

Drugs in Breastmilk: Benefits versus Risks

Department of Health and Human Services

Food and Drug Administration-Center for Drug Evaluation and Research

“Evaluation of the Safety of Drugs and Biological Products used during Lactation”

ADEPT - Lactation Workshop

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The background consists of several overlapping, semi-transparent geometric shapes in various shades of green and teal. A large, dark teal shape is at the top, with a lighter green shape below it. A wide, medium-teal horizontal band is in the center, containing the text. Below this band, there are more overlapping shapes in dark teal and light green, creating a layered, mountain-like effect.

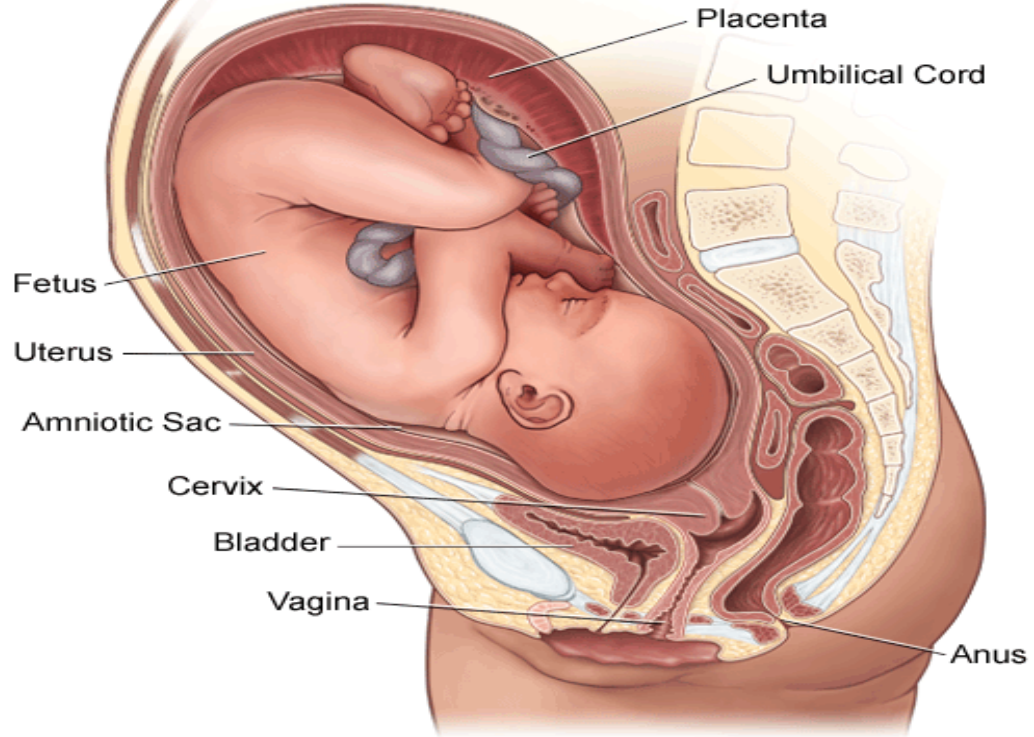
I have no conflicts of interest
involving this presentation.





Six blindfolded wise men
examine an elephant . . .

Fetus in Utero



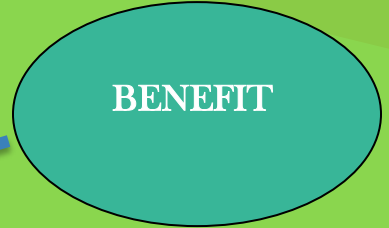
Medication While
Breastfeeding:
Is this a problem?



