

# Update on **Medication** in Lactation

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# Why We Care

- Most moms take something
- Most meds ok with breastfeeding
- Most pharmacies don't teach this
- Many providers don't know this
- Most EMR systems not based on current evidence
- Many moms quit breastfeeding/pumping unnecessarily

# Why We Care

What has changed?

The milk hasn't changed

Moms are still programmed to make perfect milk for their babies

Babies are still programmed to breastfeed



# Why We Care

Some things have changed

CA CC 43.3 1977

AB1025 10/12/2001

SB1275 2004

JCAOH 4/1/2010

SB502 10/6/2011

SB402 10/9/2013

ACA 3/23/2010



# Baby Friendly - 10 Steps

1. Have a written breastfeeding policy that is routinely communicated to a health care staff
2. Train all health care staff in the skills necessary to implement this policy
3. Inform all pregnant women about the benefits and management of breastfeeding
4. Help mothers initiate breastfeeding within one hour of birth
5. Show mothers how to breastfeed and how to maintain lactation, even if they are separated from their infants
6. Give infants no food or drink other than breast milk, unless medically indicated
7. Practice rooming in – allow mothers and infants to remain together 24 hours a day
8. Encourage breastfeeding on demand
9. Give no pacifiers or artificial nipples to breastfeeding infants
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or birth center

# Preventive Services covered by the Affordable Care Act

- There are 22 covered preventive services for Women, Including Pregnant Women
  - The eight new prevention-related health services marked with an asterisk (\*) must be covered with **no cost-sharing** in plan years starting on or after August 1, 2012
1. **Anemia** screening on a routine basis for pregnant women
  2. **Bacteriuria** urinary tract or other infection screening for pregnant women
  3. **BRCA** counseling about genetic testing for women at higher risk
  4. **Breast Cancer Mammography** screening every 1 to 2 years for women over 40
  5. **Breast Cancer Chemoprevention** counseling for women at higher risk
  6. **Breastfeeding comprehensive support and counseling from trained providers, as well as access to breastfeeding supplies, for pregnant and nursing women \***
  7. **Cervical Cancer** screening for sexually active women
  8. **Chlamydia Infection** screening for younger women and other women at higher risk
  9. **Contraception:** Food and Drug Administration-approved contraceptive methods, sterilization procedures, and patient education and counseling, not including abortifacient drugs\*
  10. **Domestic and interpersonal violence** screening and counseling for all women\*
  11. **Folic Acid** supplements for women who may become pregnant

# Preventive Services covered by the Affordable Care Act

12. **Gestational diabetes** screening for women 24 to 28 weeks pregnant and those at high risk of developing gestational diabetes\*
13. **Gonorrhea** screening for all women at higher risk
14. **Hepatitis B** screening for pregnant women at their first prenatal visit
15. **Human Immunodeficiency Virus (HIV)** screening and counseling for sexually active women\*
16. **Human Papillomavirus (HPV) DNA test:** high risk HPV DNA testing every three years for women with normal cytology results who are 30 or older\*
17. **Osteoporosis** screening for women over 60 depending on risk factors
18. **Rh Incompatibility** screening for all pregnant women and follow-up testing for women at higher risk
19. **Sexually Transmitted Infections (STI) counseling** for sexually active women\*
20. **Tobacco Use** screening and interventions for all women, and expanded counseling for pregnant tobacco users
21. **Urinary tract or other infection screening** for pregnant women
22. **Well-woman visits** to obtain recommended preventive services\*

# Future Trends

- You will likely be seeing more breastfeeding patients
- They will likely have questions about medications
- You will likely not have a lot of time to do a thorough risk/benefit analysis



# Risk/Benefit Analysis

Often the known benefits of breastfeeding  
outweigh the  
theoretical risks of medication exposure



# Medication in Mother's Milk

- The breast is a fancy sweat gland
- In general, about 1% of maternal dose gets into milk
- Can we give medication to baby?
- Many parameters:
  - MW, pH, PB,  $\frac{1}{2}$  life, oral bioavailability
- Thomas Hale, Pharm D (bible)

