Spring 6-2015

Induced Lactation

Katherine M. Evans
University of Vermont, kmevans@uvm.edu

Induced Lactation

Katherine Evans, MS-IV
University of Vermont College of Medicine
Women's Health Teaching Seminar
June 23, 2015

Definitions

- Induced Lactation: triggering breast milk production in a woman who has never been pregnant
- Relactation: triggering breast milk production in a woman who has given birth but who either did not breastfeed or stopped breastfeeding
- Galactorrhea: pathologic secretion of breast milk in non-puerperal women or post-partum breast milk production that persists despite lack of breast stimulation ("inappropriate lactation")

So relactation applies to women "who previously breastfed a biologic child even years before and now is adopting a newborn."

Utility of Induced Lactation

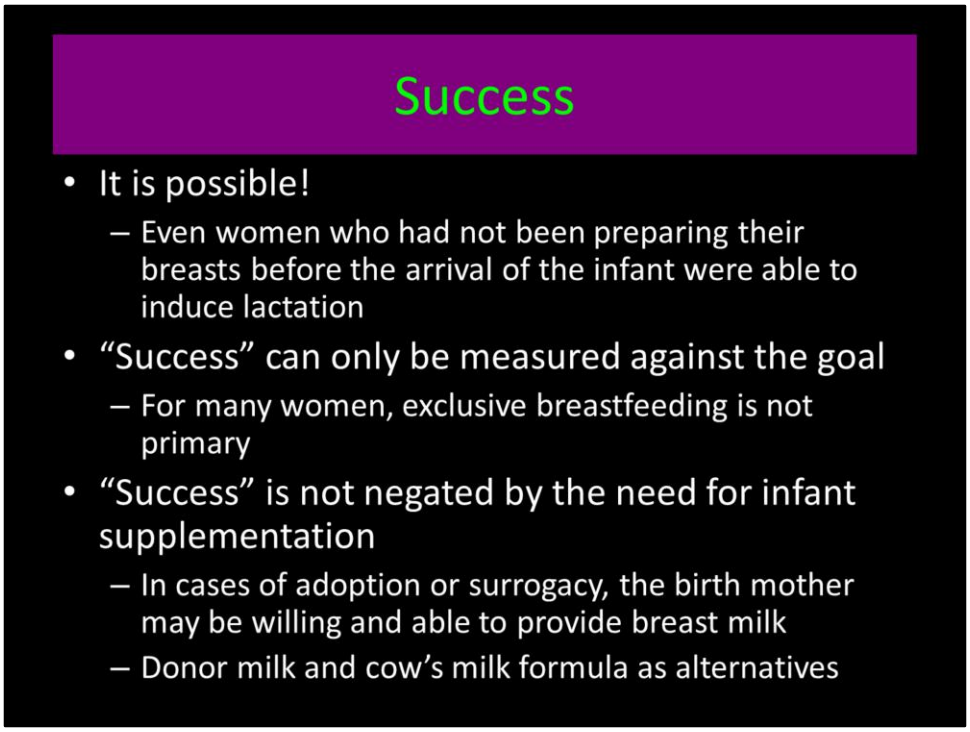
- Adoption
- Surrogacy
- Same-Sex Couples
- Maternal-Infant Separation
- Emergencies/Natural Disasters

Note: women in any of these categories can fall into either the induced lactation OR the relactation camp, depending on circumstances

Positive attitude, motivation, and commitment are key.
This means being grateful and celebrating even when only tiny drops are produced.

Auerbach & Avery: had women rank in order the reason(s) behind wanting to induce lactation. Here is the ranked list.

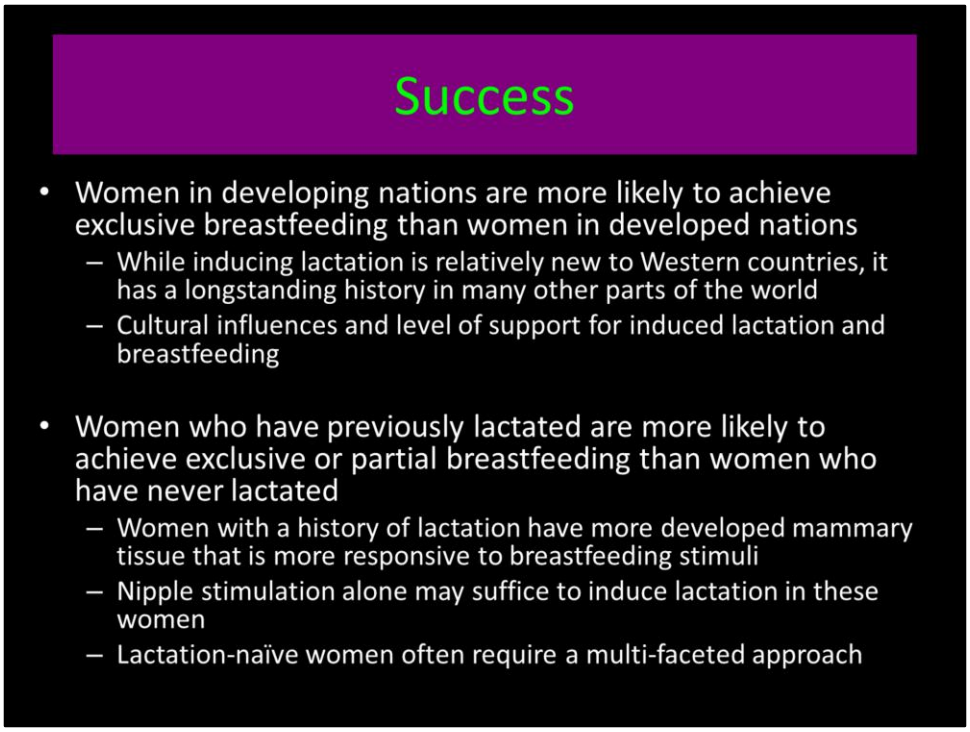
1. Mother-infant relationship
2. Emotional benefits to baby
3. Body contact with baby
4. Nutritional benefits to baby
5. Nuturant fulfillment of mother
6. Ability to produce milk
7. Breastfeeding as a reflection of femininity
8. Amount of milk produced
9. Physical changes in mother



Auerbach & Avery: 76% had positive experience

Note: inducing lactation is a PROCESS – it does not happen overnight. Peak production usually occurs 10-12 weeks after the first drops are made, which in itself may takes weeks to occur.
→once baby arrives and is put to breast, onset of lactation is between 1-6 weeks; closer to 1-2 if the baby is receiving at-breast supplementation.

