



# Lecture 7

## Drugs affecting breast milk and lactation

### Objectives :

- ★ Recognize the main pharmacological characters that control the passage of drugs from milk to baby.
- ★ Identify the adverse effects of major pharmacological categories on babies.
- ★ Describe the best and safest medication to be given to breast feeding women if she is suffered from different diseases as epilepsy, infection, diabetes, heart failure, hypertension.
- ★ Know drugs that can inhibit lactation and should be avoided in breast feeding
- ★ Know drugs that may enhance lactation.

- Additional Notes
- Important
- Explanation –Extra-

before starting, please check our [reproductive block correction](#)

For any correction, suggestion or any useful information do not hesitate to contact us: [Pharmacology434@gmail.com](mailto:Pharmacology434@gmail.com)

# Breastfeeding

## Introduction

- **Breastfeeding** 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.
- Drugs ingested by the mother diffuse or are transported from the maternal plasma to the alveolar cells of the breast.
- The concentration of drugs achieved in breast milk is usually low (< 1 %).
- However, **even small amounts of some drugs** may be of significance for the suckling child.

## Pharmacokinetics changes in pediatrics

- Higher gastric pH
- increase gastric emptying time
- decreased serum albumin
- Higher concentrations of free drug
- Higher percentage of body water
- Lower rate of metabolism due to immaturity of liver enzymes.
- Renal clearance is less efficient: ( ↓ Renal blood flow- ↓ GFR).
- **Premature babies** have very limited capacity for metabolism and excretion.

## Classification of Pediatric Population

### 1-Newborn

**less than one month old:**  
**1-Preterm neonates:** born before 38 weeks of pregnancy  
**2-Full-term neonates:** 38-42 weeks of gestational age.

### 2-Infants (Babies)

**1 month – 12 months of age.**

### 3-Children

**1 -12 years of age:**  
**1-Toddler Child:** 1-5 years  
**2–Older child:** 6-12 years

### 4-Adolescent

**•13-18 years.**

# Factor controlling passage of drugs into breast milk

## 1-Factor related to drugs

1-Molecular Weight	<ul style="list-style-type: none"><li>• <b>Very small molecules</b> (&lt; 200 Daltons) such as <b>alcohol</b>, equilibrate rapidly between plasma and breast milk via the aqueous channels surrounding alveoli.</li><li>• <b>Large molecules drugs</b> (&gt;800 Daltons) are <b>less likely</b> to be transferred to breast milk than low molecular weight.</li><li>• <b>Insulin:</b> MW &gt; 6,000 daltons</li><li>• <b>Heparin:</b> MW 40,000 daltons</li></ul>
2-Lipid Solubility of the drug	<ul style="list-style-type: none"><li>• Lipid Soluble Drugs pass <b>more freely</b> into the breast milk than water soluble Drugs.</li></ul>
3-Degree of Ionization	<ul style="list-style-type: none"><li>• Ionized form of drugs are <b>less likely</b> to be transferred into breast milk (e.g. <b>Heparins</b> pass poorly into breast milk)</li></ul>
4-PH Of Drug	<ul style="list-style-type: none"><li>-PH of milk is slightly <b>more acidity</b> than maternal blood.</li><li>-<b>Weak basic drugs</b> tend to concentrate in breast milk and become trapped <b>secondary to ionization</b>.</li></ul>
5-Weak Acidic Drugs	don't enter the milk to a significant extent and <b>tend to be concentrated in plasma</b>
6-Plasma Protein Binding of drugs	<ul style="list-style-type: none"><li>• Drugs circulate in maternal circulation in <b>unbound (free)</b> or <b>bound</b> forms to albumin.</li><li>• <b>Only unbound</b> form gets into maternal milk.</li><li>• Definition of good protein binding &gt; 90%</li><li>• e.g. warfarin</li></ul>
7-Half life of the drug	<ul style="list-style-type: none"><li>• Avoid the use of drugs with <b>long half lives</b></li><li>• short half life (<math>t_{1/2}</math>) are preferable.</li><li>• <b>Oxazepam (short) vs diazepam (long)</b></li></ul>
8-Volume of Distribution	Transfer of drug from maternal blood to milk is <b>low</b> with drugs that have <b>large volume of distribution (Vd)</b>

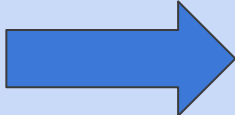
- Monoclonal antibodies, pass **very poorly** into milk **after** the first 1st week postpartum. (because it is protein and has large MW)
- The epithelium of the breast alveolar cells is **most permeable to drugs during the 1<sup>st</sup> week postpartum**, so drug transfer to milk may be greater during the 1st week of an infant's life.