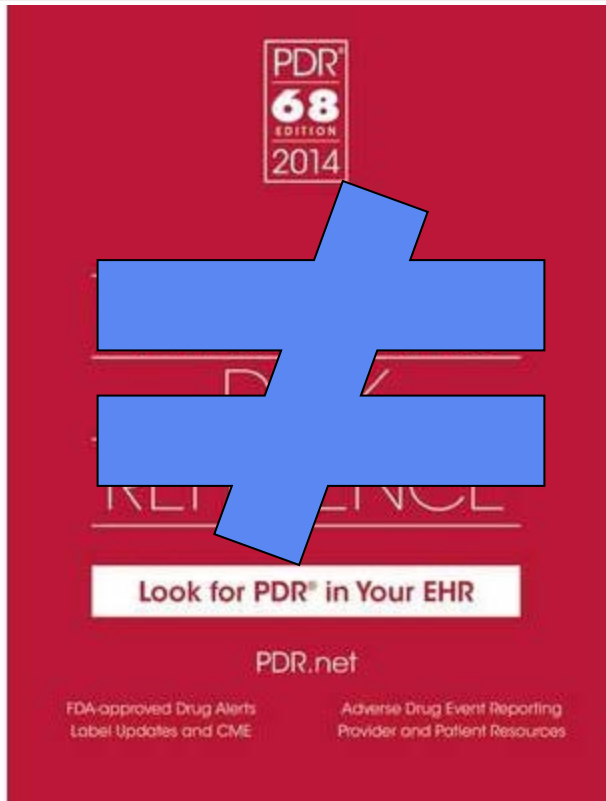
# Meds Moms Should Take

If the medication returns the body to a normal physiologic state, then it is in the best interest of both Mom and baby, for a nursing Mom to take these meds:

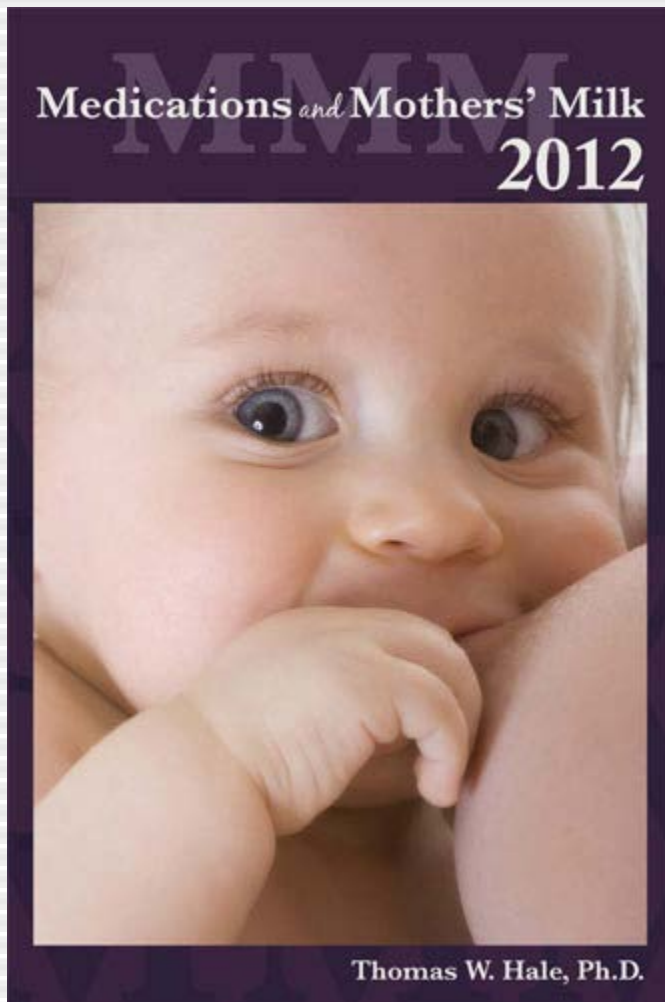
Insulin

Synthroid

# Unreliable Reference



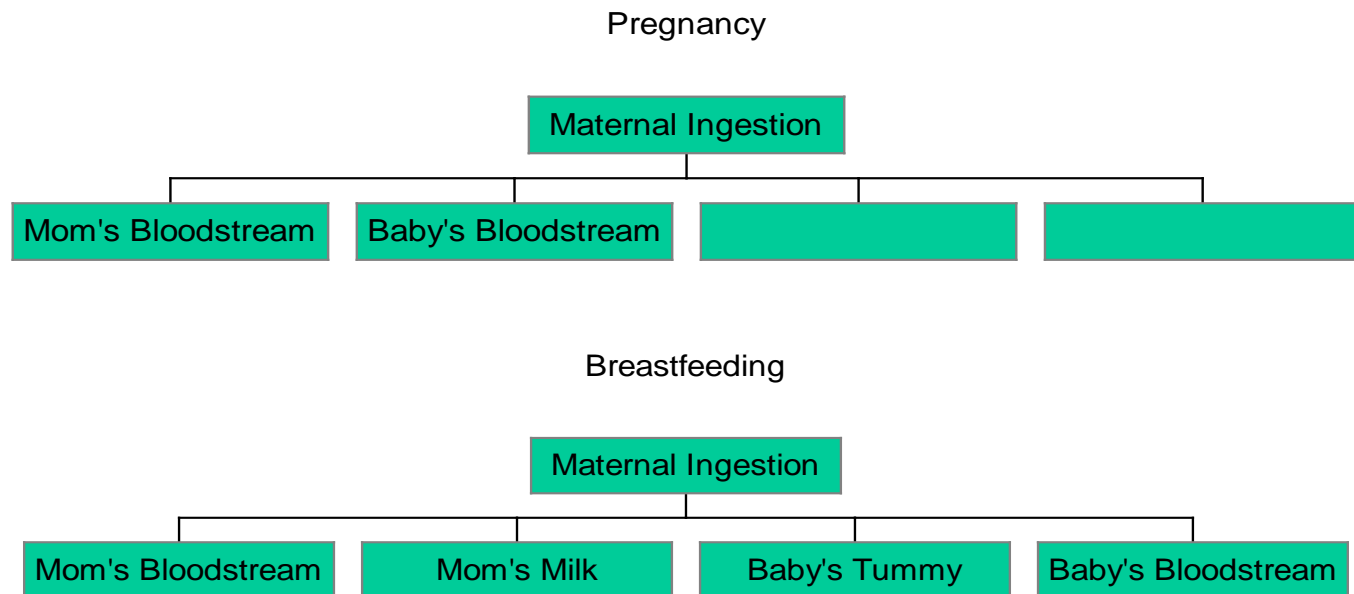
# Reliable Reference



*Medications and Mothers' Milk*  
by Thomas W. Hale, Ph.D.

# Maternal Medication Analysis

## The Journey



# Medication Risk/Benefit Ratio

Hale Rating L1 - Safest

Hale Rating L2 - Safer

Hale Rating L3 - Moderately Safe

Hale Rating L4 - Possibly hazardous

Hale Rating L5 - Contraindicated

- Based on ingestion volumes of 150cc/kg/day and maximum maternal concentrations
- Includes the American Academy of Pediatrics' review of medication for use in breastfeeding mothers
- Details on individual studies
- Alternatives proposed
- Also includes pregnancy risk

# Critical Analysis

Parameter	Definition	+ Breastfeeding
T 1/2	Half Life	SHORT
PHL	Peds Half Life	SHORT
M/P	Milk/Plasma Ratio	<1
PK	Peak Concentration	SHORT
PB	Protein Binding	HIGH
Oral	Oral Bioavailability	LOW
Vd	Volume of Distrib.	DWAI
pKa	Cousin of pH	LOW
MW	Molecular Weight	>200-500



# Critical Analysis

- $T_{1/2}$  = MEDICATION HALF LIFE
- PHL = PEDIATRIC HALF LIFE
  - In general, the shorter the better for nursing moms and babies
  - Keep in mind that there are asterisks \*