Risk: Benefit

RISK

BENEFIT



The Compelling Reasons to Breastfeed

- Species Specificity
- Nutritional Advantages
- Infection Protection
- Immunological Protection
- Allergy Protection
- Psychological Benefits
- Disaster Preparedness



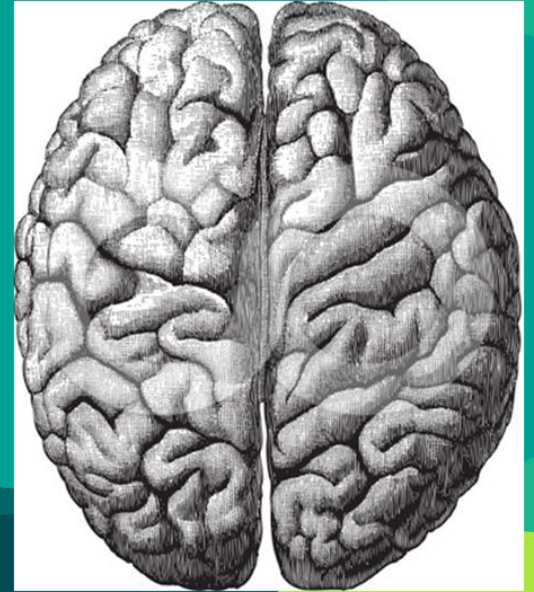
What is the Evidence?

- Cochrane Reviews confirm advantages:
 - Brain development
 - Immunological protection
 - Infection protection
 - Ect.



Food for the Brain

- Cholesterol
- Taurine
- DHA (docosahexaenoic acid)



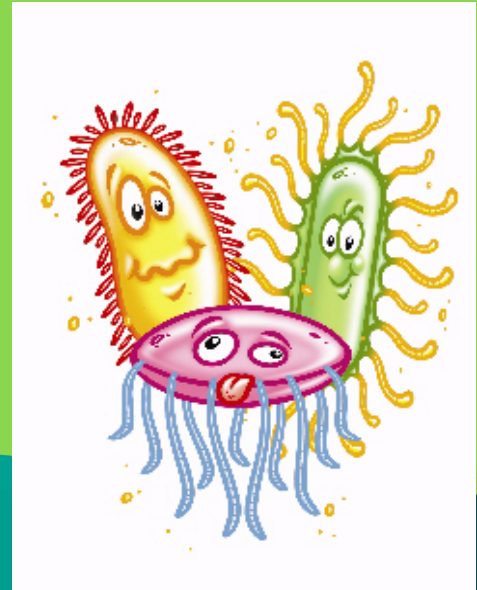
Protection Against Obesity

- Milk constituents
- Can not overfeed a breastfeeding infant
- Observations of infants feeding by bottle



Infections that Are Lower in Incidence in Breastfed Infants

- Respiratory tract infection
- Otitis media
- Pneumonia
- Urinary infection
- Necrotizing enterocolitis
- Diarrhea
- Invasive bacterial infection



Breastfeeding Protects Against



- Childhood cancers
- Lymphoma
- Acute lymphatic leukemia
- Crohn's disease
- Celiac disease
- Childhood onset diabetes

When there is:

↓ illness = ↓ clinic visits

↓ severity of illness = ↓ hospitalizations

↓ need for medical care = ↓ costs



And All This Reduces Health Care Costs



Known Benefits of Breastfeeding for the Mother

- Improved postpartum recovery
- Psychological benefits, including a feeling of empowerment and the development of a strong human bond between mother and infant
- Decreased risk of osteoporosis
- Reduced risk of pre-menopausal breast cancer and ovarian cancer
- Reduced risk of pregnancy initiated long-term obesity



Female breast from infancy to lactation with corresponding cross-section and duct structure