# Factor controlling passage of drugs into breast milk

## 2-Factor related to Mother

1-Dose of the drug	-
2-Route of Administration:	<p>-Route of administration affect the concentration of the drug in maternal blood.</p> <p>-Maternal use of <b>topical preparations (creams, nasal sprays or inhalers)</b> are expected to carry <b>less</b> risk to a breastfed infant than systemically administered drugs.</p>
3-Time of Breastfeeding:	<p>-The <b>concentration</b> of the drug in the milk at the time of feeding.</p> <p>-Lactating mother should take medication just <b>after nursing and 3-4 hours before the next feeding.</b> (to allow time for drug to be cleared from the mother's blood → drug concentration in milk will be low).</p>
4-Health Status:	<p><b>Breastfeeding is contraindicated in case of:</b></p> <ul style="list-style-type: none"> <li>•HIV-positive women</li> <li>•Active, untreated TB in mother</li> <li>•Herpes on breast</li> <li>•Use of illegal drugs by mother</li> <li>•Certain medications used on a chronic basis.</li> </ul>
5-Maternal Drug Concentration	-

## 3-Factors related to Neonates

<p><b>The amount of a drug to which the baby is exposed as a result of breast feeding depends on:</b></p> <ul style="list-style-type: none"> <li>•The <b>amount</b> of milk consumed.</li> <li>•The <b>amount</b> of drug absorbed from GI.</li> <li>•The <b>ability</b> of the baby to eliminate the drug.</li> </ul>	<ul style="list-style-type: none"> <li>•Age</li> <li>•Body weight</li> <li>•Health status</li> </ul> 	<p><b><u>special cautions are required in:</u></b></p> <ul style="list-style-type: none"> <li>- Premature infants</li> <li>- Low birth weight</li> <li>- Infants with G6PD deficiency</li> <li>- Infants with impaired ability to metabolize /excrete drugs e.g. hyperbilirubinemia.</li> </ul>
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## Neonatal hyperbilirubinemia

## Neonatal Methemoglobinemia

Premature infants or infants with inherited **G6PD** deficiency are susceptible to **oxidizing drugs** that can cause → hemolysis of RBCs → ↑ bilirubin (hyperbilirubinemia) → ↑ Kernicterus .

Infants under 6 months of age are particularly prone to develop **methemoglobinemia** upon exposure to some oxidizing drugs.

Examples for oxidizing drugs:

Antibiotics: **sulfonamides, trimethoprim**

Antimalarials: **Primaquine**

**Methemoglobin** is an oxidized form of hemoglobin that has a decreased affinity for oxygen → **tissue hypoxia**.

### Drugs contraindicated during lactation

- Anti cancer drugs: **Doxorubicin, cyclophosphamide, methotrexate**
- Radiopharmaceuticals e.g. **radioactive iodine**
- CNS acting drugs: **amphetamine, heroin, cocaine**
- Lithium- Chloramphenicol- Atenolol- Potassium iodide**

### Drugs that can suppress lactation

- These drugs reduce prolactin**
- Levodopa** (dopamine precursor) -**Bromocriptine** (dopamine agonist).
  - Estrogen**: combined oral contraceptives that contain high-dose of estrogen and a progestin.
  - Androgens**
  - Thiazide diuretics**

### Drugs that can augment lactation

- Dopamine antagonists** : they stimulate prolactin secretion → galactorrhea e.g.
- Metoclopramide** (antiemetic) -**Domperidone** (antiemetic)
  - Haloperidol** (antipsychotic)
  - Methyl dopa** (antihypertensive drug) -**Theophylline** (used in asthma)

## Antibiotics

Penicillins, <u>Ampicillin</u> , <u>amoxicillin</u>	No significant adverse effect, can cause <b>allergic reactions, diarrhea</b>
Cephalosporins	No significant adverse effect
Macrolides: <b>erythromycin, clarithromycin</b>	Can cause <b>alterations to infant bowel flora</b>
Quinolones	Theoretical risk of arthropathies → <b>Should be avoided</b>
Chloramphenicol	“Gray baby” syndrome → <b>avoid</b>
Tetracyclines	Absorption by the baby is probably prevented by chelation with milk calcium. → <b>Avoid</b> due to possible risk of teeth discoloration.
Sulfonamides <b>(co-trimoxazole)</b>	hyperbilirubinemia -neonatal jaundice→ <b>Should be avoided</b> in premature infants or infants with G6PD deficiency

## Sedative/hypnotics

Barbiturates ( <b>phenobarbitone</b> )	Lethargy, sedation, poor suck reflexes with prolonged use.
Benzodiazepines: <b>Diazepam, Lorazepam</b>	<b>Single use</b> of low doses is probably <u>safe</u> . Lethargy, sedation in infants with prolonged use.