Induced lactation can be successful whether the infant's arrival is anticipated or not. Often the adoption process is tricky and getting a timeline may be impossible; also, this same concept applies to inducing lactation in the case of maternal-infant separation (i.e. maternal death/illness which occurs suddenly).



WOMEN WHO THINK THEY WILL PRODUCE MILK ARE MUCH MORE LIKELY TO ACTUALLY PRODUCE MILK!!! CONFIDENCE AND POSITIVITY.

- Knowledge of breastfeeding → High exposure to breastfeeding starting from childhood, which increases confidence
- Beliefs surrounding breastfeeding and child care → Unrestricted vs. restricted breastfeeding; close contact with mother
- Encouragement to breastfeed → Expectation is to breastfeed; Uncommon to perceive lactational insufficiency (vs. in the West)
- Support for mothering (particularly, of adoption)
- Infertility and body confidence → Developing nations: adoption less likely due to issues of infertility
- Pregnancy and breastfeeding history → As above, adoptive mothers in developing nations are more likely to have lactated previously
- Use of pharmaceutical galactagogues and factors impacting hormone levels → Obesity increases estrogen → decreases prolactin

Having knowledge and support and breastfeeding more frequently. Do not begin counseling women by saying “it’s impossible for you to produce enough milk to exclusively breastfeed” as this becomes a self-fulfilling prophecy.

There is no example of behavioral changes taking place without these things (i.e. psychological mindset intact and primed, social support, education) being present! Induced lactation is no different.

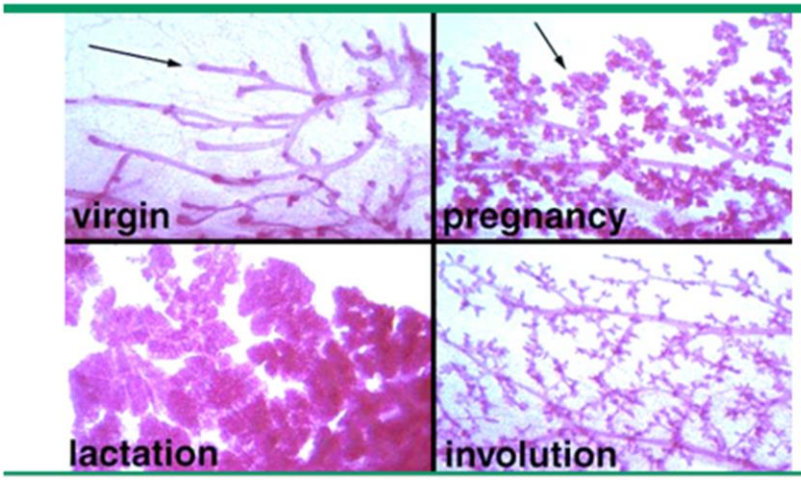
Hormonal influences triggering lactation.

The maturation that occurs in early pregnancy is known as "mammogenesis II" and involves the proliferation of both lobular and ductal systems within the breast glandular tissue (progressing into type 4 lobules, which are NOT present in the breasts of women who have never been pregnant).

Note that progesterone and estrogen are strong inhibitors of prolactin. So while prolactin is able to exert a minor effect in completing breast maturation and enabling the production of colostrum, full milk production is unable to occur in the presence of progesterone. Progesterone inhibits the mRNA synthesis of milk proteins triggered by prolactin; estrogen prevents prolactin from entering milk secretory cells effectively.

Nipple and breast stimulation are known to rise serum prolactin levels slightly. This is essentially the ONLY stimulus for prolactin secretion. However, oxytocin in released in response to not only breast/nipple stimulation, but also to sensory stimuli (sight, smell, hearing, touch, taste.

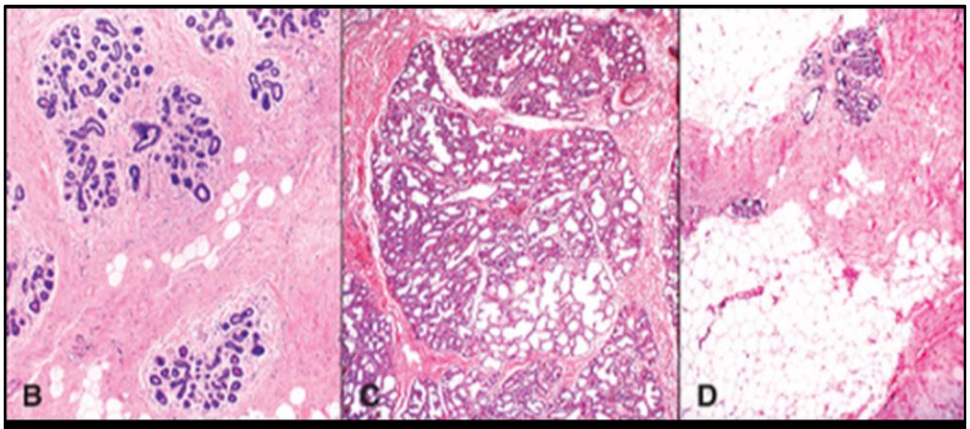
Development of mammary gland



Reproduced with permission from Lothar Hennighausen.

