

# ***Drugs affecting breast milk and lactation***

**Prof. Hanan Hagar/Dr. Saeed Sheikh  
Pharmacology Unit  
College of Medicine**

# Learning issues

Student should be able to :

- **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.**

# LACTATION

- ***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.



# DRUGS AND LACTATION

- **Most drugs administered to breast feeding woman are detectable in milk.**
- **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.**
- **There are many pharmacokinetic and pharmacodynamics changes in pediatrics.**

# Pediatric population are classified into:

- **Newborn:** less than one month old
  - **Preterm neonates:** born before 38 weeks of pregnancy
  - **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

# Pharmacokinetics changes in pediatrics

- Higher gastric pH
- 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.

## Physiologic Differences between Neonates and Adults of Pharmacokinetic Importance (Hilligoss 1980)

|   | Neonate | Adult |
|---|---------|-------|
| Gastric acid output (mEq/10kg/hr)                   | 0.15 ↓  | 2     |
| Gastric emptying time (min)                         | 87 ↑    | 65    |
| Total body water (% of body weight)                 | 78 ↑    | 60    |
| Adipose tissue (% of b.wt.)                         | 12 ↓    | 12-25 |
| Serum albumin (gm/dL)                               | 3.7 ↓   | 4.5   |
| Glomerular filtration rate (ml/min/m <sup>2</sup> ) | 11 ↓    | 70    |

# Factors controlling passage of drugs into breast milk

## Factors related to drugs :

- Molecular weight
- Lipid solubility
- Degree of ionization
- Drug pH
- Protein binding
- Half life
- Oral bioavailability



# Factors controlling passage of drugs into breast milk

## **Maternal factors:**

- Dose of drug
- Route of administration
  - Time of breast feeding
  - Health status
  - Maternal drug concentration

# Factors controlling passage of drugs into breast milk

## **Infants factors:**

- Age
- Body weight
- Health status

# Factors related to drugs

## **Molecular weight:**

- Very small molecules (< 200 Daltons) such as **alcohol**, equilibrate rapidly between plasma and breast milk via the aqueous channels surrounding alveoli.
- Large molecules drugs (>800 Daltons) are less likely to be transferred to breast milk than low molecular weight.
- **Insulin:** MW > 6,000 daltons
- **Heparin:** MW 40,000 daltons

- Monoclonal antibodies, pass very poorly into milk after the first 1st week postpartum.
- 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 infants life.

## **Lipid solubility of the drug:**

Lipid soluble drugs pass more freely into the breast milk than water soluble drugs.

