Low Milk Supply

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Objectives

- List 2 reasons for insufficient breast development during pregnancy
- Describe 2 reasons why a woman may have absence of lactation postpartum
- Recite 3 reasons for low milk supply postpartum that are not due to prenatal breast development
- Identify 2 behavioral means of increasing milk supply
- Describe 2 indications for using herbs or prescription medications to increase milk supply
- Counsel on the use of 3 herbal galactogogues, including risks and side effects

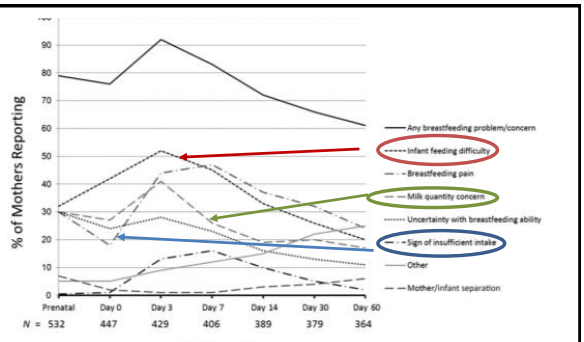
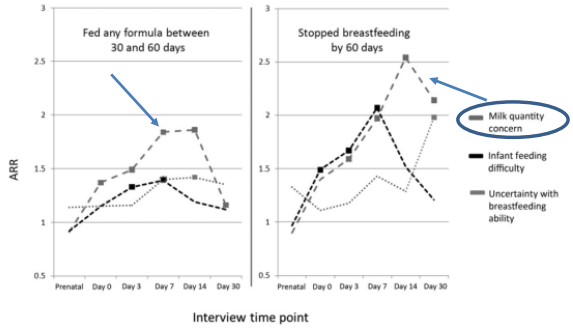


FIGURE 2
Prevalence of maternally reported breastfeeding concerns (main categories) by interview time point. At the prenatal interview, women were asked about their breastfeeding concerns. At each postpartum interview, women who had breastfed or expressed their breast milk since the previous interview were asked to describe any problems or concerns they had (currently or since the previous interview) about feeding their infant. Main categories in legend are presented top to bottom in order of prevalence at the day 3 interview. "Maternal health and medication" and "too much milk" main categories are not shown (prevalence ≤ 2% at any time point). Prevalence results are not adjusted for confounders.

Pediatrics 2013;132e865-3875



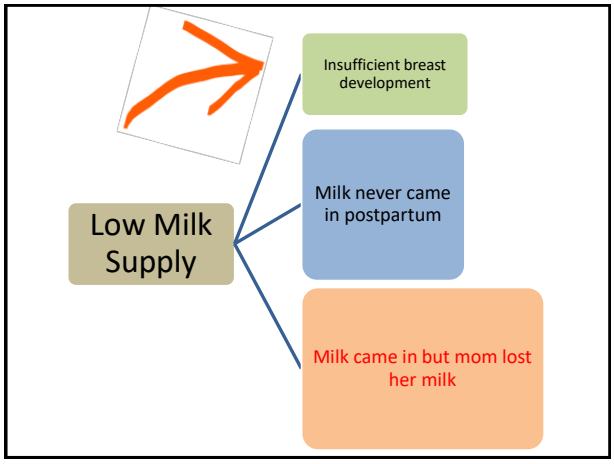
Concern re milk quantity is the most common reason to stop nursing at 60 days

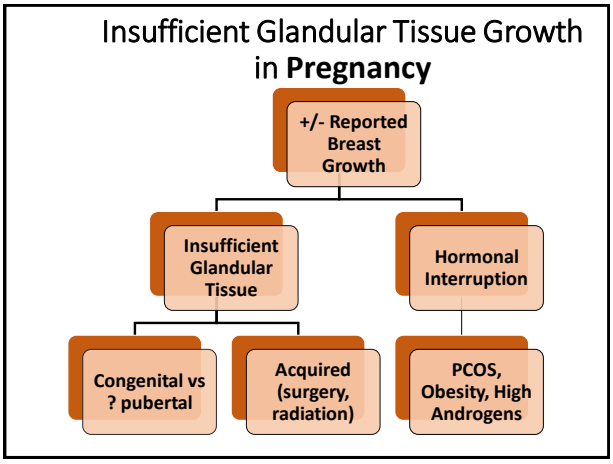
Pediatrics 2013;132e865-3875

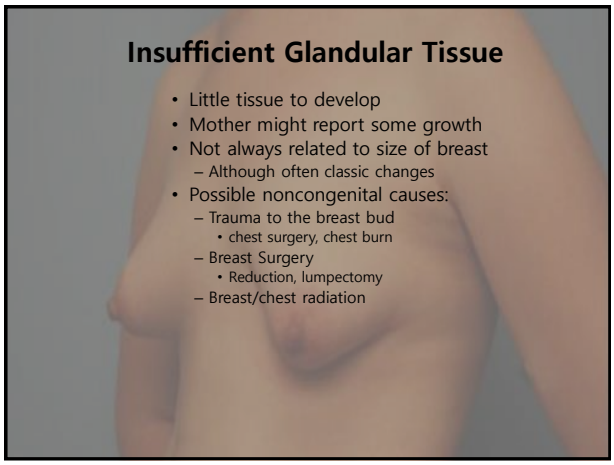
Low milk supply—Real or Perceived?