Graphic 76317 Version 2.0

Schanler RJ, Potak DC. Physiology of lactation.



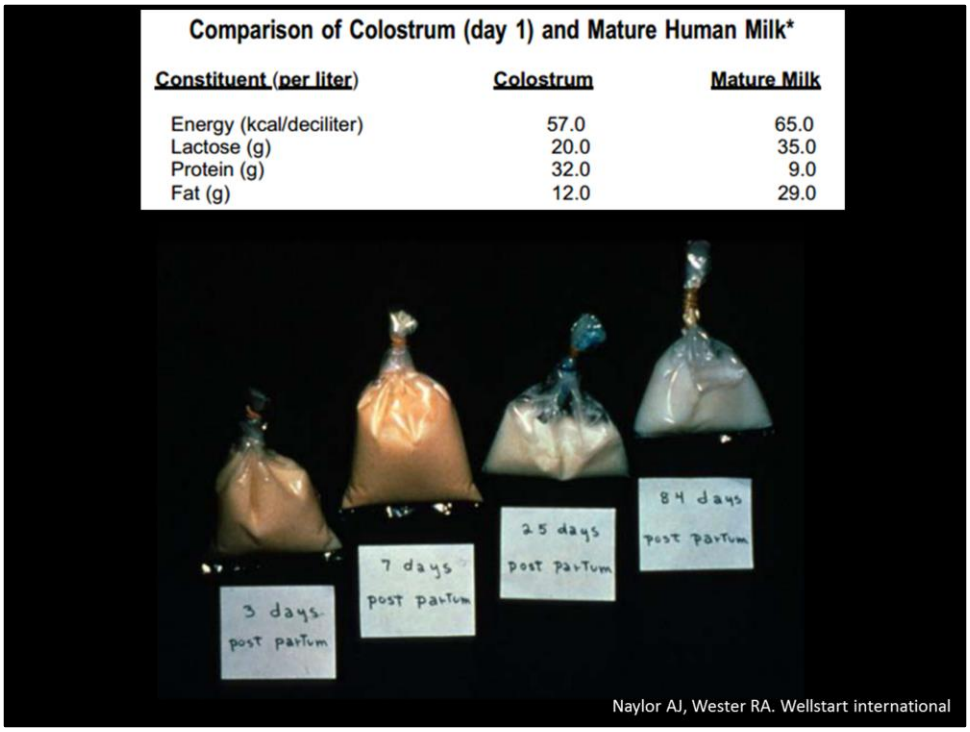
- B: Nulligravid → few small lobules, abundant stroma
- C: Pregnancy → many large lobules
- D: Postmenopausal → involution of lobules, stroma replaced by adipose

Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran pathologic basis of disease.

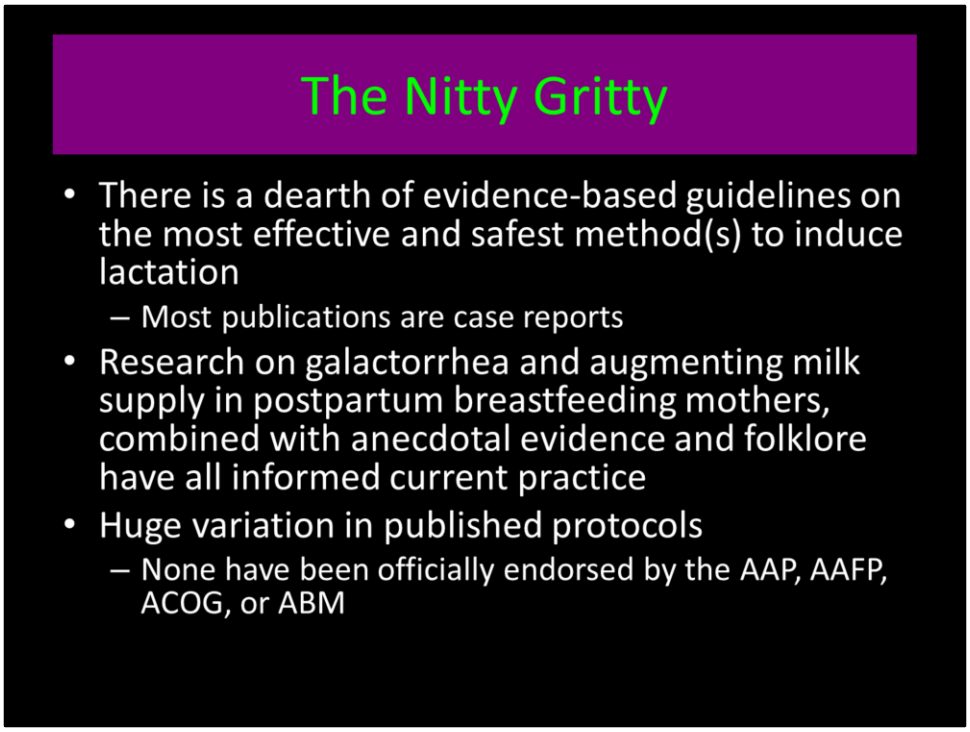
The density of a young woman's breast stems from the predominance of fibrous interlobular stroma and the paucity of adipose tissue. Before pregnancy the lobules are small and are invested by loose cellular intralobular stroma. Larger ducts connect lobules. C, During pregnancy, branching of terminal ducts produces more numerous, larger lobules. Luminal cells within lobules undergo lactational change, a precursor to milk formation. D, With increasing age the lobules decrease in size and number, and the interlobular stroma is replaced by adipose tissue.

