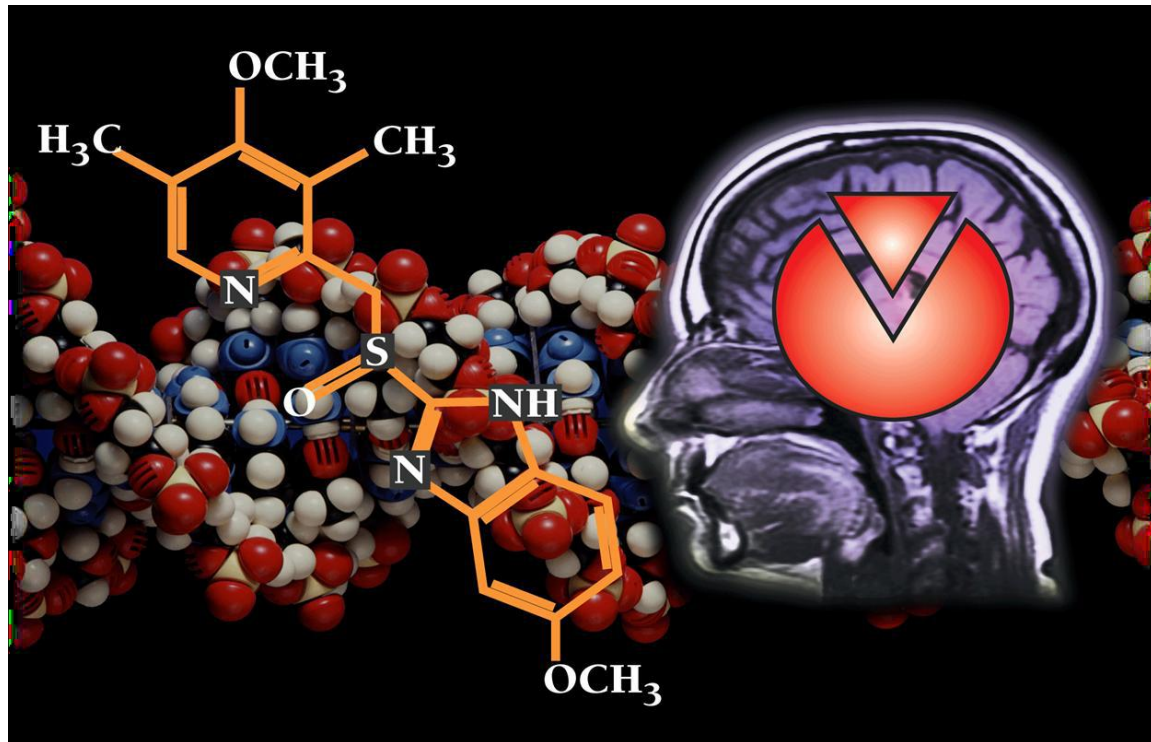


04-Drugs affecting breast&Milk and lactation



Note: text in blue and textboxes with thick light blue margins are additional info. **Text in red is important**

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introduction

- ✓ **Breast feeding** is very important because breast milk is the healthiest form of milk for babies.
- ✓ **It provides the baby with immunoglobulins (IgA, IgM) that** are essential for protection against gastroenteritis and other infections.
- ✓ Most drugs administered to breast feeding woman are detectable in milk.
- ✓ The concentration of drugs achieved in breast milk **is usually low**. However, even small amounts may be of **significance for the suckling child because its drug metabolic and eliminating mechanisms are immature especially premature infants.**

Pediatric population are classified into:

- **Newborn**: less than one month old
 - **Preterm neonates**: born before 38 weeks of pregnancy (it's the harmful stage)
 - **Full-term neonates**: 38-42 weeks of gestational age
- **Infants (babies)**: 1 month – 12 months of age
- **Children**: 1 -12 years of age
 - **Toddler (young child)**: 1-5 years
 - **Older child**: 6-12 years
- **Adolescent**: 13-18 years