# Critical Analysis

- **M/P = MILK / PLASMA RATIO**
  - This is the ratio of medication that reaches the milk compared with the concentration of medication in maternal plasma
  - When the M/P is  $<1$ , the medication is safer, less likely to enter the milk

# Critical Analysis

- **PK = Peak Concentration**
  - This is the time it takes for the medication to reach its peak serum concentration
  - If the P/K is short, this allows for discrete timing of medication and nursing
    - To minimize medication exposure for the baby, Mom can nurse the baby prior to taking the medication. The subsequent nursing session can be delayed until the medication peak has passed

# Critical Analysis

- **PB = Protein Binding**
- The higher the PB, the better for breastfeeding
- If a medication is highly bound to protein in the maternal circulation, it is less likely to cross over into the milk

# Critical Analysis

- Oral Bioavailability
  - This is a really important one!!
  - For breastfeeding, low is better
  - If the medication has low oral bioavailability, then not much medication is going to get past the stomach
  - Examples are insulin and heparin

# Critical Analysis

- **Volume of Distribution**
- How widely the drug is distributed throughout the body
- The higher the  $V_d$ , the more likely the drug is to leave the circulation and deposit in fat or muscle

# Critical Analysis

- **pKa** – the pH at which the drug is equally ionic and nonionic
- For breastfeeding, the lower the better

# Critical Analysis

- **Molecular Weight**
- This is another **really important** indicator of medication in milk
- Calculated in Da units
- For breastfeeding, the higher the better
- MW >200-500 it's difficult if not impossible for the medication to enter the milk
- Examples are insulin (MW 6000) and heparin (MW 30,000)



# Critical Analysis

- Molecular Weight of organic compounds is calculated based on the number of atoms times the Molar Mass (MM) (g/mol)
- Ethanol (CH<sub>3</sub>CH<sub>2</sub>OH)

#	Atom	MM	Subtotal Mass
2	C	12.01	24.02
6	H	1.01	6.06
1	O	16.00	16.00

Total MW = 46.08

<http://www.lenntech.com/calculators/molecular/molecular-weight-calculator.htm>

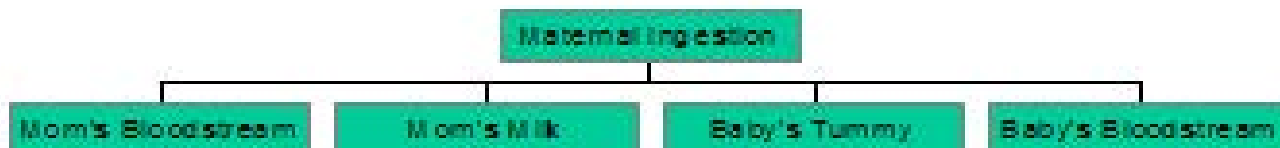
# Maternal Medication Analysis

## The Journey

Pregnancy



Breastfeeding



# Preferred Meds for Common Conditions

- **Contraception**
  - Estrogen fights with Prolactin so standard BCPs not recommended. Estrogen also significantly reduces the lactose and protein production in the alveolar epithelial cells of the breast.
  - Any hormonal contraceptive can negatively impact milk supply during artificial lactogenesis

# Preferred Meds for Common Conditions

- Depression
  - SSRIs: Zoloft (L2) is safest, Paxil (L2) and Luvox (L2) well studied and appear to be safe. Prozac (L2) has longest half life, reports of colic, losing position on the safe list as of 2014
- Smoking Cessation
  - Bupropion (Wellbutrin, Zyban) also good for depression (L3)
  - Nicotine Patch/Gum produce serum nicotine levels 1/3 that of smoking 1 pack cigarettes
- Fever
  - Tylenol (L1, AAP usually compatible)
  - Motrin (L1, AAP usually compatible)