Physiologic Basis for Inducing Lactation

- Production of milk ("lactogenesis") occurs in stages
  - Lactogenesis I begins during pregnancy and yields colostrum
  - Lactogenesis II occurs postpartum and yields mature milk
    - Withdrawal of estrogen and progesterone → prolactin activates receptors on primed alveoli to begin making milk
    - Oxytocin → activates smooth muscle to squeeze milk out of lobules
  - Lactogenesis III ("Galactopoeisis") maintains production
    - Adequate removal of milk is the stimulus for further milk production



Colostrum: for the first 2-4 days after birth
Transitional: 7-10 days after delivery
Mature: by 14 days after delivery



Variation: should breast pumping occur before hormones or after? Do galactagogues (including herbs) work? Timing of all of this?!?!?

AAP: American Academy of Pediatrics
AAF: American Academy of Family Physicians
ACOG: American College of Obstetricians and Gynecologists
ABM: The Academy of Breastfeeding Medicine

Photo: Lenore Goldfarb, PhD, IBCLC
Nipple stimulation: this is the ONLY intervention listed in some induced lactation protocols

Nipple stimulation: stimuli listed in decreasing order of efficacy.
Ideally, frequent nipple stimulation (5 minutes per breast several times daily) beginning 6 weeks before baby arrives.
Ideally, hospital-grade electric pump to double pump every 3 hours for 8 weeks before baby arrives.

Remember that breastfeeding is not robotic; it is the intimate interaction between two individuals who nurture one another. Thus, an environment of calm, peace, and skin-to-skin contact decrease the stress that may interfere with effective milk let-down/transfer and latch.

At-Breast Supplementation

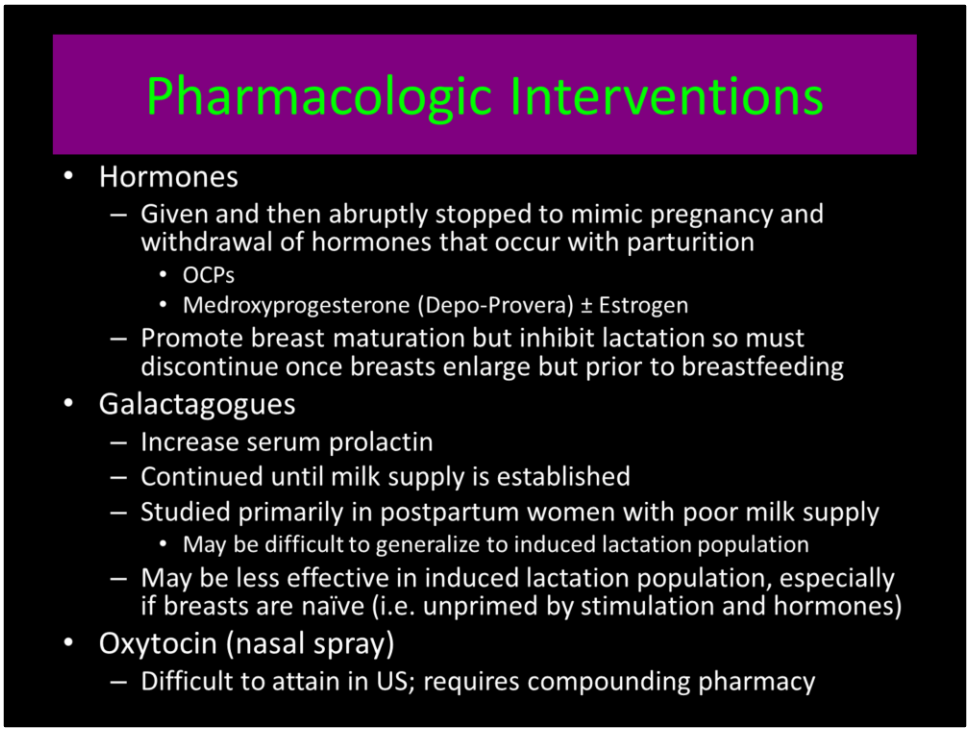
Medela Supplemental Nutrition System (SNS)

- Relies on gravity
- Two tubes

Lact-Aid Nursing Trainer System

- Relies on baby's suckling
- One tube

SNS: http://www.selfexpressions.com/supnursys.html
Lact-Aid: http://www.medscape.com/viewarticle/540786_5



OCPs: best to stop their usage 24-48 hours [other sources say stop 4 weeks before] before baby arrives (if possible to plan so exactly).

Thearle & Weissenberger study: Depo 2.5-40mg + estrogen 0.05-0.4mg daily over 6-9 months
Nemba study: one dose of Depo 100 mg, 1 week before receiving chlorpromazine 25 mg qid or metoclopramide 10 mg qid.

Galactagogues

Agent	Mechanism of Action	Recommended Dosage	Availability in the United States	Side Effects	Hale's Lactation Risk Category*
Metoclopramide	Dopamine antagonist; crosses blood-brain barrier	Oral: 10-15 mg, 3 times per day	Yes	Diarrhea, sedation, depression, tremor, bradykinesia	L2
Domperidone**	Peripheral dopamine antagonist; crosses blood-brain barrier minimally	Oral: 10-20 mg, 3-4 times per day	NO	Dry mouth, skin rash or itching, headache, gastrointestinal disturbance	L1
Sulpiride	Selective dopamine antagonist	Oral: 50 mg, 2 times per day	No	Tremor, bradykinesia, acute dystonic reactions, sedation	L2
Chlorpromazine	Central nervous system tranquilizer; blocks dopamine receptors	Oral: 25 mg, 4 times per day reported; use not recommended because of associated adverse reactions	Yes	Sedation, lethargy, tremor, bradykinesia, weight gain	L3
Fenugreek	Herbal supplement; reputation as a galactagogue, but mechanism of action unknown	Oral: 2-3 capsules, 3 times per day; variable	Yes	Maple syrup odor in urine and sweat, diarrhea, hypoglycemia, dyspnea	L3
Blessed Thistle	Herbal supplement; reputation as a galactagogue, but no data support this use	Unknown	Yes	None	L3

Wittig SL, Spatz DL.