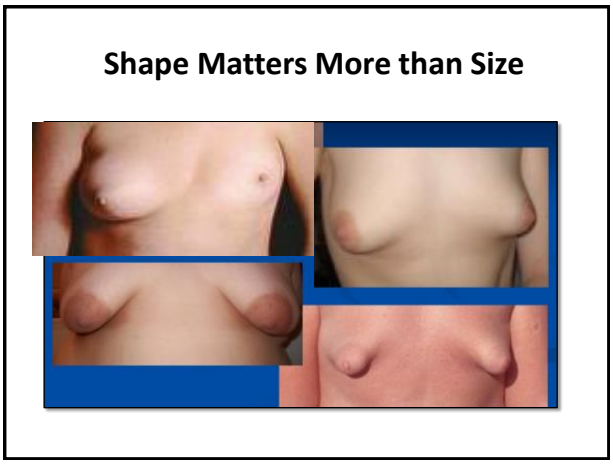
Managing Perceived Low Milk Supply

- Perceived vs real?- Weigh the infant
- Gaining weight well?
  - Evaluate the infant's symptoms
  - Identify a possible reason for the infant's behavior
- If not gaining well, the milk supply is either normal or low
  - Decreased transfer
  - Mother can pump plenty of milk despite the infant not gaining well









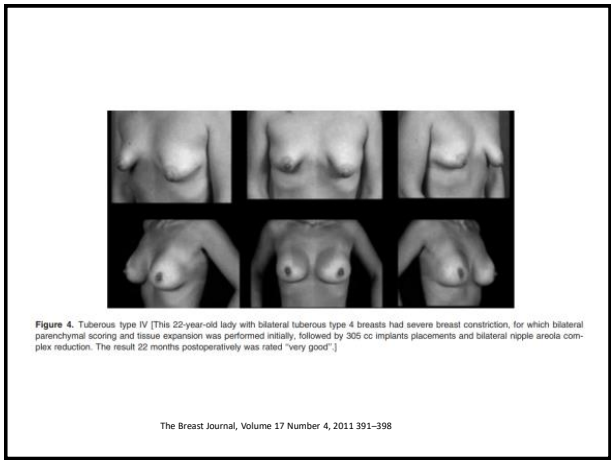


Figure 4. Tuberous type IV [This 22-year-old lady with bilateral tuberous type 4 breasts had severe breast constriction, for which bilateral parenchymal scoring and tissue expansion was performed initially, followed by 305 cc implants placements and bilateral nipple areola complex reduction. The result 22 months postoperatively was rated "very good".]

The Breast Journal, Volume 17 Number 4, 2011 391–398

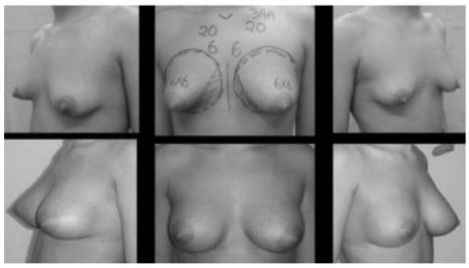
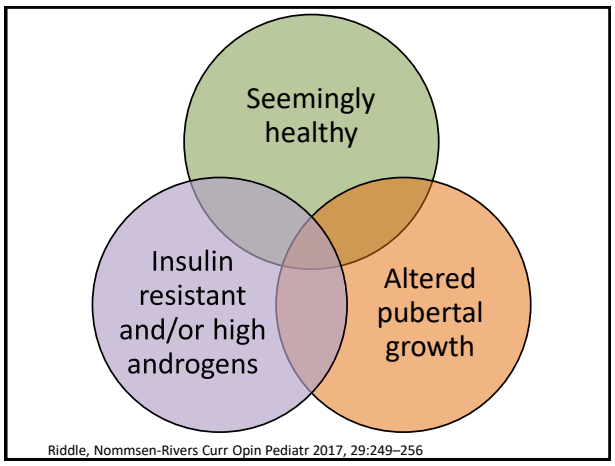
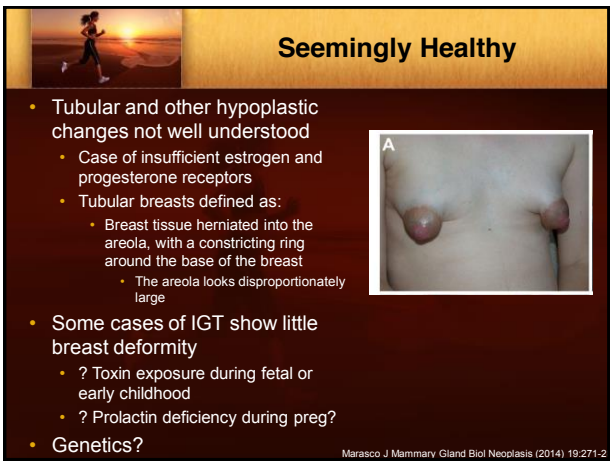