# Preferred Meds for Common Conditions

- Hypertension
  - Apresoline good choice for eclampsia, gestational, pp HTN (L2, AAP usually compatible)
  - Beta blockers - Labetalol and Inderal (L2, AAP usually compatible) safer choices than Tenormin (L3, AAP significant side effects, caution)
  - Diuretics that have been well studied and are safe include HCTZ (L2, AAP usually compatible) and Lasix (L3, AAP not reviewed)
  - ACE inhibitors: neonates are particularly sensitive to ACE inhibitors, esp. during the first month. Captopril and Enalapril have AAP approval and L2 rating.
- Mastitis
  - Dicloxacillin (L1)
  - Keflex (L1)
  - Augmentin (L1)
  - Trimethoprim/Sulfamethoxazole (L3, AAP usually compatible)
- Seizures
  - Dilantin at first glance appears safer than Phenobarb (both L3); half life of Phenobarb is 53-140 hours, while half life of Dilantin is 6-24 hours

# Preferred Meds for Common Conditions

- Diabetes

- Insulin (L1) has  $MW > 6000$  and zero oral bio-availability
- Type II Drugs
  - Sulfonylureas (Diabinese is L3) oral hypoglycemic works in pancreas
  - Biguanides (Glucophage is L3) oral antihyperglycemic works in liver
  - Thiazolidinediones (Avandia is L3) oral antidiabetic decreases insulin resistance

- Nausea

- Zofran (L2)
- Reglan (L2)

# Preferred Meds for Common Conditions

- **Headaches**

- Tylenol, Motrin, Naproxyn Codeine (all AAP approved).
- Avoid Aspirin because of Reyes Syndrome
- Migraine may need Imitrex (L3) or sq triptan
- Beta blockers; many ok
- Ergotamines (Cafergot L4) should NOT be used because they decrease Prolactin level

- **UTI**

- Septra (L3), Macrobid (L2)
- Most antibiotics are safe

# Apps

- LactMed – NIH app
  - Summary, Drug Levels, Effects in Infants, Effects on Lactation, Alternative Drugs, Drug Class, References, Full Record





# Apps

- **Epocrates**

- Lactation ratings safe, probably safe, safety unknown, possibly unsafe, unsafe.
- CYP450
- Images



# Apps

- Thomas Hale online app is called
- **InfantRisk Center** - from Texas Tech
- \$9.95
- Many articles
- Medication Lactation ratings
- Recruits research participants

# Risk-Benefit Analysis



Consider that the known benefits of human milk may outweigh the theoretical risks of medication exposure