Witting

Galactagogues will NOT make the milk supply; only skin-to-skin and nipple stimulation can do this. However, they may be helpful in augmenting supply and initiating production.
Mixed/variable efficacy. Should be combined with nipple stimulation.

Metoclopramide

- Significant neurological (extrapyramidal) side effects
- Strong association with depression
- Use limited to 14 days for the purposes of induced lactation
- Not as effective as domperidone

Agent	Mechanism of Action	Recommended Dosage	Availability in the United States	Side Effects	Hale's Lactation Risk Category*
Metoclopramide	Dopamine antagonist; crosses blood-brain barrier	Oral: 10-15 mg, 3 times per day	Yes	Diarrhea, sedation, depression, tremor, bradykinesia	L2

Wittig SL, Spatz DL.

Domperidone

- Reports of adverse cardiac events with IV formulation has prompted the FDA to make it illegal in the US to prescribe any formulation for any reason (although no adverse cardiac effects have been described from the oral formulation)

Agent	Mechanism of Action	Recommended Dosage	Availability in the United States	Side Effects	Hale's Lactation Risk Category*
Domperidone**	Peripheral dopamine antagonist; crosses blood-brain barrier minimally	Oral: 10-20 mg, 3-4 times per day	NO	Dry mouth, skin rash or itching, headache, gastrointestinal distur-bance	L1

Modified from Wittig SL, Spatz DL.

Domperidone made "orphan" status for hypoprolactinemia in breastfeeding and this opens the door for it to be studied exclusively in women looking to augment/induce lactation. Dr. Thomas Hale is largely behind these efforts to study the safety of the drug in both mother and baby, and to eventually reintroduce it to the market. http://www.emeraldcoastbreastfeeding.com/2011/09/15/domerpidone/

Herbal Supplements

- Fenugreek
  - Caution in women with diabetes mellitus (risk of hypoglycemia)
  - Caution in women with asthma (may exacerbate symptoms)
- Blessed Thistle
  - Potential adverse: allergies (in the ragweed family)

Agent	Mechanism of Action	Recommended Dosage	Availability in the United States	Side Effects	Hale's Lactation Risk Category*
Fenugreek	Herbal supplement; reputation as a galacta-gogue, but mechanism of action unknown	Oral: 2-3 capsules, 3 times per day; variable	Yes	Maple syrup odor in urine and sweat, diarrhea, hypoglycemia, dyspnea	L3
Blessed Thistle	Herbal supplement; reputation as a galacta-gogue, but no data support this use	Unknown	Yes	None	L3

Wittig SL, Spatz DL.

Fenugreek: 1830 mg tid

-avoid in pregnancy → stimulates uterine contractions

Blessed Thistle: 1170 mg tid

Mother's Milk Tea [Internet].

http://www.traditionalmedicinals.com/products/mothers-milk/

Fenugreek: 35 mg
Blessed Thistle: 35 mg
Marshmallow root

Antipsychotics

- Sulpridie (unavailable in US)
- Clorpromazine

Agent	Mechanism of Action	Recommended Dosage	Availability in the United States	Side Effects	Hale's Lactation Risk Category*
Sulpiride	Selective dopamine antagonist	Oral: 50 mg, 2 times per day	No	Tremor, bradykinesia, acute dystonic reactions, sedation	L2
Chlorpromazine	Central nervous system tranquilizer; blocks dopamine receptors	Oral: 25 mg, 4 times per day reported; use not recommended because of associated adverse reactions	Yes	Sedation, lethargy, tremor, bradykinesia, weight gain	L3

Wittig SL, Spatz DL.

Others

- Thyrotropin Releasing Hormone (TRH)
  - Promotes release of Prolactin and TSH
- Milk thistle
- Fennel
- Alfalfa
- Oats
- Marshmallow root
- Stinging Nettle
- Theophylline (coffee, tea)
- Goats rue
- Placenta
- Growth hormone (in animal models)

Encapsulated placenta

Photo: encapsulated placenta; http://doula-services.com/placenta-encapsulation/

On The Horizon

- SQ recombinant human prolactin (r-hPRL)
  - Studied in women with lactation insufficiency who were pumping for their preterm infants and in women with documented lactation deficiency
    - Prolactin was shown to increase milk volume and immunoglobulin secretion into breast milk, mimicking normal lactogenesis
  - Clinical trials for wider application ongoing
    - INDUCED LACTATION!

http://pediatrics.aappublications.org/content/127/2/e359.full.pdf
https://clinicaltrials.gov/ct2/show/NCT00181610

Case Report Strategies

- Szucs (long notice)
  - Domperidone 10 mg qid 20 weeks before
  - Domperidone 20 mg qid 19 weeks before
  - Norethindrone and ethyinyl estradiol (OCPs) 20 weeks before (for 12 weeks, but stopped after 10)
  - Began pumping 6-7 times/day & taking fenugreek (1200 mg tid→1830 mg) and blessed thistle (340 mg bid→1020 mg) after OCPs stopped
- Wilson (long notice)
  - Ethynodiol diacetate/ethinyl estradiol 1mg/35mcg for 8 weeks 12 weeks before
  - On week 3 of OCPs, added domperidone
  - Herbal tea: fenugreek
  - Began pumping 4-5 times/day after OCPs stopped

