|-------------------|-----------------------|
| • Amiodarone | |
| • Barbiturates | Cytotoxic |
| • Contraceptives | Ergot alkaloid |
| • Cytotoxic drugs | Radio pharmaceuticals |
| • Aspirin | Lithium |
| • Ephedrine | Chloramphenicol |
| • Tetracycline | Atropine |
| • Chloramphenicol | Thyroxine |
| | Iodine and mercury |

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Drug that suppress lactation

- Bromocriptine
- Bendroflumethiazide
- Estradiol
- OCP
- L-dopa
- Trazodone

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Guidelines

- Drug which have no data on safety during lactation should be avoided.
- If women who are breastfeeding must take a drug that may harm the baby, they must stop breastfeeding.
- When possible, drugs should be taken immediately after breastfeeding or before the baby's longest period of sleep.
- Some drugs require a doctor's supervision during their use. Taking them safely while breastfeeding may require adjusting the dose, limiting the length of time the drug is used, or timing when the drug is taken in relation to breastfeeding.

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Drugs requiring TDM

- Drug acting on CVS- Digoxin, Amiodarone
- Antibiotics- aminoglycosides
- Antiepileptics- phenobarbitone, phenytoin, valproic acid, carbamazepine, gabapentine
- Psychopharmacological agents- lithium, amitriptyline, nortriptyline, clozapine
- Immunosuppressants- cyclosporine, tacrolimus
- Antiinfective- cycloserine, ethambutol, pyrazinamide, streptomycin

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