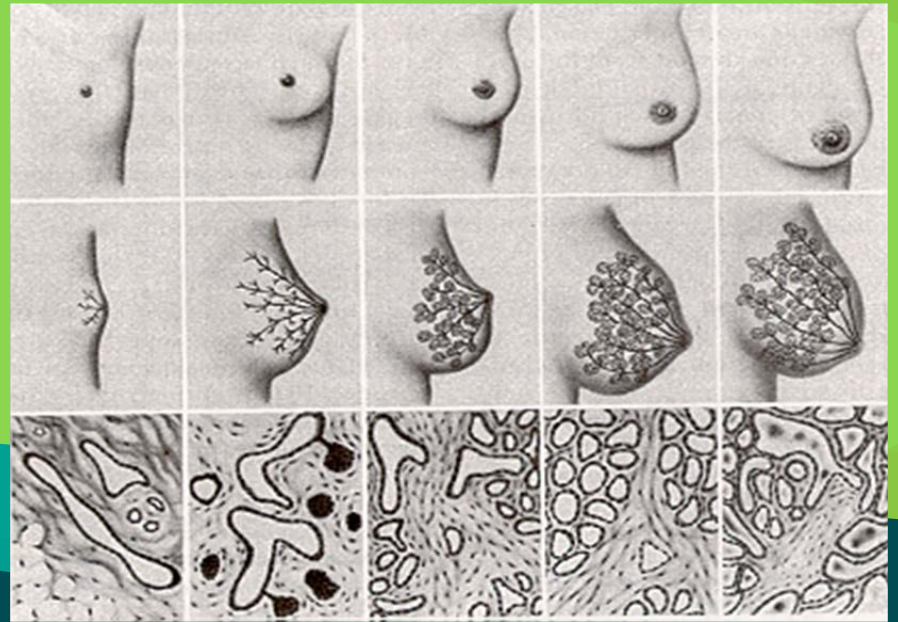
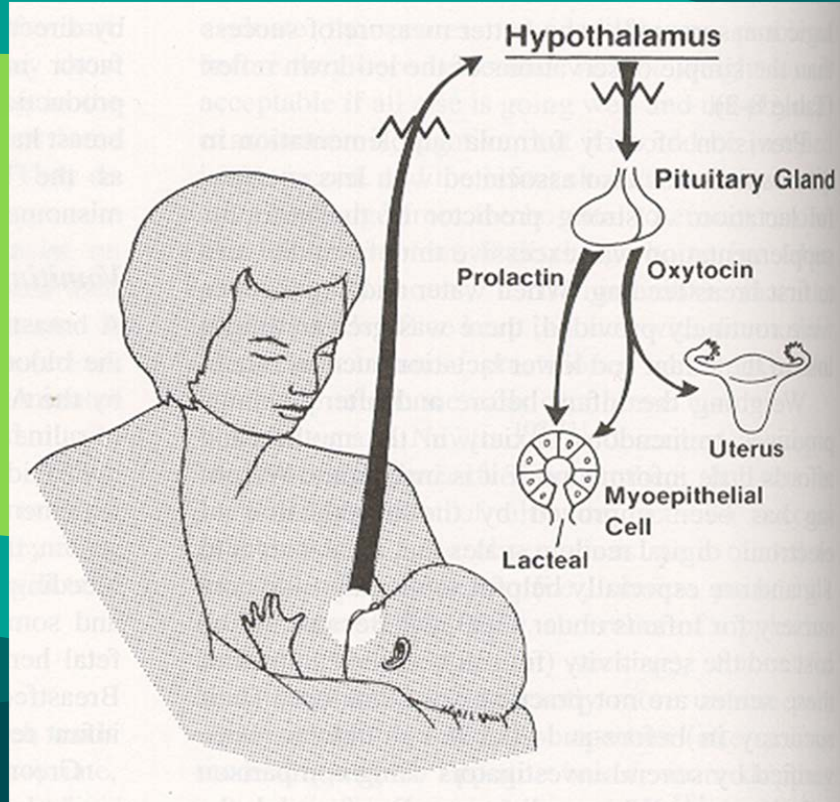


Diagram of ejection reflex arc



How Do Drugs Pass into Milk?

Properties

Plasma \longrightarrow Milk

Infant - Can the infant absorb, detoxify, and excrete drug?