Figure 1. Tuberous type I [25 year old patient with bilateral tuberous type 1 breasts. Preoperative and 6 months postoperative result following bilateral inferomedial quadrant parenchymal scoring and differential subglandular augmentation with 335 and 295 cc implants.]



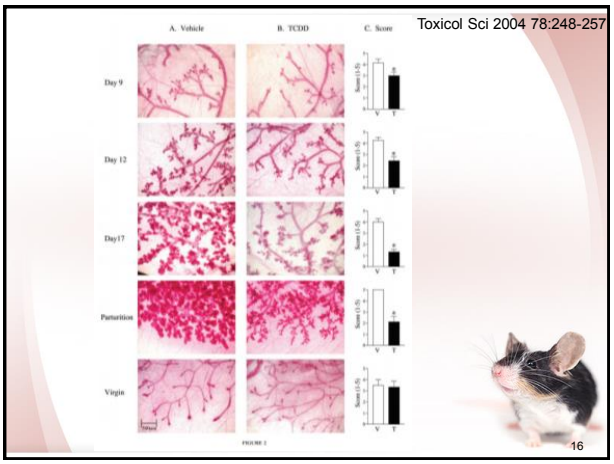
Riddle, Nommsen-Rivers Curr Opin Pediatr 2017, 29:249–256

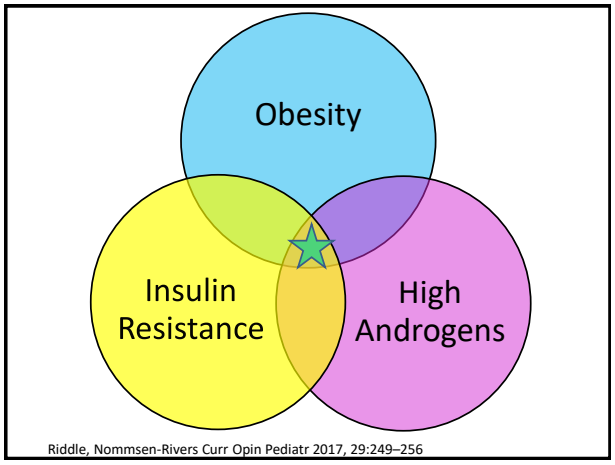


Altered Pubertal Breast Growth

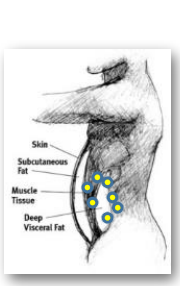
- May occur in utero or occur in early childhood
  - Exposure to estrogenic contaminants
    - Organochloride pesticides (e.g.DDT) associated with precocious puberty
    - Bisphenol A (estrogenic)=> speeds growth and puberty in rats
- Role of obesity
  - Does increased fat in the breast change MG development?

Environ Health Perspect 114:471–475 (2006).