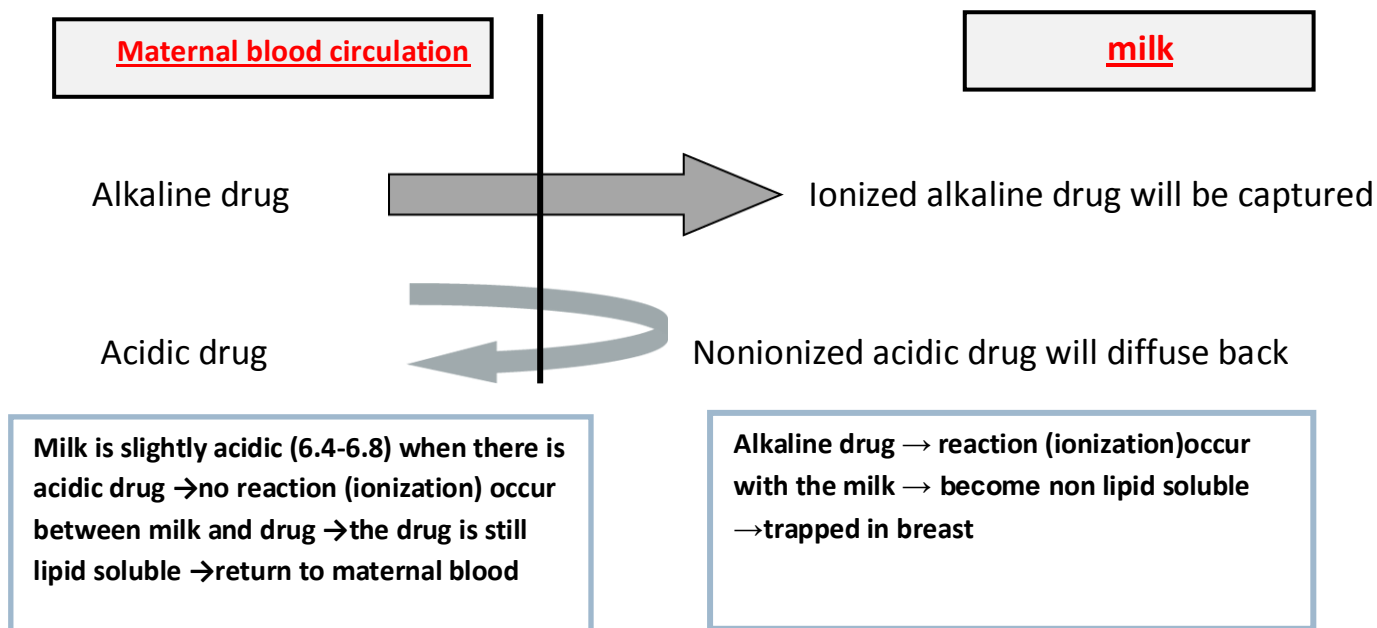
Metabolism & excretion in pediatrics

- Neonates especially premature babies have **limited capacity for metabolism and excretion.**
- Neonates have very **limited rate of metabolism due to immaturity of liver enzymes that is not fully developed until 8 weeks of age.**
- **Renal clearance is less efficient: well developed after 3-5 months.**
- The epithelium of the breast alveolar cells is most permeable to drugs during the 1st week postpartum, so drug transfer to milk may be greater during the 1st week of an infant's life.

Factors controlling passage of drugs into breast milk

1. Physiochemical character of the drug

- **Lipid solubility of the drug:** lipid soluble drugs pass more freely in the breast milk
- **Molecular weight:** low molecular weight drugs are more likely to be transferred to breast milk than high molecular weight
- **Degree of ionization:** non-ionized form of drugs are more likely to be transferred into breast milk.
- **pH of the plasma and milk:**
 - Weakly alkaline drugs tend to be concentrated in milk.
 - Weakly acidic drugs don't enter the milk to a significant extent and tend to be concentrated in plasma.
- **Effect of pH of the plasma and milk**



2. Plasma protein binding of drugs

Highly plasma protein-bound drugs pass less into milk.

3. Drug concentration in maternal serum

Transfer of drug from mother's blood to milk is low with drugs of the following characters:

- Large volume of distribution (V_d) (it's well distributed and taken up by tissue → less amount will be in blood → less amount will be secreted in milk)
- Short half life ($t_{1/2}$).

The amount of a drug to which the baby is exposed as a result of breast feeding depends on:

- The **concentration** of the drug in the milk at the time of feeding.
- The **amount** of milk consumed.
- The **amount** of drug absorbed.
- The **ability** of the baby to eliminate the drug.

General considerations to minimize risk to nursing infant:

- The safest drug should be chosen **e.g. Acetaminophen** than **aspirin** for analgesia
- Use, whenever possible, a **topical form** of medication instead of an **oral form**.
- Choose medications with the **lowest lipid solubility**.
- Choose medications with the **shortest half-life** and **highest protein-binding** ability.
- Lactating mother should take medication **just after nursing** and 3-4 hours before the next feeding.
- Drugs **with no safety data** should be avoided or lactation should be discontinued.

Drugs that should be avoided during lactation

- **Radioactive iodine**

- **Potassium iodide**

- **Anticancer drugs :**

Doxorubicin, cyclophosphamide, methotrexate

- **CNS acting drugs :**

Amphetamine, heroin, cocaine

- **Lithium** (anti –mania)

- **Atenolol**(the drug is excreted in high amounts in milk)

Drugs that can suppress lactation (**inhibit prolactin**)

- **Levodopa** (dopamine precursor)
- **Bromocriptine** (dopamine agonists) (**for treatment of hyperprolactinemia**)
- **Androgens**
- **Estrogen, oral contraceptives that contain high-dose of estrogen and a progestin.**
- **Thiazide diuretics**
- Ergot derivatives (**not imp**)

Drugs that can augment lactation

Dopamine antagonists :

they stimulate prolactin secretion e.g.