Route of Administration of Drug

1. Oral
2. Intravenous (IV)
3. Intramuscular (IM)
4. Transdermal Drug Delivery System (TDDS)

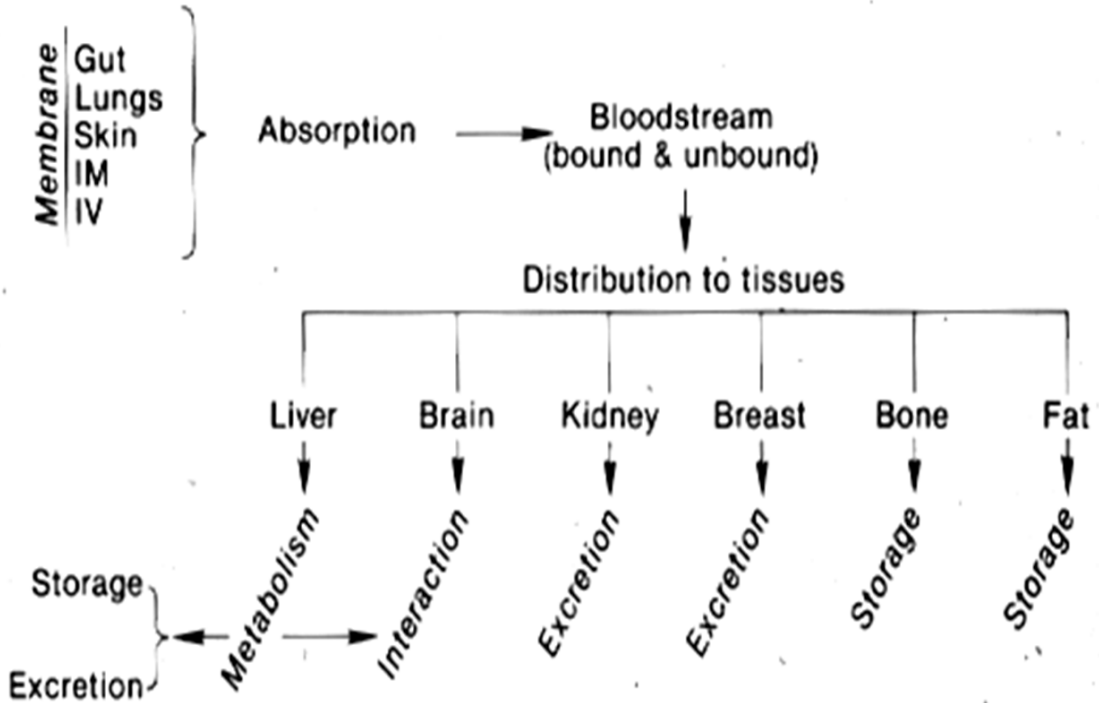


Drug Characteristics

- Absorption rate
- Half-life of peak serum time
- Dissociation constant
- Volume of distribution

Drug Characteristics

- Size of Molecule
- Degree of Ionization
- pH of Substrate
 - Plasma 7.4
 - Milk 6.8
 - Solubility
 - In water
 - In lipids
 - Protein binding more to plasma than to milk protein



Predicated Distribution Ratios of Drug Concentrations in Milk and Plasma

| | <u>Milk/Plasma Ratio</u> |
|---|--------------------------|
| Highly lipid-soluble drugs | ~ 1 |
| Highly protein-bound drugs in maternal serum | < 1 |
| Small (mol. wt. < 200) water-soluble drugs | ~ 1 |
| Weak acids | ≤ 1 |
| Weak bases | ≥ 1 |
| Actively transported drugs | > 1 |

M/P

Milk/Plasma Ratio



Effect on Nursing Infant

1. Absorption from GI tract
2. Infant's ability to detoxify
3. Infant's ability to excrete



Minimizing Effect of Maternal Medication



Adjustments can be made to minimize the effect:

1. Do not use long-acting form of the drug
2. Schedule dose so least amount possible gets into the milk
3. Watch the infant for any unusual signs or symptoms
4. Choose the drug that produces the least amount in the milk
5. Temporarily pump and discard