Case Report Strategies

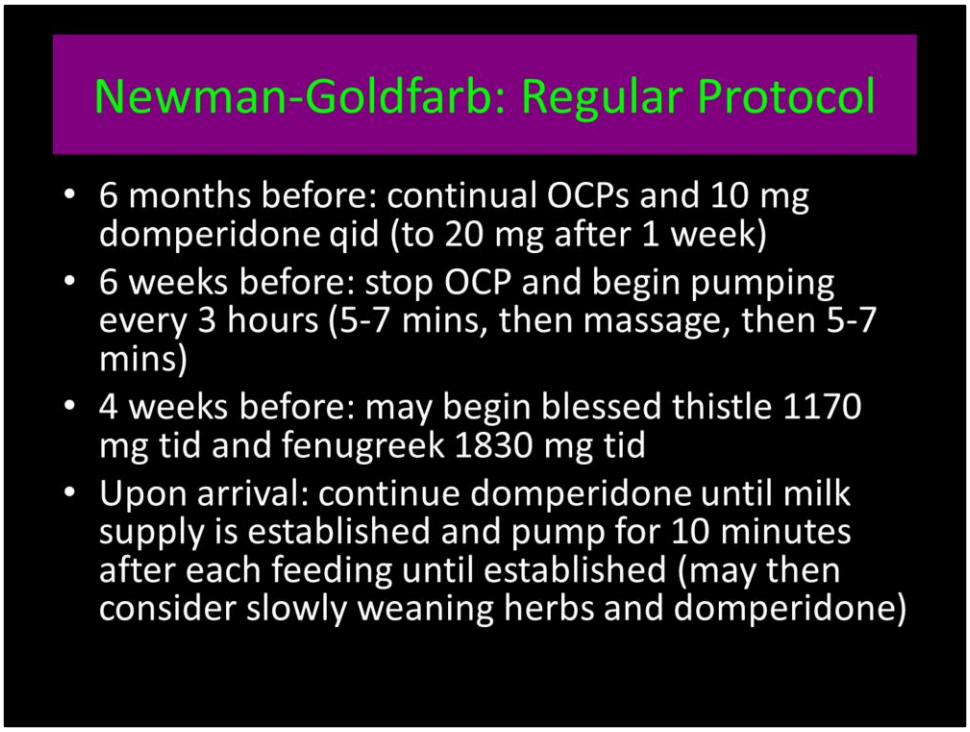
- Cheales-Siebenaler (short notice)
  - Pumped every 3-4 hours combined with at-breast supplementation
    - Oxytocin (syntocinon) nasal spray before each pumping
  - Metoclopramide 10 mg tid
- Nemba (short notice: all saw milk within 14 days)
  - All: infant suckling, psychosocial support and readiness
  - Lactation-naive:
    - Single 100 mg dose of medroxyprogesterone
    - 1 week later, begin chlorpromazine 25 mg qid and/or metoclopramide 10 mg qid until adequate lactation established
  - Lactation-experienced:
    - Chlorpromazine 25 mg qid and/or metoclopramide 10 mg qid until adequate lactation established

Lawrence & Lawrence Strategies

- Approach 1
  - Begin manual breast stimulation 8 weeks prior
- Approach 2
  - May utilize OCP continually, but need to be discontinued about 4 weeks prior
  - Double pump (gradually increase from 5 minutes 3x/d to 10 minutes every 4 hours)
  - Initiate domperidone
- Approach 3
  - 2 weeks of OCPs with breast stimulation

Ruth Lawrence, MD

Book (Breastfeeding: A Guide for the Medical Profession)
Ruth A. Lawrence, MD (University of Rochester)
https://www.urmc.rochester.edu/people/20996369-ruth-a-lawrence/articles



This is the “classic” protocol, but due to the FDA making prescribing domperidone illegal, and owing to the substantial negative (and sometimes irreversible) side effects of metoclopramide, the protocol is essentially impossible to follow in the USA.

Newman-Goldfarb: Accelerated Protocol

- Yasmin (drospirenone or Microgestin with domperidone 20 mg tid for 30-60 days until breast enlarges
- Then stop the hormone and begin pumping every 3 hours, also start blessed thistle and fenugreek

Yasmin = Drospirenone 3 mg & ethinyl estradiol 0.03 mg (30 mcg)
Microgestin = norethindrone 1.5 mg & ethinyl estradiol 0.03 mg (30 mcg)

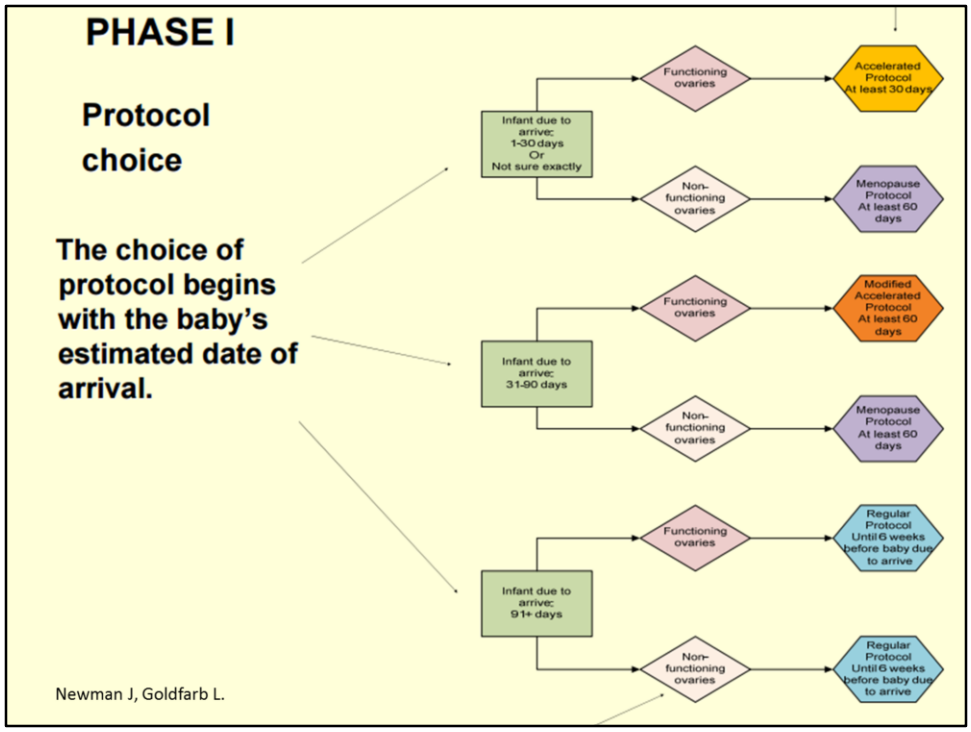
Newman-Goldfarb: Menopause Protocol

- Either Provera 2.5 or Prometrium 100 mg (avoid Ortho 1/35 if over age 35)
- Domperidone 10 mg qid for 1 week then up to 20 mg qid
- Stay on both until breast enlargement (but at least 60 days) → then stop hormones and continue dompeidone and start pumping and using herbs as previously described