Riddle, Nommsen-Rivers Curr Opin Pediatr 2017, 29:249–256



↑ Insulin Levels

↑Glucose Metabolism by Liver
↓ Glucose Uptake by Muscles

Free Fatty Acids

Gestational DM

Increased Insulin resistance

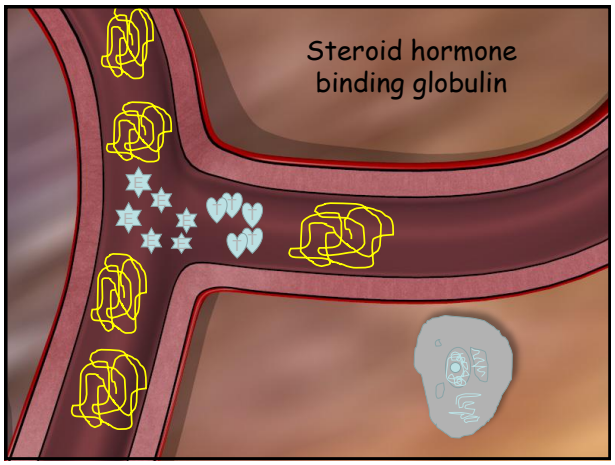
+ Pregnancy

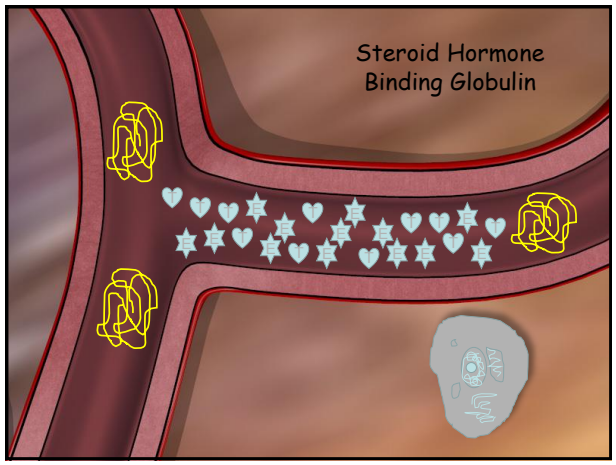
Higher insulin levels

Decreased SHBG from Liver

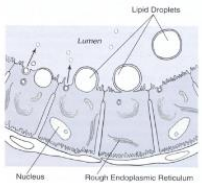
Increased Free Androgens

Irregular menses PCOS





Role of Insulin in Milk Protein Synthesis



*RNA surrounds each lipid droplet

*RNA sequences can be measured in different stages of milk production

*protein tyrosine phosphatase, receptor type, F (PTPRF) may serve as a biomarker for insulin resistance and delay in lactation.
~overexpressed in insulin-resistant mothers
~suppresses increase in milk output

Lemay DG, Ballard OA, Hughes MA, Morrow AL, Horseman ND, et al. (2013) RNA Sequencing of the Human Milk Fat Layer Transcriptome Reveals Distinct Gene Expression Profiles at Three Stages of Lactation. PLoS ONE 8(7): e67531. doi:10.1371/journal.pone.006753

Insulin's Role in Milk Production

- Mammalian research- insulin has a central role in milk protein synthesis
- PTPRF (protein tyrosine phosphatase, receptor type F) suppresses insulin action
- PTPRF might be too high (over expression of the gene that signals to make this) in insulin resistant women
  - Particularly causing delay in lactation

PLOS One July 2013 8(7)

Insulin's Role in Milk Production

- Strong association between obesity and shorter breastfeeding duration
  - After controlling for other confounders
  - Even in the most supportive countries-Norway

Nommsen-Rivers Adv Nutr 2016;7:407–14;

High Androgens and Low Supply?

- High androgens associated with
  - PCOS
  - Gestational DM
  - Obesity
  - Pre-eclampsia
  - Gestational HBP
- Androgens thought to play a role in low supply, but no correlations found

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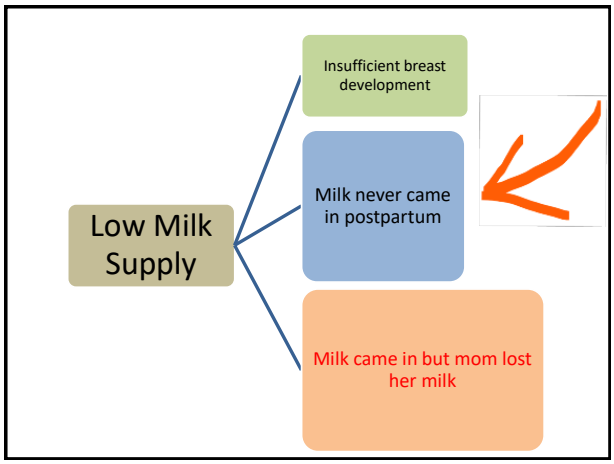
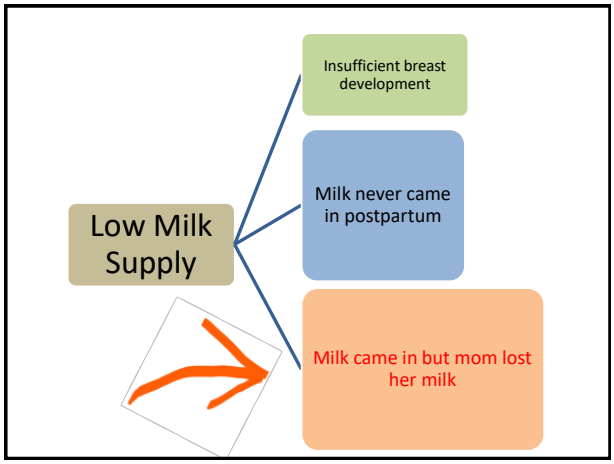


