Induced Lactation

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Induced Lactation

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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 take 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.
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 $\rightarrow$ prolactin activates receptors on primed alveoli to begin making milk
    • Oxytocin $\rightarrow$ 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

<table>
<thead>
<tr>
<th>Constituent (per liter)</th>
<th>Colostrum</th>
<th>Mature Milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/deciliter)</td>
<td>57.0</td>
<td>65.0</td>
</tr>
<tr>
<td>Lactose (g)</td>
<td>20.0</td>
<td>35.0</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>32.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>12.0</td>
<td>29.0</td>
</tr>
</tbody>
</table>
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
Physiologic Interventions

• Nipple Stimulation = Essential
  – Baby suckling
  – Manual massage
  – Breast pump

• Skin-to-Skin = Essential

• Supplemental Feeding Systems
  – Provide at-breast supplementation
    • Baby’s suckling is most effective breast stimulation
    • Flow of milk provides continued stimulus to infant
  – May be effective alone or in conjunction with preparatory efforts

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
Pharmacologic Interventions

• Hormones
  – Given and then abruptly stopped to mimic pregnancy and withdrawal of hormones that occur with parturition
    • OCPs
    • Medroxyprogesterone (Depo-Provera) ± Estrogen
  – Promote breast maturation but inhibit lactation so must discontinue once breasts enlarge but prior to breastfeeding

• Galactagogues
  – Increase serum prolactin
  – Continued until milk supply is established
  – Studied primarily in postpartum women with poor milk supply
    • May be difficult to generalize to induced lactation population
  – May be less effective in induced lactation population, especially if breasts are naïve (i.e. unprimed by stimulation and hormones)

• Oxytocin (nasal spray)
  – Difficult to attain in US; requires compounding pharmacy

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.
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

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of Action</th>
<th>Recommended Dosage</th>
<th>Availability in the United States</th>
<th>Side Effects</th>
<th>Hale’s Lactation Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>Dopamine antagonist; crosses blood-brain barrier</td>
<td>Oral: 10-15 mg, 3 times per day</td>
<td>Yes</td>
<td>Diarrhea, sedation, depression, tremor, bradykinesia</td>
<td>L2</td>
</tr>
</tbody>
</table>

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.
Fenugreek: 1830 mg tid
  - avoid in pregnancy → stimulates uterine contractions
Blessed Thistle: 1170 mg tid
http://www.traditionalmedicinals.com/products/mothers-milk/

Fenugreek: 35 mg
Blessed Thistle: 35 mg
Marshmallow root
## Antipsychotics

- Sulpiride (unavailable in US)
- Chlorpromazine

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

*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)

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

- **Szuc (long notice)**
  - Domperidone 10 mg qid 20 weeks before
  - Domperidone 20 mg qid 19 weeks before
  - Norethindrone and ethynyl 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/ethynyl 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-naïve:
    • 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

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 domperidone 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
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

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

I make milk.

What’s your superpower?

Potential Donors [Internet].
References


PMIDs

ABM: 21332371
Auerbach: 7193971
Bryant:16809652
Cheales-Siebenaler:10578774
PMIDs
Emery:8715241
Gribble:17004343
Kleinman:7420228
Kulski:7193419

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PMIDs
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Perrin:25288606
Powe:21262884
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Schnell:25583321
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Thearle:6598379
Wilson:25311827
Wittig:18327104