Specific Drug Categories



Categories of Drugs by Risk (AAP Classification)

- Contraindicated drugs (category I)
- Drugs of abuse (category II)
- Temporary cessation of breastfeeding (pump and discard milk) (category III)
- Pharmacologic properties that guide decision making when the drug has not been studied during lactation

Cytotoxic Drugs that May Interfere with Cellular Metabolism of the Nursing Infant

| Drug | Reason for Concern, Reported Sign or symptom in Infant, or Effect on Lactation |
|------------------|---|
| Cyclophosphamide | Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia |
| Cyclosporine | Possible immune suppression; unknown effect on growth or association with carcinogenesis |
| Deoxorubicin* | Possible immune suppression; unknown effect on growth or association with carcinogenesis |
| Methotrexate | Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia |

*Drug is concentrated in human milk

Drugs of Abuse for Which Adverse Effects on the Infant during Breastfeeding have been Reported*

| Drug | Reported Effect or Reasons for Concern |
|---------------|---|
| Amphetamine** | Irritability, poor sleeping pattern |
| Cocaine | Cocaine intoxication: irritability, vomiting, diarrhea, tremulousness, seizures |
| Heroin | Tremors, restlessness, vomiting, poor feeding |
| Marijuana | Only 1 report in literature; no effect mentioned; very long half-life for some components |
| Phencyclidine | Potent hallucinogen |

*The Committee on Drugs strongly believes that nursing mothers should not ingest drugs of abuse, because they are hazardous to the nursing infant and to the health of the mother.

** Drug is concentrated in human milk.

Radioactive Compounds that Require Temporary Cessation of Breastfeeding*

| Compound | Recommended Time for Cessation of Breastfeeding |
|---|--|
| Copper 64 (^{64}Cu) | Radioactivity in milk present at 50 h |
| Gallium 67 (^{67}Ga) | Radioactivity in milk present for 2 wk |
| Indium 111 (^{111}In) | Very small amount present at 20 h |
| Iodine 123 (^{123}I) | Radioactivity in milk present up to 36 h |
| Iodine 125 (^{125}I) | Radioactivity in milk present for 12 d |
| Iodine 131 (^{131}I) | Radioactivity in milk present 2-14 d, depending on study |
| Iodine ^{131}I | If used for treatment of thyroid cancer, high radioactivity may prolong exposure to infant |
| Radioactive sodium | Radioactivity in milk present 96 h |
| Technetium 99m ($^{99\text{m}}\text{Tc}$), $^{99\text{m}}\text{Tc}$ microaggregates, $^{99\text{m}}\text{Tc O}_4$ | Radioactivity in milk present 15 h to 3 d |



* Consult nuclear medicine physician before performing diagnostic study so that radionuclide that has the shortest excretion time in breast milk can be used. Before study, the mother should pump her breast and store enough milk in the freezer for feeding the infant; after study, the mother should pump her breast to maintain milk production but discard all milk pumped for the required time that radioactivity is present in milk. Milk samples can be screened by radiology departments for radioactivity before resumption of nursing.

Maternal Medication Is Usually Compatible with Breastfeeding

Drug

Reported Sign or Symptom in Infant or Effect on Lactation

1) Caffeine



Irritability, poor sleeping pattern, excreted slowly; no effect with moderate intake of caffeinated beverages (2-3 cups per day)

2) Methadone

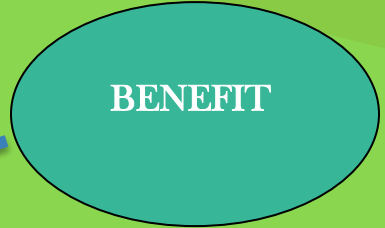


None

Risk: Benefit

RISK

BENEFIT



Breastfeeding is the most precious gift
a mother can give to her infant.



When there is infection or disease it may be
a life saving gift.
When there is poverty it may be the only gift.

Lawrence 1992