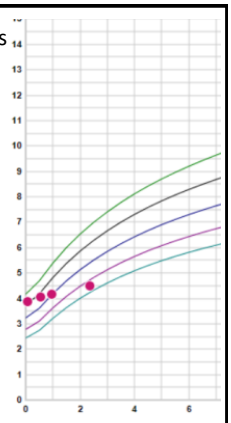
Case of Early Excessive Weight Loss

- You are seeing a dyad, G1P1 day 9 pp
- Male born at 38 weeks, bw 7 lb 1 oz, healthy
- On day 4 baby's weight was 6 lb 2 oz, down 13%
  - They began supplementing 1 oz/feeding pc
- He is nursing every 2.5 hours, both sides, day and night, and mom pumps 8 ml after feeding
- Mom's breasts don't feel full yet



Case of Insufficient Growth at 2 Months

- You are seeing female for a 2 month exam
- G3P3, Born term NSVD, 40 weeks gest
- Baby's nursing pattern
  - 4 times from am to supper time
  - Cluster feeds in evening
  - Sleeps 11 hours over night
- Baby is content
- Mom never worried re feeding issues
  - Baby is happy
  - She doesn't feel 'empty'
- You measure a pre/post feed weight
  - Baby transfers 95 ml



What is the most likely reason for the drop in weight %?

First Steps to Increase Milk Supply

- Max nipple stimulation
  - 8 times a day
    - No more than a 5-6 hr break at night
    - Nursing usually more effective than pumping
- Complete breast drainage
- Avoid meds that decrease supply
- Reduce stress/rest
- Sufficient calories

Galactogogues

Common Galactogogues

- Stinging Nettle
- Ginger
- Garlic
- Basil
- Fenugreek
- Fennel
- Anise
- Blessed Thistle
- Milk Thistle
- Marshmallow root
- Goats Rue
- Moringa Leaf
- Shatavari
- Torbangun
- Black Seed
- Turmeric
- Dill
- Alfalfa

Common Foods Believed to Increase Supply Based on Culture, Little Research

- Herbs and Spices
  - Garlic, ginger, basil, onions, caraway, anise, coriander, dill, cumin
- Hops
- Chamomile, marshmallow
- Green Leafy Vegetables and sprouts
- Grains- oats, quinoa, barley, rice
- Nuts and nut butters
- Brewers yeast

Mother-food.com

Galactogogues that Decrease Blood Sugar/Improve Insulin Sensitivity

- Black Seed
- Fenugreek
- Fennel
- Shatavari
- Goats rue
- Milk Thistle (Silymarin)
- Turmeric
- Ginger
- Dill
- Garlic
- Coriander
- Cumin
- Alfalfa

Galactogogues that are Phytoestrogens

- Fennel
- Fenugreek (and increases testosterone)
- Shatavari
- Milk Thistle (Silymarin)
- Hops
- Alfalfa

Considerations in Galactogogue Use

- Response is going to vary depending on mom's ability to make milk
  - Mothers who make a lot of milk will have a greater response
- Results of studies done on women with no risk factors for low supply don't apply to women who have risk factors
- Certain herbs/meds are a better fit for some than others
- Research is generally low quality. Best evidence is cultural experience
- No data on how long herbs take to be effective

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Ginger

- Popular use in Thailand
  - Known as a vasodilator
- RCT, double blind controlled trial
  - Healthy mothers with newborns > 37weeks gest
    - 500mg of ginger caps bid vs placebo, ~ 15 in each group
    - Started within 2 hours of delivery
    - Groups closely equal for Cesarean, parity, etc
  - Breastmilk volumes recorded days 3 and 7 pp
    - Test weights day 3, pumping volumes day 7

Breastfeeding Med 11(7) 2016

TABLE 2. RESULTS COMPARING THE DIFFERENCES IN BREAST MILK VOLUME AND SERUM PROLACTIN BETWEEN THE GINGER AND PLACEBO GROUP

Group	Ginger (n = 30)	Placebo (n = 33)	Mean difference (95% CIs)	p
Breast milk volume on day 3 (mL/24 hour), mean ± SD	191.0 ± 71.2	135.0 ± 61.5	56.0 (20.9 to 91.0)	<0.01*
Serum prolactin level (ng/mL), mean ± SD	321.5 ± 131.8 (n = 15)	331.4 ± 100.7 (n = 21)	−32.1 (−86.8 to 22.6)	0.74
Breast milk volume on day 7 (mL/hour), mean ± SD	80.0 ± 58.5	112.1 ± 91.6	−9.8 (−69.5 to 49.8)	0.24

*Statistically significant $p < 0.05$.

