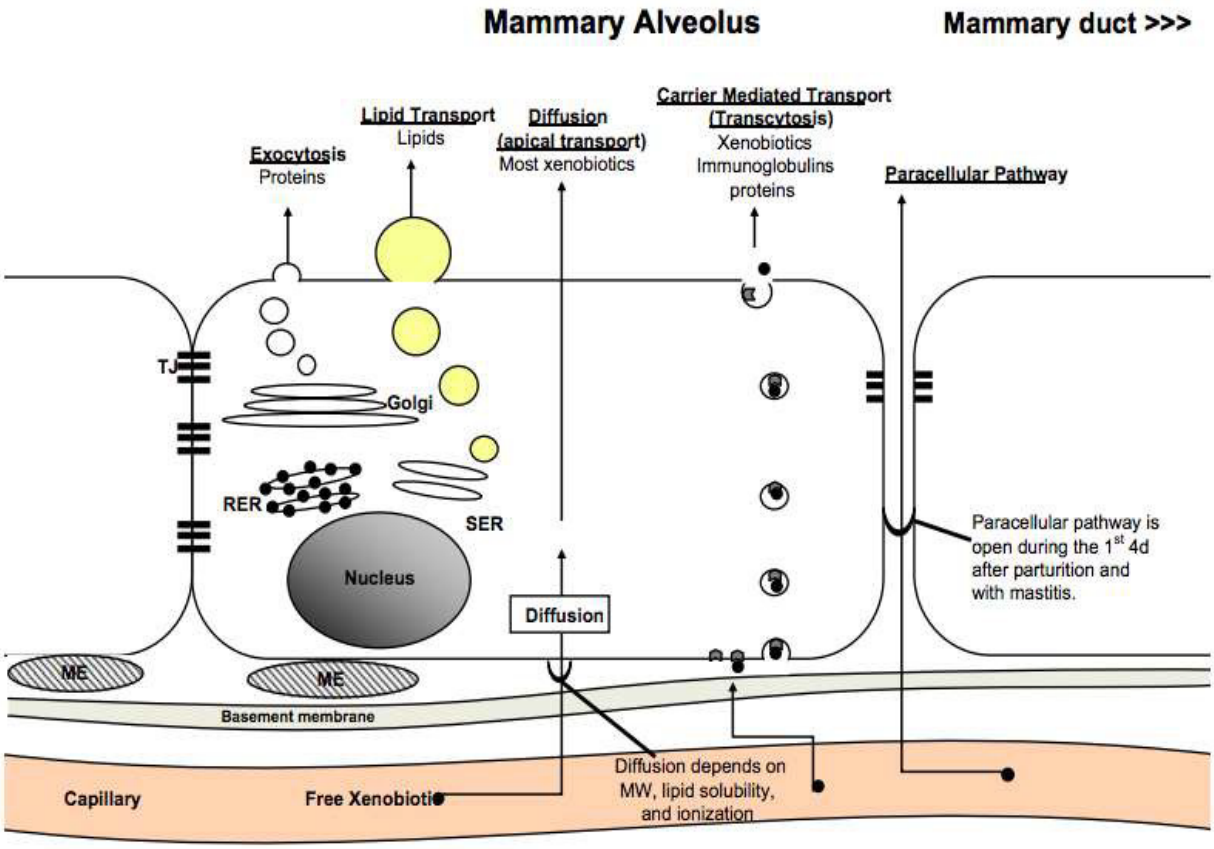
Clinical Pharmacology & Toxicology Pearl of the Week

~ Medications and Breastfeeding ~

- ✓ Almost all drugs appear in human breast milk to some degree
- ✓ As with all xenobiotics, the dose determines the potential for toxicity

How is breast milk synthesized?

- ✓ The mammary alveolus is similar to the pulmonary alveoli
  - Inner alveolus is only one cell layer away from capillaries
- ✓ Alveolar cell synthesizes proteins and transports lipids into the inner alveolus making the bulk of the breast milk
- ✓ Xenobiotics can enter breast milk through three mechanisms:
  - Active carrier transport: Used for immunoglobulins and proteins. Xenobiotics transported includes nitrofurantoin, penicillins, and ranitidine
  - Passive diffusion: Major pathway for drug transfer. Dependent on xenobiotic concentration gradient, molecular size, lipid solubility, and ionization
  - Paracellular pathway: Diffusion down concentration gradient. Only open during first four days of breast feeding and during inflammatory conditions including mastitis.



Source: Hendrickson et al, Clinical Toxicology 2012, 50:1, 1-14

Factors that determine xenobiotic potency in breast milk

I. Maternal determinants:
   a. Maternal absorption, distribution, metabolism, and elimination pharmacokinetics
      i. Example: Ultra-rapid metabolizers of codeine to morphine via CYP-2D6 may transfer larger quantities to their infant in their breast milk.

II. Xenobiotic determinants:
   a. Ability to diffuse through membranes: lower molecular weight, lipid solubility, and higher maternal free drug concentration

III. Human milk determinants:
   a. Milk pH is 7.0. Tends to ion-trap weak bases, increasing their concentrations
   b. Example: Amphetamines, opioids
   c. High lipid of milk leads to high concentrations of lipophilic xenobiotics

IV. Infant determinants:
   a. Infant absorption, distribution, metabolism, and elimination pharmacokinetics
   b. Volume of meals relative to body weight (highest at birth and trends down)
   c. Drug tolerance can develop if exposed to xenobiotic in utero

Do I need to pump and discard after drinking alcohol?

- ✓ Breast milk is generated as needed on demand. There is no storage of milk within breast tissue.
- ✓ Drug levels within the breast milk are dependent on current maternal blood levels.
- ✓ Discarding breast milk is discouraged
  - Can potentially lead to:
    - Decreased milk supply
    - Switch to formula feeding
    - Discontinuation of breast feeding
    - Discontinuation of required medications
- ✓ Breast feeding while actively intoxicated is discouraged due to risk of sedation and smothering the child

Infant alcohol exposure calculation
Maternal ETOH level 21 mmol/L (BAC 0.1%)
Infant meal: 100mL = 2.1 mmol ETOH
2.1 mmol ETOH in 5 kg child = 0.52 mmol/Kg
Comparison: 1 std drink in 70 kg adult = 5.2 mmol/Kg

Contraindications to breast feeding

- ✓ Infant with classic galactosemia or maple syrup urine disease
- ✓ Maternal HIV
- ✓ Severe maternal illness preventing mother from caring for child
- ✓ Communicable disease that may be transmitted to child (Ex: TB, brucellosis)
- ✓ Active maternal substance abuse (risk of transmission to child, risk of inability to care for child
- ✓ Certain medications may preclude breastfeeding in the short term

Drug safety in breastfeeding resources

- ✓ Mother to Baby - https://mothertobaby.org/
- ✓ Lactmed - https://www.ncbi.nlm.nih.gov/books/NBK501922/

References:

1. Robert G. Hendrickson & Nathanael J. McKeown (2012) Is maternal opioid use hazardous to breast-fed infants? Clinical Toxicology, 50:1, 1-14.
2. Drugs and Lactation Database. (LactMed). National Library of Medicine.
3. Mother to Baby, Organization of Teratology Information Specialists.
4. Contraindications to Breastfeeding | Breastfeeding special circumstances | CDC

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found HERE.

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