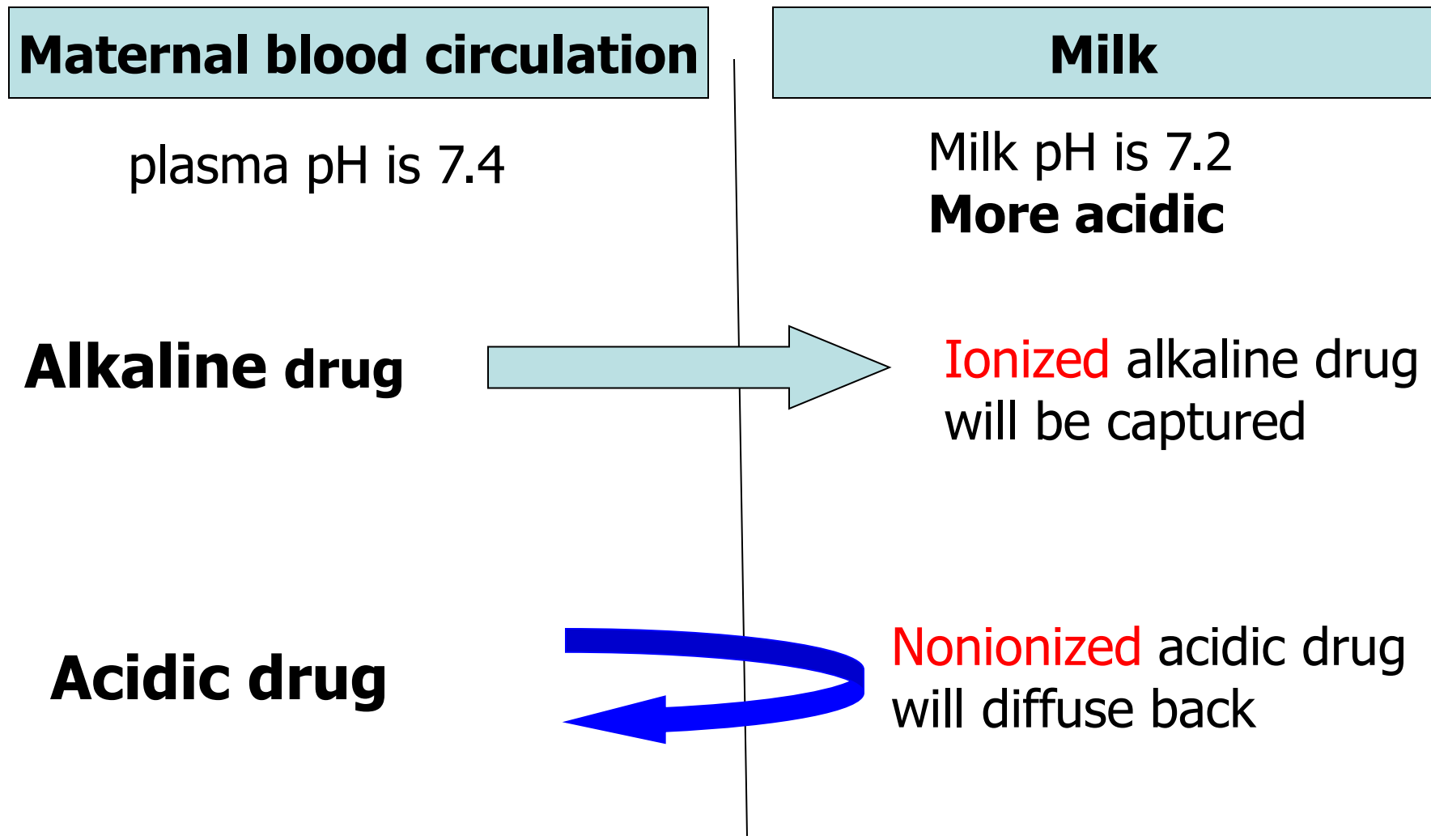
## **Degree of ionization:**

- Ionized form of drugs are less likely to be transferred into breast milk.
- e.g., heparins pass poorly into breast milk

## pH of drug:

- pH of milk is slightly more acidic than maternal blood.
- Weak basic drugs tend to concentrate in breast milk and become trapped secondary to ionization.
- **Weak 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



## Plasma protein binding of drugs

- Drugs circulate in maternal circulation in unbound (**free**) or bound forms to albumin.
- **Only** unbound form gets into maternal milk.
- Definition of good protein binding > 90%
- e.g. warfarin

## Half life of drug

- Avoid the use of drugs with long half lives
- short half life ( $t_{1/2}$ ) are preferable.
- Oxazepam *vs* diazepam



## **Volume of distribution**

Transfer of drug from maternal blood to milk is low with drugs that have large volume of distribution ( $V_d$ ).

## **Factors related to mother**

- Dose of the drug
- Route of administration
- Time of breast feeding
- Health status
- Maternal drug concentration

# Factors related to mother

## Route of administration

- Route of administration affect the concentration of the drug in maternal blood.
- Maternal use of **topical preparations (creams, nasal sprays or inhalers)** are expected to carry less risk to a breastfed infant than systemically administered drugs.

# Factors related to mother

## Time of breastfeeding

- The **concentration** of the drug in the milk at the time of feeding.
- Lactating mother should take medication just **after nursing and 3-4 hours before the next feeding.**

(to allow time for drug to be cleared from the mother's blood – drug concentration in milk will be low).

# Health status

## Breastfeeding is contraindicated in case of:

- Mother HIV
- Active, untreated TB in mother
- Herpes on breast
- Use of illegal drugs by mother
- Certain medications

# **Factors related to neonates**

- Age
- Body weight
- Health status

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

- The **amount** of milk consumed.
- The **amount** of drug absorbed from GI.
- The **ability** of the baby to eliminate the drug.

# Age & Health status

## Special cautions are required in

- Premature infants
- Low birth weight
- Infants with G6PD deficiency
- Infants with impaired ability to metabolize /excrete drugs e.g. hyperbilirubinemia.





# Neonatal hyperbilirubinemia

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

## **Examples for oxidizing drugs:**

**Antibiotics** sulfonamides, trimethoprim

**Antimalarials:** Primaquine

# Neonatal Methemoglobinemia

- Infants under 6 months of age are particularly prone to develop methemoglobinemia upon exposure to some oxidizing drugs.
- **Methemoglobin** is an oxidized form of hemoglobin that has a decreased affinity for oxygen → **tissue hypoxia.**

# Drugs contraindicated during lactation

- Only few drugs are totally contraindicated
- **Anticancer 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

|   |   |
|---|---|
| <b>Penicillins</b><br><b>Ampicillin</b><br><b>amoxicillin</b> | <b>No significant adverse effect</b><br><b>allergic reactions, diarrhea</b>   |
| <b>Cephalosporins</b>   | <b>No significant adverse effect</b><br><b>Alterations to infant bowel flora</b>  |
| <b>Macrolides</b><br>erythromycin<br>clarithromycin           |   |
| <b>Sulfonamides</b><br>(co-trimoxazole)                       | hyperbilirubinemia -neonatal jaundice<br><b>Should be avoided</b> in premature infants or<br>infants with G6PD deficiency |