Higher volumes on day 3 but not day 7
Day 3 was a 24 hr total (test weights, day 7 was a 1 hr measurement)
Ginger did not raise PRL

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Fenugreek

Trigonella foenum-graecum

- Phytoestrogen
- Improves insulin sensitivity
- Considered possibly safe by the FDA in medicinal amounts
- Dose- 500mg-610mg caps of crushed seeds, 2-3 caps 3x/day
- Evidence is mixed

Lactmed/Toxnet Dec 2018
Breastfeeding Med 13(10) 2018
Breastfeeding Med 13(5) 2018

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Fenugreek

Trigonella foenum-graecum

- Possible side effects
  - Infant flatus/abd pain
  - Maple syrup odor for infant and mother
  - Drop in blood sugar if at risk
  - Legume, so can cross react with peanuts in allergic people
  - Liver toxicity has been reported
  - May interact with warfarin
  - Exacerbate asthma
  - Decrease cholesterol

Lactmed, Toxnet 2018

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Fenugreek+ Ginger + Tumeric

- Randomized Double Blind Controlled Trial in Thailand
- 25 mothers in each group, everyone 1 mo pp, bfeeding exclusively
- 200mg fenugreek/120mg ginger/100mg turmeric tid
- Used a hand pump to establish total 24 hour volumes for baseline
- Then did the same after 2 and 4 weeks on the herbal supplements or placebo

Breastfeeding Med 13(10) 2018

Fenugreek+ Ginger + Tumeric

TABLE 3. BREAST MILK VOLUME AND PERCENTAGE CHANGE BETWEEN THE HERBAL SUPPLEMENT GROUP AND PLACEBO GROUP

	Milk volume (mL/day)			Milk volume (% change)		
Time	Herbal supplement (n=25)	Placebo (n=25)	p	Herbal supplement (n=25)	Placebo (n=25)	p
Week 0	710±216	736±179	0.425	—	—	—
Week 2	1,030±264*	805±181	0.003	49±32*	11±20	<0.001
Week 4	1,399±312*	896±185	<0.001	103±38*	24±22	<0.001

*Significant differences at $p<0.05$.

Breastfeeding Med 13(10) 2018

Goats Rue
Galega officinalis

- Unclear mechanism of action
- A few poorly designed trials showing effectiveness
  - Most studies were in combination with other herbs
- Clinically may increase glandular tissue
- Risks- hypoglycemia, anti-coagulant effect

Shatavari- Asparagus Racemosus (Wild Asparagus)

- Root is the active, safe part of plant
- Long hx of use in India
- Side effects- headache, slight risk of a decrease in milk supply
- Interacts with Lithium
- Dose is 800mg-1000mg 3x/day

Shatavari-only 1 RCT

- India- double blind, placebo controlled study
- 60 subjects randomized
  - Not all had deficient lactation
    - Some had anxiety, pain, infant fussiness
  - Treatment vs placebo caps
    - 1 cap tid of shatavari powder or rice powder
- Outcome measures were
  - Change in PRL from baseline
  - Maternal satisfaction with improved infant behavior
  - Infant weight gain
- Results after 30 days
  - Mean PRL increased by 32.9 vs 9.6% for treatment/placebo groups
  - Mean infant weight increased by 16.1% vs 5.7% for treatment/placebo

Iranian J of Pharm Res 2011 10(1) 167-172

Silymarin + Phosphatidylserine + Goats Rue (SPG)

Eur J Clin Nutr 2016 70, 1151-1154

- Silymarin- a standardized preparation extracted from the seeds of milk thistle.
- Phosphatidylserine increases oral absorption of silymarin. It is a phospholipid that is mainly taken for brain function
- RCT of SPG vs placebo to 100 mothers of premies (27-32 weeks) from days 3-28 pp
  - 50 in each group
- Mothers pumped every 2-3 hours

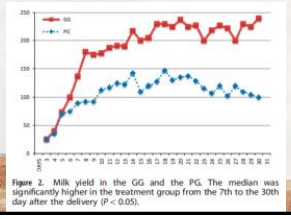

Figure 2. Milk yield in the GG and the PG. The median was significantly higher in the treatment group from the 7th to the 30th day after the delivery ($P<0.05$).

Red- herb
Blue- placebo

Moringa=Malunggay

- Used, grown and consumed in tropics
- Leaf portion increases milk supply
- Dose is 500mg-1000mg 3x/day
- Raises PRL level
- No significant side effects
  - Exception if blood thinners

Table 2. Volume of breastmilk (in ml) on postpartum days 3 to 10 of treatment and control groups.

Day Post-partum	Treatment Group (Prolacta) (amount in ml.)	Control Group (placebo) (amount in ml.)	p-value
Day 3	96.35 ± 14.3	78.56 ± 9.81	< 0.5598
Day 4	111.85 ± 11.95	89.58 ± 16.75	< 0.5598
Day 5	127.5 ± 10.33	93.70 ± 22.60	< 0.5598
Day 6	140.3 ± 11.97	101.5 ± 9.3	< 0.5598
Day 7	185.525 ± 23.40	116.6 ± 116.6	< 0.5598
Day 8	249.025 ± 46.98	128.0 ± 13.2	< 0.5598
Day 9	330.4 ± 39.5	140.3 ± 10.88	< 0.5598
Day 10	395.9 ± 36.33	150.8 ± 16.5	< 0.5598