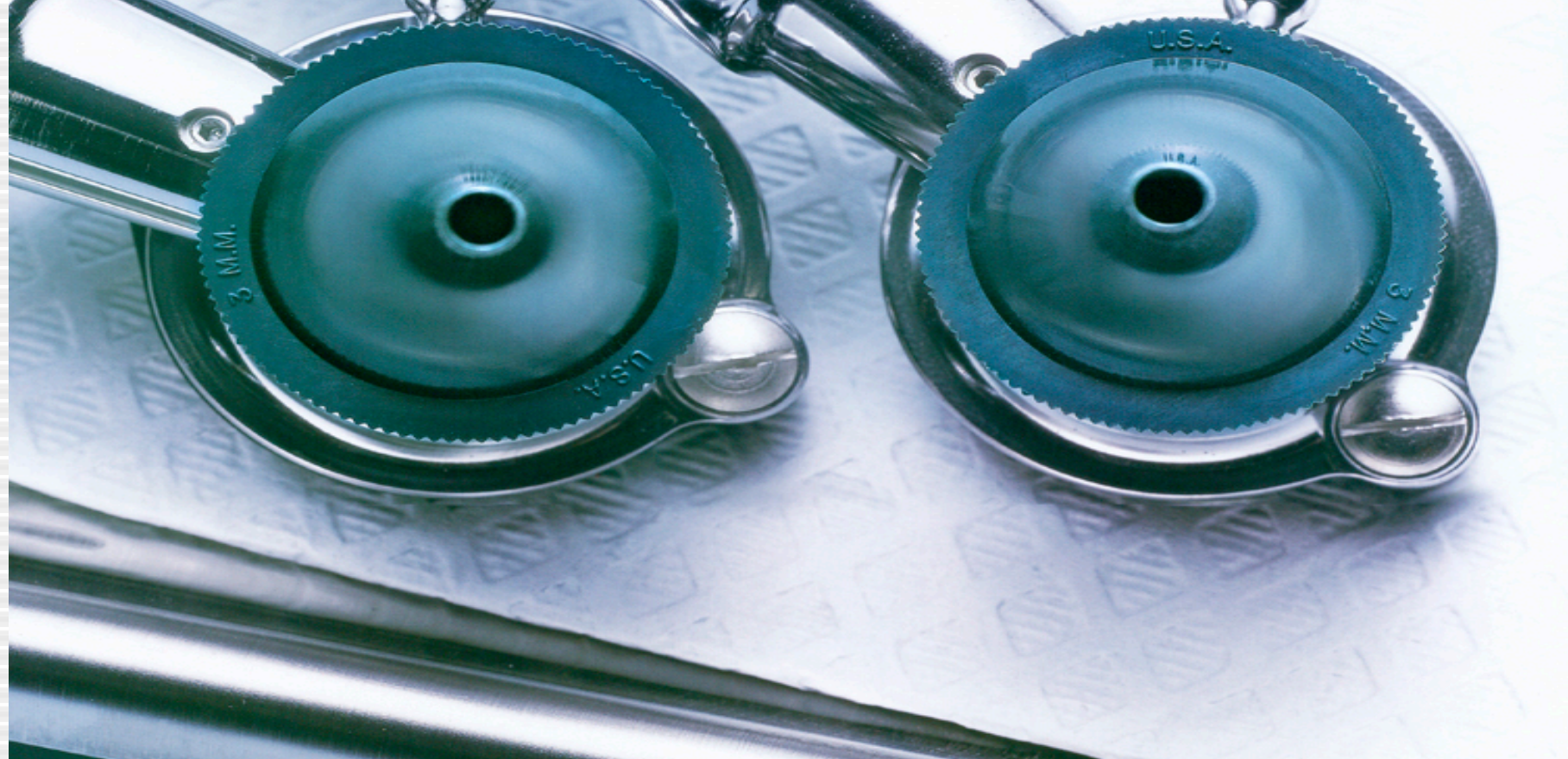
# No Question About It

“The debate is over about the importance of breastfeeding for health outcomes for women and children in the United States...

THERE IS NO DEBATE...

...we don't need any more evidence in order to reach a conclusion about whether or not breastfeeding has important health outcomes that matter for the individual and for the population of children and women in this country”

David Meyers, MD, FAAFP. First Annual Summit on Breastfeeding. June, 11, 2009.



**BREASTFEED FOR SIX MONTHS  
HELP REDUCE YOUR CHILD'S  
RISK FOR EAR INFECTIONS**

Two dandelion seed heads are shown against a vibrant green background. The seed heads are white and fluffy, with brown centers. They are positioned in the upper half of the image, one on the left and one on the right. The background is a soft, out-of-focus green, suggesting a grassy field.

**BREASTFEED FOR SIX MONTHS  
HELP REDUCE YOUR CHILD'S  
RISK FOR RESPIRATORY ILLNESSES**



**BREASTFEED FOR SIX MONTHS  
YOU MAY HELP REDUCE YOUR  
CHILD'S RISK FOR CHILDHOOD OBESITY**

# What makes breast milk so great?

- SIgA
- Lactoferrin
- Interleukin 10
- Epidermal Growth Factor
- Bifidus Factor
- Alphalactalbumin



# Known Benefit

- Protein

**Alpha-lactalbumin** is what humans are meant to digest

The dominant protein in bovine milk is **beta-lactoglobulin**, which has NO human milk counterpart.

The beta-lactoglobulin of cow's milk is responsible for antigenic (allergic) responses in humans.

1 CHEDIL EL CHAD  
EL OLTUT ERA  
NGELEKEL EL  
OLAB A DI TUL



Human milk is meant for baby humans

CHEDIL EL KEREBOU EL OLTUT  
ERA NGELEKE  
EL OLAB  
A DI TUL



Cow's milk is meant for baby cows

3 CHEDILEL KEREBOU EL OLTUT  
ERA NGELEKEL A CHEKEBIL EL TOLECHOI



WHAT IS WRONG WITH THIS PICTURE???