# Antibiotics

|   |  |
|---|--|
| <b>Quinolones</b>                       | Theoretical risk of arthropathies<br><b>Should be avoided</b>  |
| <b>Chloramphenicol</b>                  | “Gray baby” syndrome<br><b>avoid</b>   |
| <b>Tetracyclines</b>                    | Absorption by the baby is probably prevented by chelation with milk calcium. <b>Avoid</b> due to possible risk of teeth discoloration. |
| <b>Sulfonamides</b><br>(co-trimoxazole) | hyperbilirubinemia -neonatal jaundice<br><b>Should be avoided</b> in premature infants or infants with G6PD deficiency                 |

# Sedative/hypnotics

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



# Antidiabetics

**Insulin**

**Oral antidiabetics**

**Metformin**

safe

compatible

avoid due to lactic acidosis

# Analgesics

**Paracetamol**

safe

**Ibuopfen**

compatible

**Aspirin**

avoid due to theoretical risk of  
Reye's syndrome

# Oral contraceptives

Non hormonal method should be used

Avoid estrogens containing pills

Estrogens ↓ milk quantity

Progestin only pills or minipills are preferred for birth control.

## **Antithyroid drugs**

**Propylthiouracil**

**Carbimazole**

**Methimazole**

**potassium iodide**

May suppress thyroid function in infants.

Propylthiouracil should be used rather than carbimazole or methimazole.

## **Anticoagulants**

**Heparin**

Safe, not present in breast milk.

**Warfarin**

Warfarin can be used, very small quantities found in breast milk, **monitor the infant's prothrombin time during treatment.**

## **Anticonvulsants**

**Carbamazepine**

**Phenytoin**

**Valproic acid**

**Lamotrigine**

Preferable over others

Compatible with breastfeeding

Amounts entering breast milk are not sufficient to produce adverse effects

Infants must be monitored for CNS depression

**avoid**

## **Antidepressants**

**SSRI**

Paroxetine is the preferred SSRI in breastfeeding women.

|                                 |   |
|---------------------------------|---|
| <b>Cytotoxic drugs</b>          | <b>Breast feeding should be avoided</b>   |
| <b>Iodine<br/>(radioactive)</b> | <b>Permanent hypothyroidism in infant<br/>Breast-feeding is contraindicated</b> |
| <b>Lithium</b>                  | <b>Large amounts can be detected in milk<br/><br/>avoid</b>                     |
| <b>CVS drugs<br/>Atenolol</b>   | <b>Risk of bradycardia and hypoglycemia<br/><br/>avoid</b>                      |

# Drugs of choice in lactation

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

# Summary for choice of drug

- **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
- **No** active metabolites
- **well-studied** in infants



## General considerations

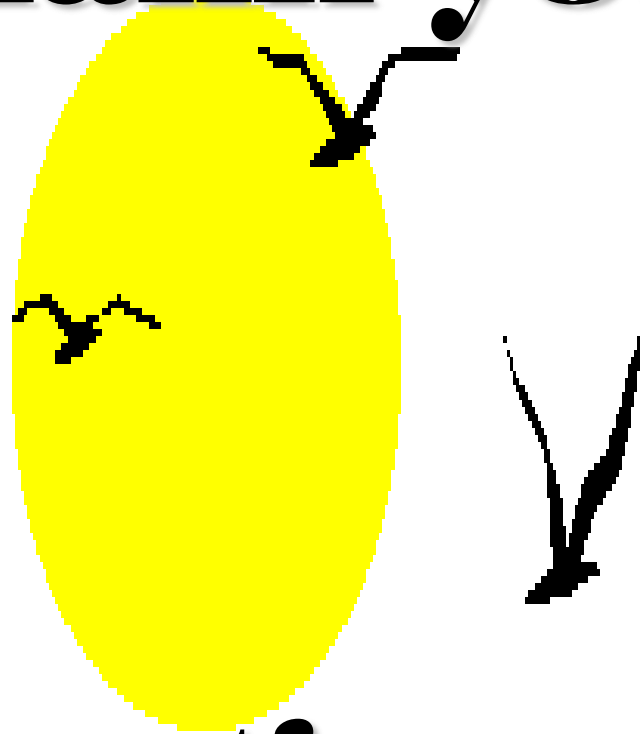
- Infants should be monitored for adverse effects e.g. feeding, sedation, irritability, rash, etc.
- Drugs with no safety data should be avoided or lactation should be discontinued

# General considerations

- Do not guess
- Use the following sources:
  - Use Medication and Mothers' Milk  
([www.iBreastfeeding.com](http://www.iBreastfeeding.com))
  - Use lactmed or toxnet  
(<http://toxnet.nlm.nih.gov> )

a free online database with information on drugs and lactation, is one of the newest additions to the National Library of Medicine's TOXNET system, a Web-based collection of resources covering toxicology, chemical safety, and environmental health.

**Thank you**



**Questions ?**