

Drugs during Lactation

- * Breast feeding for baby.
 - less gastric, respiratory, & UT infection
 - less obesity & juvenile-onset DM
 - less atopic diseases
 - lower BP & cholesterol as adults

- * Breast feeding for mother:
 - ↓ risk of pre-menopausal breast Ca
 - ↑ mother-infant bond

- * Almost all drugs enter milk by passive diffusion → the drug should be:
 - > Non polar > lipid soluble > Hydrophobic
 - > Unionized > Not protein-bound

- * Serum pH: 7.4 Milk pH: 6.8 - 7.0
 - ↳ if a drug was non-ionized in serum & traversed to milk, the pH of milk will ionize it, making it unable to diffuse back → ↑ concentration → Adverse effect

* Drug parameters affecting diffusion.

- ① pKa (ionized → polar → can't cross
Unionized → non-polar → can cross)
 - ($pH \propto \frac{milk}{plasma}$) > Basic drugs (Erythromycin)
 - ↳ unionized → will get ionized in milk (more acidic) → trapped in milk.
 - > Acidic drugs (Penicillin)
 - ↳ more ionized at higher pH
 - ↳ trapped in serum.

- ② Protein binding ($\frac{1}{2}$)
 - ↳ pr-bound drugs (Warfarin) are retained in serum → only small free portion pass → not concentrated enough to harm.

- ③ Lipophilicity (\propto)
 - ↳ water soluble won't cross effectively
 - ↳ CNS-active drugs → cross
 - ↳ suppress CNS function in baby
 - ↳ NSAIDs pass minimally
 - ↳ Sotalol pass significantly
 - ↳ becomes hydrophilic in milk & ionized → will be trapped.

- ④ Molecular weight ($\frac{1}{2}$)
 - < 200 → pass through small pores
 - in between → dissolve in lipid layer
 - > 6000 → excluded from milk

Notes!!

- * Milk pH (6.8 - 7.0), less buffering capacity, higher fat content, lower protein content.
- * 1st week of life → large gaps between alveolar & → more passage ^{Thus} The principles only apply after the 2nd week of life, as the gaps close due to prolactin
- * Colostrum → secreted in first 2 days after birth → high in Ig, lymphocytes, & macrophages. Also high in drugs, yet with small amount since it's produced in small volume.

* Factors that ↑ risk:

- ① Inherent drug toxicity
 - Antineoplastics, Radionuclides, Iodine-containing
- ② Multiple maternal therapy
 - especially if they have the same adverse effects
 - Anticonvulsants & Psychotropics
- ③ Active metabolites
 - Benzodiazepines → prolonged $T_{1/2}$ = prolonged exposure = accumulation
- ④ Drugs with long $T_{1/2}$
 - Fluoxetine
- ⑤ Gestational age
 - Premature infant = less clearance
- ⑥ Maternal drug regimen
 - chronic Tx & multiple medications

* How to reduce risk of drugs:

1. Use safe drugs
2. Give maternal dose immediately after feeding the baby
3. If single dose of hazardous material
 - ↳ no breast feeding until 5 $T_{1/2}$
 - ↳ pump milk & discard it meanwhile.
4. If once daily → dose before the infant's longest sleep period
5. No self-medication
6. Lowest effective dose for the shortest time possible.
7. Simple regimen
8. Avoid new drugs (less safe, not much info)
9. Monitor exposed infant
10. Drugs with short $T_{1/2}$ & high pr-binding

* Drugs effects on Lactation

- Dopamine Agonist (Cabergoline)
 - ↳ ⊖ prolactin → ↓ milk production
- Estrogen & OCP → ↓ lactation
- Dopamine Antagonist (Domperidone, Metoclopramide)
 - ↳ 10 mg by 3 for 7-14 days.
 - ↳ pharmacological galactagogues
 - ↳ ⊕ prolactin secretion
 - ↳ ↑ milk production

* Special situations

- ① Neonates & premature babies:
 - less elimination • high TBW
 - prolonged gastric emptying → ↑ absorption
 - less protein binding
 - less conjugation capacity by UDP-glucuronotransferase
- ② G6PD deficiency
 - Erythrocytes more susceptible to oxidative stress + only small amount will cause hemolysis
- ③ Recreational drug use
 - ↳ encourage to avoid if not → stop nursing
 - 1. Cannabis, LSD, Cocaine
 - 2. Chronic use of Alcohol → stop nursing
 - ↳ ↓ lactation + infant sedation, fluid retention, & hormone imbalance + disturb nursing
 - 3. Nicotine
 - ↳ ↓ milk production
 - 4. Caffeine
 - ↳ if > 10 cups/day → infant fussiness, jitteriness, & poor sleep.

* Drugs contraindicated during lactation:

1. Hazardous to milk production
 - Dopamine agonists (including Sympathomimetics)
 - > Propinrole > Selegiline
 - > Rotigotine > Dopamine
 - Decongestants
 - Ethanol
 - Nicotine
 - Tamoxifen / Alloxifene → Selective Estrogen receptor antagonists
2. Hazardous to infant
 - Antiarrhythmic (Amiodarone)
 - Anticholinergic
 - Antibiotics (Fluoroquinolone, Dapsone, Rifabutin, Flucytosine..)
 - CNS stimulants
 - Cytotoxic agents
 - Illicit substances
 - Immunosuppressants
 - Monoamine oxidase inhibitors
 - Radioactive substance (I^{131})
 - Tetracycline
 - Tricyclic agent (Doxepin)
 - Vit A derivatives (for psoriasis) (Isotretinoin)
 - Lithium

- Botanical galactagogues (used before starting pharmacological Tx.)
 - > Fenu greek حبة
 - > Fennel شومر
 - > Anise يانسون
 - > Milk thistle خرفش
 - > Barley شعير