- Mothers with term infants, 41 in each group
- Dose was 750mg once a day starting day 3 pp
- Not selected for risk of low supply
- Asked to pump q4 hours, volumes are per day

Torbangun- Coleus Amboinicus Lour

- Indonesian new mothers consume torbangun soup after birth for 1 month, with chicken or catfish
- Grown in the garden of the pregnant mother
  - Leaves used in the soup
- No limitations on frequency of eating the soup
- Possibly increases lactocytes along with milk excretion
  - Increased milk excretion in bovine and goats

JHL 25(1) 2009

Herbal Combinations

- Many different brands
  - Nettle
  - Blessed thistle
  - Goats Rue
  - Fennel
  - Fenugreek
  - Saw Palmetto
- Clinically seem less effective
  - Less of each herb

Concerning Reports

- Fennel- neurotoxicity in 2 bfeeding infants
- Alfalfa- drug-induced Lupus, bone marrow suppression
- Shatavari- headaches
- Moringa leaf- stomach upset for moms and babies
- Fenugreek- stomach upset for moms and babies, maple syrup smell, maternal dizziness
- Tumeric- headaches, insomnia, diarrhea

Metformin and Low Supply

- Metformin
  - Increases insulin sensitivity, increases liver update of glucose, and improves pancreatic function
  - Very commonly used for type 2 DM & PCOS
  - Derived from goats rue
- Study
  - Recruited postpartum
  - 10 in the intervention group, 5 placebo
  - All had low supply not due to bfeeding behavior, and all had 1 sign of insulin resistance
  - Gradually increased metformin dose from 750mg to 2000mg over 1 mo

Nommsen Rivers et al JHL Jan 2019

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- Average increase 68ml/day
  - Only for those taking it for 2-4 weeks
- Placebo and those taking metformin for 5 days or less generally lost supply

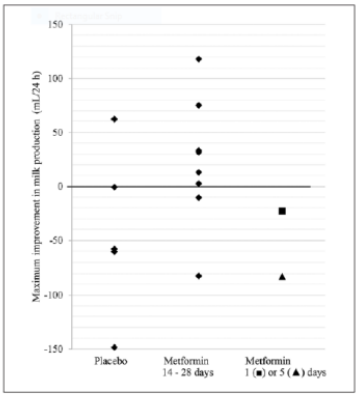

Figure 2. Maximum Improvement in Milk Production from Baseline.

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Metoclopramide

- Increases prolactin levels
  - Dopamine antagonist
- S/E- fatigue, dizziness, depression, seizures, tremors, tics, tardive dyskinesia'
- Low relative infant dose =4.4%
- Contraindications- psychiatric disorders, seizures, risk of serotonin syndrome with other serotonin agents
- Dose = 10mg 3-4x/day
- Studies are mixed- we don't know who are good responders
  - 5 Randomized placebo controlled blinded studies 1980-2011, none showed increased volumes over placebos
  - Other RCTS showed significant increases in milk supply
- Follow women closely for neurologic side effects- depression, tardive dyskinesia

ABM protocol #9 Use of Galactogogues 2018

Domperidone

- Increases prolactin levels
  - Dopamine antagonist
- Rare neurologic side effects
- Similar efficacy to metoclopramide
- Dose at 10mg 3-4 times a day
  - Relative infant dose 0.04%
- Contraindications- Long QT
- Side effects-abdominal cramps, rash, itching, prolonged QT
- Rx interactions- antifungals, erythromycin, anticholinergics, lithium
- Not FDA approved, not available in USA

Ochsner J 16:511-524 2016

Empower Trial with Domperidone

Breastfeeding Med Dec 13 2018

- Mothers assigned to domperidone 10mg tid or placebo
  - Mothers of premies born 23-29 weeks
  - 8-21 days pp
  - Pumping at least 6 times a day
  - Had a milk volume less than 150ml/kg/day or a milk volume reduction of at least 20% in the last 72 hrs
- Included 8 level 3 NICUs in Canada
- They compared starting the domperidone on day 8 vs day 22 pp, for 14 days each

Empower Trial

- Group A- took domperidone days 1-14 pp (day 1 is at enrollment on day 8)
- Group B- took domperidone days 14-28

TABLE 2. PRIMARY OUTCOME

	Group A (N=45), n (%)	*Group B (N=38), n (%)*	*Odds ratio (95% confidence interval) unadjusted*	*Odds ratio (95% confidence interval) adjusted*
Number of mothers who achieved a 50% increase in milk volume after 14-day treatment of domperidone	35 (77.8%)	25 (65.8%)	1.82 (0.69–4.81) $p=0.23^a$	1.96 (0.72–5.32) $p=0.19^b$