Antidiabetics		Analgesics	
<b>Insulin</b>	safe	<b>Paracetamol</b>	safe
<b>Oral antidiabetics</b>	compatible	<b>Ibuprofen</b>	compatible
<b>Metformin</b>	avoid due to <b>lactic acidosis</b>	<b>Aspirin</b>	avoid due to theoretical risk of <b>Reye's syndrome</b>
Oral contraceptives		Antithyroid drugs	
Non hormonal method should be used Avoid estrogens containing pills Estrogens <b>decrease</b> milk quantity Progestin only pills or minipills are preferred for birth control.		<b>Propylthiouracil</b> <b>Carbimazole</b> <b>Methimazole</b> <b>potassium iodide</b>	May suppress thyroid function in infants.  <b>Propylthiouracil</b> should be used rather than <b>carbimazole</b> or <b>methimazole</b> .
Anticoagulants		Anticonvulsants <small>(Infants must be monitored for CNS depression)</small>	
<b>Heparin</b>	Safe, not present in breast milk.	<b>Carbamazepine</b>	Preferable over others
<b>Warfarin</b>	Warfarin can be used, very small quantities found in breast milk, <b>monitor the infant's prothrombin time during treatment.</b>	<b>Phenytoin</b>	Compatible with breastfeeding
		<b>Valproic acid</b>	Amounts entering breast milk are not sufficient to produce adverse effects
		<b>Lamotrigine</b>	<b>avoid Lamotrigine</b>

## Antidepressants

SSRI

**Paroxetine** is the preferred SSRI in breastfeeding women.

## Other drugs

**Cytotoxic drugs**

Breast feeding should be **avoided**

**Iodine** (radioactive)

Permanent hypothyroidism in infant ,Breast-feeding is **contraindicated**

**Lithium**

Large amounts can be detected in milk (**avoid**)

## CVS drugs

**Atenolol**

Risk of bradycardia and hypoglycemia (**avoid**)

## Drugs of choice in lactation

**Antibiotics**

**safe:** Cephalosporins, penicillins  
**Avoid:** chloramphenicol, quinolones, sulphonamides and tetracyclines

**Antidiabetics**

**safe:** Insulin – oral antidiabetics , **Avoid:** metformin

**IMPORTANT**



## Drugs of choice in lactation

Anticoagulants	Heparin – warfarin
Antithyroid drugs	Propylthiouracil is preferable over others
Analgesics	Acetaminophen(paracetamol)
Anticonvulsants	Carbamazepine -phenytoin
Oral contraceptives	Progestin only pills or minipills are preferred for birth control.
Antiasthmatics	Inhaled corticosteroids - prednisone

**IMPORTANT**

## Summary For Choice Of Drugs

- Route of administration (topical, local, inhalation) instead of an oral form.
- Short acting
- Highly protein bound
- Low lipid solubility
- High molecular weight
- Poor oral bioavailability and No active metabolites
- well-studied in infants

# MCQs

## 1-What is “true” about “Lipid Solubility”:

- A)Lipid Molecules pass more freely
- B)Water Molecules Pass more freely
- C)Equal

## 2)Toddler Children are considered between:

- A)6-12 years
- B)1-5 years
- C)1-5 months

## 3)What is true about “Volume of distribution”:

- A)Large volume of distribution Molecules pass easier than low one.
- B)Low Volume of distribution pass easier than large one.
- c)Equal

## 4-which one of the following drugs is contraindicated during lactation :

- A)Atenolol
- B)Bromocriptine
- C)Haloperidol

## 5-which one of the following antibiotics Should be avoided in premature infants or infants with G6PD deficiency:

- A)amoxicillin
- B)Tetracyclines
- C)Sulfonamides

## 6-Metformin Should be avoided due to: A)

- lactic acidosis
- B)theoretical risk of Reye's syndrome
- C)Theoretical risk of arthropathies

# Good luck!

## Done by Pharmacology team

### 434

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