- **Metoclopramide** (*antiemetic*)
- **Haloperidol** (*antipsychotic*)
- **Phenothiazines** (antiemetic)
- **Methyl dopa** (antihypertensive drug)
- **Theophylline** (used in asthma)

Neonatal Hyperbilirubinemia (Drugs that are contraindicated in infants with glucose -6 - phosphate dehydrogenase(G6PD))

- **Premature infants or infants with inherited glucose -6- phosphate dehydrogenase (G6PD) deficiency** are susceptible to oxidizing drugs that can cause → hemolysis of RBCs → ↑ bilirubin (hyperbilirubinemia) → ↑ **Kernicterus** (**bilirubin encephalopathy**)
- **Examples for oxidizing drugs:**

Antibiotics :(**sulfonamides, trimethoprim, dapsone**_(**anti-leprosy**)_)

Antimalarials :(**Primaquine**)

Note: The baby's blood brain barrier is not fully developed. Sulfa drugs displace bilirubin from binding sites on serum albumin. Bilirubin is then free to pass to CNS that then causes brain damage leading to kernicterus (If only few amount of bilirubin is free, jaundice occurs. If an excessive amount of bilirubin is free, kernicterus occurs)

Note: Primaquine leads to G6PD deficiency; the RBCs would become more sensitive to oxidative agents that will lead to its hemolysis and release of bilirubin

Neonatal Met-hemoglobinemia

- **Methemoglobin is an oxidized form of hemoglobin** that has a decreased affinity for oxygen
→ tissue Hypoxia.
- Infants under 6 months of age are particularly susceptible to methemoglobinemia upon exposure to some oxidizing drugs as:
- **Antibiotics (sulfonamides, trimethoprim, dapsone)**
- **Topical anesthetic (benzocaine applied to the gums in baby teething gels).**

Antibiotics

Penicillins <i>Ampicillin</i> <i>amoxicillin</i>	No significant adverse effect allergic reactions, diarrhea
Cephalosporins	No significant adverse effect
Chloramphenicol	"Gray baby" syndrome (cyanosis ,CVS collapse ,etc) because the enzyme which is responsible for the congeation of the drug and make it easier to execrated is immature in the infant
Sulphonamides	hyperbilirubinemia -neonatal jaundice Should be avoided in premature infants or infants with G6PD deficiency
Macrolide : (Erythromycin)	No significant adverse effect
Quinolones (ciprofloxacin)	Risk of arthropathies Should be avoided
Tetracyclines .	Absorption by the baby is probably prevented by chelation with milk calcium. Risk of tooth discoloration

Sedative/hypnotics (high lipid soluble)

single doses are unlikely to be harmful (but Clinical monitoring is recommended)

Regular use of high doses should be avoided

Barbiturates (phenobarbitone)	Lethargy, sedation , poor suck reflexes Clinical monitoring is recommended
Benzodiazepines (diazepam)	Lethargy, sedation in infants Clinical monitoring is recommended

Anti-diabetics

Insulin	safe
Oral antidiabetics	compatible
Metformin	avoid due to lactic acidosis

Oral CONTRACEPTIVE

Non hormonal method should be used

Avoid estrogens containing pills

Estrogens ↓ milk quantity

Progestin only pills or minipill are preferred for birth control.

Others

Antithyroid drugs: Propylthiouracil Carbimazole , Methimazole potassium iodide	May suppress thyroid function in infants. Propylthiouracil should be used rather than carbimazole or methimazole
Anticonvulsants : Carbamazepine Phenytoin	Are preferable over others Amounts entering breast milk are not sufficient to produce adverse effects <i>Infants must be monitored</i>
Anticoagulants: Heparin , Warfarin	Heparin is not present in breast milk. Warfarin can be used (very small quantities found in breast milk).
Iodine (radioactive)	Permanent hypothyroidism in infant Breast-feeding is contraindicated
Cytotoxic drugs	Breast feeding should be avoided
Lithium	Large amounts can be detected in milk Avoid
CVS drugs Atenolol	Risk of bradycardia and hypoglycemia Avoid (but other beta blocker can be used)

Drugs of choice in lactation

Antibiotics	Cephalosporins, penicillins are safe Avoid: chloramphenicol, quinolones, sulphonamides and tetracyclines
Antidiabetics	Insulin – oral antidiabetics are safe Avoid: <u>metformin</u>
Anticoagulants	Heparin – warfarin
Analgesics	Acetaminophen (paracetamol)
Antithyroid drugs	Propylthiouracil is preferable over others
Anticonvulsants	Carbamazepine - phenytoin
Oral contraceptives	Progestin only pills or minipills are preferred for birth control.
Antiasthmatics	Inhaled corticosteroids - prednisone

Summary:

To minimize the ADRs of the drugs in lactation we use a drug having these characters :

- non lipid soluble (water soluble) → ionized
- High molecular weight
- acidic drug
- Short half life
- high volume of distribution

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