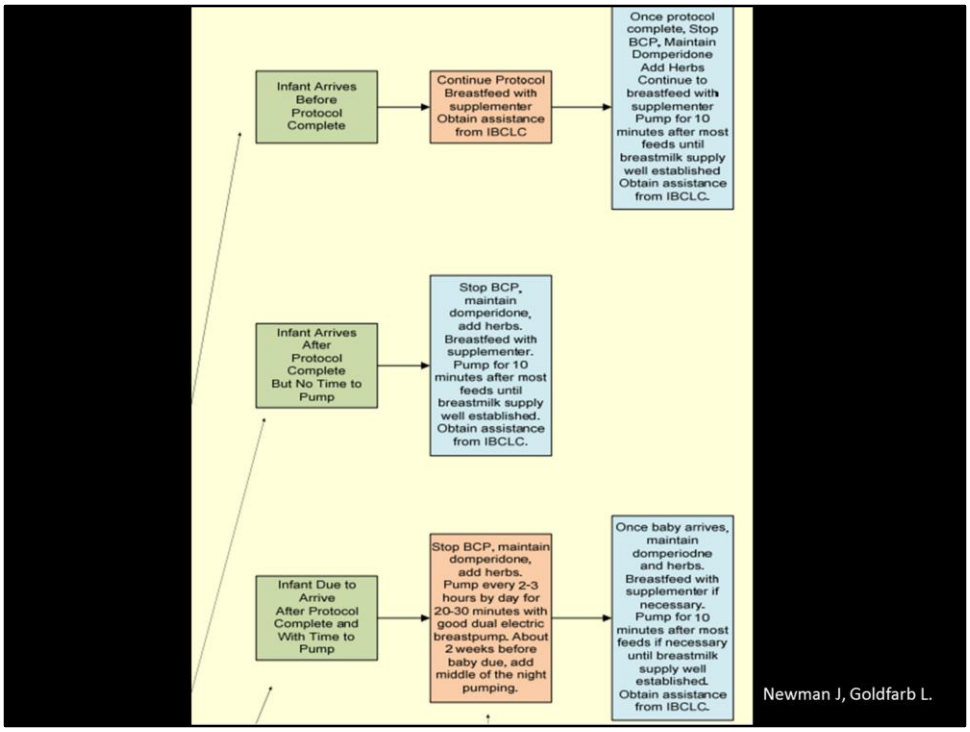
Ortho 1/35 = norethindrone 1 mg & ethinyl estradiol 0.035 mg (35 mcg)
Provera = medroxyprogesterone acetate
Prometrium = micronized progesterone

Newman-Goldfarb: Protocol Decision Tree

- Selecting the appropriate Newman-Goldfarb protocol for induced lactation
  - Estimated arrival of infant
  - Functional status of mother's ovaries
- Flowchart to guide protocol selection
  - Decision points for whether or not the mother has completed the protocol prior to the infant's arrival



http://www.asklenore.info/breastfeeding/induced_lactation/ilca2007decision_tool.pdf



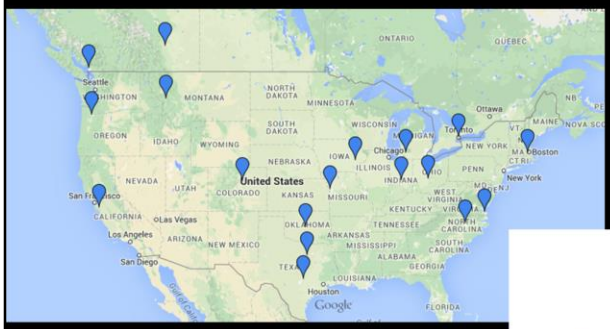
http://www.asklenore.info/breastfeeding/induced_lactation/ilca2007decision_tool.pdf

Induced Milk Composition

- Is it really the same?
  - The majority of women who induce lactation appear to lack colostrum
    - Milk produced is closer in composition to transitional or mature milk
    - Women who have previously given birth and breastfeed the infant, and/or who have prepared their breasts with hormones may be more likely to produce colostrum-type milk
  - Likely very similar and with comparable amounts of protein
    - Note that the protein may be proportionally higher in albumin and lower in IgA
    - Studies have been unable to assess fat content, owing to small sample size of paucity of research

Donor Milk

- Difficult to receive insurance coverage
- Costs ~$4.50 per ounce



HMBANA active milk banks [Internet].

Mothers' Milk Bank Northeast
Share the Health

Mothers' Milk Bank Northeast [Homepage on the Internet]

http://www.nann.org/advocacy/agenda/reimbursement-for-donor-breast-milk-for-preterm-infants.html

http://milkbankne.org/
https://www.hmbana.org/locations

Donor Milk: Recruiting Donors

Potential Donors [Internet].

References

Academy of Breastfeeding Medicine Protocol Committee. ABM Clinical Protocol #9: Use of galactogogues in initiating or augmenting the rate of maternal milk secretion (First Revision January 2011). Breastfeed Med. 2011;6(1):41-9.

Asklenore.com [homepage on the Internet]. Montreal (Canada): Candadian Breastfeeding Foundation; 2002 [cited 2015 Jun 9]. Available from: http://www.asklenore.info/index.shtml

Auerbach KG, Avery JL. Induced lactation. A study of adoptive nursing by 240 women. Am J Dis Child. 1981;135(4):340-3.