# Specific Anti-infective, Immunologic and Growth Factor Activities of Human Milk

- SIgA provides protection to infants against pathogens in the immediate environment of the mother-infant dyad. Loading dose day 1 (4g); after day 4 dose is less (1g).
- SIgA is the most important immunomodulating factor in human milk. It coats the gut and binds pathogens to it. SIgA has been shown in vitro to be active against E.coli, C. tetani, C.diphtheriae, L. pneumoniae, S. pyogenes, S. mutans, S. sanguinis, S. mitis, group B strep, H. influenzae, h. pylori, C. difficile, Candida albicans, to mention a few....
- An exclusively breastfed infant receives at least 0.5 gm of SIgA per day in the first month of life, which is 50 times the dose given to a patient with hypoglobulinemia. Colostrum contains the 'loading dose' (at least 4 grams) of SIgA
- The SIgA in human milk stimulates the infant's own production of SIgA: it is the baby's first immunization!!

# Lactoferrin

- Lactoferrin is bactericidal, antiviral, anti-inflammatory and cytokine modulating.
- Lactoferrin is bacteriostatic because it binds to iron, thus deprives siderophilic pathogens opportunity to grow.
- Lactoferrin also prevents inflammation, including NEC
- Lactoferrin has been shown in vitro to be active against CMV, HIV, RSV, herpes simplex type 1, hepatitis C, poliovirus, to name a few
- Gastric hydrolysis enhances antiviral activity against HSV, CMV and HIV. (Colostrum 500-600mg/dL, Mature milk 50mg/dL)
- Antiadhesive for *E. coli*; anti-invasive for *Shigella* – prevents growth
- Affects neonatal intestinal growth and recovery from injury, thereby reducing intestinal infection
- Lactoferrin is produced in the milk ducts and may be one of the factors that protects breastfeeding mothers from later ductal cancers

# Interleukin 10

- Interleukins are chemical messengers that tell cells to do something
- Cytokine: hormone like protein secreted by many cell types, which regulates the intensity and duration of the immune response
- Stimulates B-cell proliferation and antibody production, so helps fight infection
- Blocks mast cell degranulation, and MAY HELP DECREASE CHILDHOOD ASTHMA

# More Human Milk Activity

- Lysosyme: bacteristatic against Enterobacter and most gram-positive bacteria. Concentration increase over time.
- Casein has been shown to inhibit adherence of H pylori to human gastric mucosa and of Streptococcus pneumonia and Haemophilus influenzae to human respiratory-tract epithelial cells. Also is strong growth promoting factor for Bifid bacteria (bifidus factor).
- Bifidus factor: Bifid bacteria are are gram-positive, nonmotile anaerobic bacilli that are the predominant intestinal flora of breastfed babies. Presence of bifidus suppresses the growth of enteropathogens in newborns' intestines.



# Bifidus Factor

- Lactose promotes infant intestinal colonization with lactobacillus bifidus, which lays down a protective lining in the GI tract, preventing penetration of pathogenic bacteria
- “Bifid Blanket” is the protective lining
- It takes a breastfed GI tract 2 weeks to recover from 1 formula insult

# Known Benefit

- **HAMLET – Human  $\alpha$ -lactalbumin Made Lethal to Tumor cells** (Anders Hakansson, PhD)
- Anti-cancer molecules in human milk
- Fluke discovery while trying to figure out why breast milk kills bacteria
- Protein-lipid complex that kills tumor cells while sparing healthy cells
- HAMLET shows broad anti-tumor activity in >60 different lymphomas and carcinoma cell lines in vitro

# Anti-infective, Immunologic and Growth Factor Properties in Human Milk

sIgA	IgG	IgM	IgD	IgE
Lactoferrin	Lysosyme	Epidermal Growth Factor	Cytokines	Bifidus Factor
Casein	IgA	Lipase	Nerve Growth Factor	C3 Complement
Lymphocytes	Macrophages	Neutrophils	Hormones	FFA