In each group, a majority increased supply by 50%

TABLE 4. SECONDARY OUTCOMES: MILK VOLUMES CHANGE AT END OF TREATMENT

	Group A (N=45)	*Group B (N=38)*	p-*Value*
Mean % volume change at end of the 14-day domperidone treatment (%) (standard deviation)	146 (129)	103 (161)	0.09[a]

Reasons to NOT Use Galactogogues

- Not as substitutes for optimal nursing/pumping
  - Back to work and pumping less
- Increasing breast volume without drainage:
  - Increased risk of plugs/mastitis
  - Increased FIL may counteract
- Situations of NO milk or minimal drops 1-2 weeks after birth
  - Expensive and not effective

When to use Galactogogues

- Relactating
  - Retrieving lost supply
- Induced lactation
  - Adoption, surrogate
- Pump reliance
  - Premies
  - Late preterm
  - Infants are not nursing
- Insufficient glandular tissue

Induced Lactation

You are seeing a woman who would like to induce lactation. She is generally healthy, but she has had repeated losses during pregnancy, and has decided to stop trying to get pregnant.

She and her partner have hired a surrogate, and the surrogate just became pregnant. She is due in 8 months.

She would like you advice on inducing lactation

She is generally healthy, never carried a fetus to full term.

She takes no medications, and she has no allergies.

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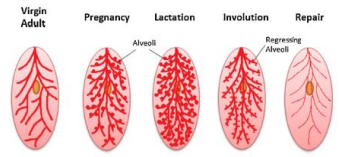
Breast Development



Options for Breast Development:
- Combined OCP or Progesterone
  - Skip placebo week
  - 1-6 months of preparation
- Medication to increase PRL
  - Domperidone vs metoclopramide
- Consider goats rue or metformin

R/o contraindications for hormones
- HBP- use progesterone only
- Migraines with aura
- H/o DVT, stroke, thrombophilia
- Breast cancer
- Mood instability/depression
- Other

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Anticipatory Guidance on Expectations

- Nulliparous mothers are expected to have least milk volume
  - Inability to take hormones for breast development adds to this challenge
- Multiparous mothers are expected to have more milk
  - Inability to take hormones may decrease volume

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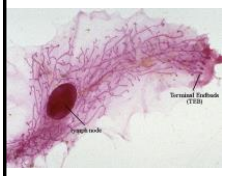
Other Considerations for Breast Development



- If hyperprolactinemia, might not need an increase in PRL
- H/o PCOS, type 2 DM, or morbid obesity
  - May see less breast development
- Duration of breast prep depends on when they anticipate bringing infant home
  - Try to stop 6 weeks before she starts nursing
- The combined birth control patch has higher levels of estrogen
- More likely to be successful without hormonal prep:
  - Weaned in the last year
  - Multip
  - H/o high supply
  - Can still express drops of milk

Pumping and Milk Expression

- Choose a pump
  - During the breast development stage
    - Some insurances will cover for induced lact
  - See back 3-4 weeks before pumping starts
    - review pump use, check flanges
- Review pumping details
  - When to start
    - When hormones stop
    - Ideally 6 weeks before having infant
  - Frequency, duration
    - Every 3 hours with no more than a 5 hour break at night

What to Take After Stopping Hormones?

- Continue domperidone or metoclopramide
- Continue goats rue or metformin
- Add galactogogues that pt desires to try them. Considerations:
  - Moringa leaf 1000-1500mg tid
  - Shatavari 800-1000mg tid
  - Torbangun
  - Fenugreek 1200-1300mg tid
  - Blessed Thistle
  - Milk Thistle
- Add one by one, to see effectiveness

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Collecting and Storing Expressed Milk

- Expression will SLOWLY increase!
- Manage expectations
  - Expect calls/messages of disappointment
  - Lots of encouragement needed
- Collect drops using a TB syringe or other w/butterfly, needle clipped off
- Place in tiny container, date, freeze
  - 11ml, 30ml containers
- Add cooled droplets from next expression
- Bring to the hospital for use immediately after birth

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Counsel on Hospital Routine in 3rd Visit

- Learn hospital routine/policies on adoption, surrogacy, and nursing
  - Meet/talk to LC
- Skin to Skin
- Frequency of nursing/pumping
- Infant sleep cycles
- Rooming in
- Hospital routines for blood sugar testing, supplementation
  - Bring thawed milk
- Infant feeding cues
- Risk of NAS if adopting
- Consider a newborn care class

From Global Health Media

Conclusions

- Low milk supply can be associated with prenatal, intrapartum, and/or postpartum complications.
- Low milk supply can occasionally be the first sign of a maternal medical problem.
- Galactogogues do not take the place of frequent, effective feeding and/or pumping.
- Galactogogues are only effective in the setting of frequent, thorough breast emptying.

Conclusions

- Studies on herbs are of low quality
- We don't know how the herbs work
- We don't know who are good responders
- We don't know interactions with prescription medications