Bryant CA. Nursing the adopted infant. J Am Board Fam Med. 2006;19(4):374-9.

Cheales-Siebenaler NJ. Induced lactation in an adoptive mother. J Hum Lact. 1999;15(1):41-3.

Cox LM. What is placental encapsulation and why is that the new thing in natural birthing? [Internet]. Kew Gardens (NY); Doula Services Network; 2015 [cited 2015 Jun 9]. Available from: http://doula-services.com/placenta-encapsulation/

Emery MM. Galactogogues: drugs to induce lactation. J Hum Lact. 1996;12(1):55-7.

Goldfarb L. The premature infant – a mother's perspective [Internet]. Montreal (Canada): Canadian Breastfeeding Foundation; 2002 [cited 2015 Jun 9]. Available from: http://www.asklenore.info/breastfeeding/mothers_story.shtml

PMIDs
ABM: 21332371
Auerbach: 7193971
Bryant:16809652
Cheales-Siebenaler:10578774

References

Gribble KD. The influence of context on the success of adoptive breastfeeding: developing countries and the west. Breastfeed Rev. 2004;12(1):5-13.

HMBANA active milk banks [Internet]. Fort Worth (TX): Human Milk Banking Association of North America; 2015 [cited 2015 Jun 9]. Available from: https://www.hmbana.org/locations

Kleinman R, Jacobson L, Hormann E, Walker WA. Protein values of milk samples from mothers without biologic pregnancies. J Pediatr. 1980;97(4):612-5.

Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran pathologic basis of disease. 8th ed. Philadelphia: Saunders Elsevier, 2010. Chapter 29, The Breast; p 1066-95.

Kulski JK, Hartmann PE, Saint WJ, Giles PF, Gutteridge DH. Changes in the milk composition of nonpuerperal women. Am J Obstet Gynecol. 1981;139(5):597-604.

Lawrence RA, Lawrence RM. Breastfeeding: a guide for the medical profession. 7th ed. Maryland Heights (MO): Elsevier Mosby; 2011.

Mothers' Milk Bank Northeast [Homepage on the Internet]. Newton Upper Falls (MA); Mother's Milk Bank Northeast; 2015 [cited 2015 Jun 9]. Available from: http://milkbankne.org/

Mother's Milk Tea [Internet]. Sebastopol (CA): Traditional Medicinals Wellness Teas; 2013 [cited 9 Jun 2015]. Available from: http://www.traditionalmedicinals.com/products/mothers-milk/

PMIDs

Emery:8715241
Gribble:17004343
Kleinman:7420228
Kulski:7193419

References

Naylor AJ, Wester RA. Wellstart international lactation management self-study modules, level I. 4th Ed. Shelburne (VT): Wellstart International; 2013.

Nemba K. Induced lactation: a study of 37 non-puerperal mothers. J Trop Pediatr. 1994;40(4):240-2.

Newman J, Goldfarb L. Newman-Goldfarb protocols for induced lactation: decision tool [Internet]. Montreal (Canada); 2007 [cited 2015 Jun 9]. Available from: http://www.asklenore.info/breastfeeding/induced_lactation/ilca2007decision_tool.pdf

Perrin MT, Wilson E, Chetwynd E, Fogleman A. A pilot study on the protein composition of induced nonpuerperal human milk. J Hum Lact. 2015;31(1):166-71.

Potential Donors [Internet]. Newton Upper Falls (MA): Mother's Milk Bank Northeast; 2015 [cited 2015 Jun 9]. Available from: http://milkbankne.org/donate/ask-a-milk-donor/

Powe CE, Puopolo KM, Newburg DS, Lonnerdal B, Chen C, Allen M, Merewood A, Worden S, Welt CK. Effects of recombinant human prolactin on breast milk composition. Pediatrics. 2011;127(2):359-66.

Ruth A. Lawrence, M.D.: University of Rochester Medical Center [Internet]. Rochester (NY): University of Rochester Medical Center, Departments of Pediatrics and Obstetrics and Gynecology; 2015 [cited 2015 Jun 9]. Available from: https://www.urmc.rochester.edu/people/20996369-ruth-a-lawrence/articles

PMIDs
Nemba:7932939
Perrin:25288606
Powe:21262884

References

Ryan T. Breastfeeding your adopted baby [Internet]. 2012 [cited 2015 Jun 9]. Available from: https://breastfeedingusa.org/content/article/breastfeeding-your-adopted-baby

Schanler RJ, Potak DC. Initiation of breastfeeding. In: UpToDate, Abrams SA , Duryea TK (Eds), UpToDate, Waltham, MA. (Accessed on June 8, 2015).

Schanler RJ, Potak DC. Physiology of lactation. In: UpToDate, Abrams SA (Ed), UpToDate, Waltham, MA. (Accessed on June 8, 2015).

Schnell A. Breastfeeding without birthing: mothers through adoption or surrogacy can breastfeed! J Hum Lact. 2015;31(1):187-8.

Szucs KA, Axline SE, Rosenman MB. Induced lactation and exclusive breast milk feeding of adopted premature twins. J Hum Lact. 2010;26(3):309-13.

The nutritional value of breast milk from non-pregnant mothers. Nutr Rev. 1981;39(8):308-9.

Thearle MJ, Weissenberger R. Induced lactation in adoptive mothers. Aust N Z J Obstet Gynaecol. 1984;24(4):283-6.

Wilson E, Perrin MT, Fogleman A, Chetwynd E. The intricacies of induced lactation for same-sex mothers of an adopted child. J Hum Lact. 2015;31(1):64-7.

Wittig SL, Spatz DL. Induced lactation: gaining a better understanding. MCN Am J Matern Child Nurs. 2008;33(2):76-81.

PMIDs

Schnell:25583321
Szucs:20571140
Nutritional:7024859
Thearle:6598379
Wilson:25311827
Wittig:18327104