# Anti-infective, Immunologic and Growth Factor Properties in BBM

sIgA		IgM		IgE
Lactoferrin	Lysosyme	Epidermal Growth Factor		Bifidus Factor
Casein	IgA	Lipase	Nerve Growth Factor	C3 Complement
			Hormones	FFA

# Anti-infective, Immunologic and Growth Factor Properties in artificial milk


# A Baby Fed Artificial Milk:

- Has 2-7 times increased risk of allergies
- Has 3 times increased risk of ear infections
- Has 3 times increased risk of gastroenteritis
- Has 3.8 times increased risk of meningitis
- Has 2.4 times increased risk of type I diabetes
- Has 2 times increased risk of SIDS
- Has 1.5-1.9 times increased risk of Inflammatory bowel disease
- Has 3 times increased risk of childhood leukemia

# What to do for low milk supply

- Any amount of human milk is better than none
- Artificial milk does not negate all the benefits of human milk
- Artificial lactogenesis is a big job

# OTC Galactagogues

atole, avena, accupuncture, barley, basil, beer, brewer's yeast, cardamon, cinnamon, coconut, fennel seed, fenugreek, fish soup, garlic, ginger, goat's rue, LLL, marshmallow root, milk thistle, millet, nettle, nuts, oatmeal, olives, olive oil, sesame seeds, thyme, turmeric, whole grains.....



# OTC Galactagogues

- Oatmeal - in ANY form
- Fenugreek - start with 3 tablets tid
- Brewer's yeast - start with 3 tablets tid
  
- So many cultural recipes....

# Rx Galactagogues

Metoclopramide

vs

Domperidone

# RX Galactagogues

- Metoclopramide (Reglan)
  - Thought to act by increasing prolactin levels
  - Side effect profile more concerning
  - FDA black box warning
  - Easy to find
  - Inexpensive
  - Sig: 10mg tid

# RX Galactagogues

- Domperidone (Motilium)
  - Thought to act by increasing prolactin levels
  - Safer side effect profile
  - **FDA withdrew approval**
  - Compounding pharmacy
  - Expensive
  - Sig: 10-20mg tid-qid

# Lactation Resources

Academy of Breastfeeding Medicine

[www.bfmed.org](http://www.bfmed.org)

Protocols downloadable for free

Breastfeeding Medicine journal available  
by subscription

# ABM Protocols

- 1. Hypoglycemia
- 2. Going Home/Discharge
- 3. Supplementation
- 4. Mastitis
- 5. Peripartum BF Management
- 6. Cosleeping and Breastfeeding
- 7. Model Hospital Policy
- 8. Human Milk Storage
- 9. Galactagogues
- 10. BF the Near Term Infant
- 11. Neonatal Ankyloglossia
- 12. NICU Grad Going Home
- 13. Contraception and BF
- 14. BF Friendly Office
- 15. Analgesia/Anesthesia & BF Mother
- 16. BF & Hypotonic Infant
- 17. Cleft Lip/Palate
- 18. Maternal Antidepressants
- 19. Prenatal BF Promotion
- 20. Engorgement
- 21. BF & Drug Dependant Woman

# Induced Lactation

- Newman – Goldfarb Protocol
- [www.healthychildren.org/English/family-life/family-dynamics/adoption-and-foster-care/pages/Inducing-Lactation-Breastfeeding-for-Adoptive-Moms.aspx](http://www.healthychildren.org/English/family-life/family-dynamics/adoption-and-foster-care/pages/Inducing-Lactation-Breastfeeding-for-Adoptive-Moms.aspx).

# Medication References

- <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>
- [www.bfmed.org](http://www.bfmed.org)
- Epocrates
- Medscape
- Infant Risk Center (Thomas Hale)
- [www.caduceusmedicalgroup.com](http://www.caduceusmedicalgroup.com)



Criteria for receiving breast milk:

**BEING BORN**

## From Dr. Ruth Lawrence...

“Breastfeeding is the most precious gift a mother can give her infant.  
If there is illness or infection, it may be a life-saving gift.  
If there is poverty, it may be the only gift.”



**NURSE THE BABY**  
**YOUR PROTECTION AGAINST TROUBLE**