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Hormone Imbalances and Milk Supply: How Polycystic Ovary Syndrome May Fit into the Picture

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2003 La Leche League International Conference

Session 130: Hormone Imbalances and Milk Supply: How Polycystic Ovary Syndrome May Fit into the Picture

Friday, July 4, 2003 7:00 PM – 8:30 PM (1900-2030)

Lisa Marasco, MA, IBCLC

| OBJECTIVES | CONTENT | TIME FRAME | CONTENT SPECIALIST | TEACHING METHOD |
|---|---|------------|--------------------|-------------------------------|
| Describe the physiology of mammogenesis. | I. Phases of Mammogenesis a. In Utero b. First 2 Years of Life c. Puberty II. Major hormones of mammogenesis a. Insulin b. Cortisol c. Thyroxine d. Prolactin e. Growth Hormone | 10 minutes | Lisa Marasco (LM) | Lecture Slides Handouts |
| Describe the hormonal shift of lactogenesis II. List three major hormones of the Lactogenic Complex. | III. Lactogenesis IV. Lactogenesis II V. Lactogenic Complex VI. Milk Synthesis | 20 min | LM | Lecture Slides Handouts |
| List four hormonal imbalances that are known to impact lactation. List 5 major symptoms and 3 possible hormonal imbalances in PCOS. Give three possible ways PCOS might impact lactation. | VII. Primary Lactation Failure a. Mechanical b. Endocrine c. Insufficient Mammary Tissue d. Literature Review VIII. Overview of Polycystic Ovary Syndrome IX. Potential impact of PCOS on lactation X. Marasco thesis study findings | 40 min | LM | Lecture Slides Handouts |
| Define "targeting" of galactogogues. Describe dilemma of short-term treatments for insufficient milk supply related to insufficient mammary tissue, and potential for longer-term treatments. | XI. Counseling for insufficient milk XII. Dilemma for current baby XIII. Galactogogues XIV. Potential for future babies XV. Hypoplasia: reversible? XVI. Case histories | 30 min | LM | Lecture Slides Handouts |
| Question and Answer. | Participant Questions Discussed. | 10 min | LM | Discussion. |

Hormone Imbalances and Milk Supply:

How Polycystic Ovary Syndrome May Fit into the Picture

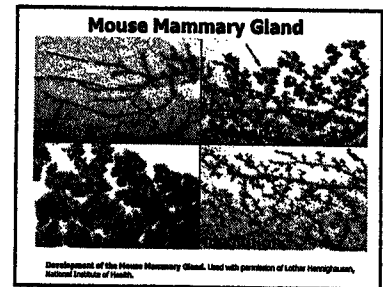
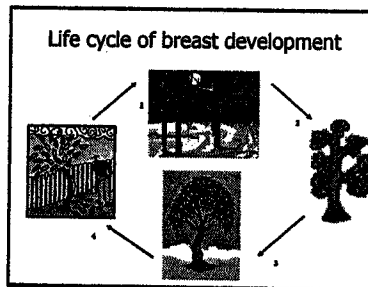
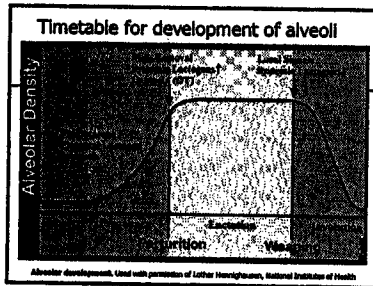
Lisa Marasco MA IBCLC

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Overview of mammarygenesis and lactogenesis

- Mammary gland undergoes three major phases of growth and development before pregnancy: *in utero, first two years of life, puberty*
- Puberty: estrogen stimulates ductile growth, progesterone stimulates growth of alveoli
- Full differentiation of the gland requires
 - Insulin: stimulates stem cells to proliferate
 - Cortisol: assists in further formation of alveoli
 - Thyroxine: stimulates pituitary, which affects proper production of prolactin and Growth Hormone
 - Prolactin & GH: Integral to alveolar development; prolactin also necessary for development of *estrogen receptors*.

- During pregnancy, estrogen, progesterone, prolactin [and HPL] help to complete breast growth, as may GH via IGF-I.
- Coxa Found that changes in breast volume during pregnancy were positively related to the concentration of HPL.
- Sources of mammary stimulating hormones:
 - Pituitary: Prolactin, Growth Hormone, TSH
 - Ovary: estrogen, progesterone
 - Placenta: HPL, Chorionic gonadotropin
 - Pancreas: Insulin
- Hormones synthesized locally within the breast by *paracrine activity* include: prolactin, progesterone, estrogen, relaxin, epidermal GF

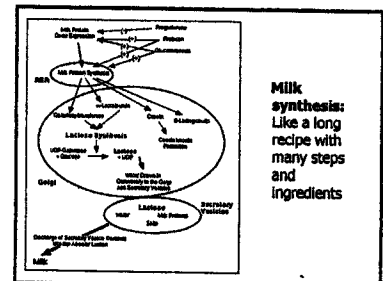


Lactogenesis

- Progesterone interferes with PRL at the alveolar cell *prolactin receptor level* to inhibit lactation before birth; progesterone and pharmacologic amounts of androgens *reduce prolactin binding*
 - "Maintenance of steroid inhibition (progesterin or androgen)... are effective in preventing *pp* milk synthesis and secretion."
- Lactogenesis II begins at parturition with removal of placenta; apparent within 2-4 days on average

Hormones necessary to begin lactation (Lactogenic Complex)

- Prolactin: needed for lactose synthesis
- Insulin: needed for lactose synthesis, maintenance/survival of lactocytes during lactation (Hartmann)
- Cortisol: low levels cause more alpha-lactalbumin to be made for lactose synthesis; *high levels are inhibitory* (i.e. chronic/extreme stress)
- Lactose synthesis is key to milk secretion




Understanding true lactation failure

- **Delayed**
- **Secondary supply failure- generally caused by an outside force**
- **Primary supply failure- refers to problems specific to mother's body and are most often irremediable**

Causes of Primary Failure


- **Mechanical interference**
 - Breast surgery/biopsies, especially peri-areolar incisions
 - Breast reduction
 - Breast augmentation
 - Blunt trauma
 - Radiation therapy
 - Damage from abscess or severe mastitis?



- **Endocrine disturbances**
 - **Retained placental fragments- high progesterone suppresses prolactin efficacy**
 - **Hypopituitarism- insufficient stimulation of lactation hormones and/or release**
 - **Hemorrhage/Sheehan's (insult vs. infarct): damage to pituitary**
 - **Uncontrolled diabetes-**
 - *breast is a sensitive target-organ for insulin; insulin necessary for lactogenesis, breast growth?*
 - *Diabetic women tend to have lower levels of PRL, PL, PTH during pregnancy and postpartum*

- **Hypothyroidism-**
 - *Joseph 1993: "Reproductive failure- infertility, pregnancy wastage, failure of lactation- occurred in 37.3% of hypothyroid and 36.5% of hyperthyroid cases against 16.3% of euthyroid and 16.7% of healthy controls."*
 - *Hurlley: "Hypothyroidism retards ductal and alveolar growth."*
 - *Miyake 1988: insufficient stimulation of hormones, sometimes even when euthyroid due to treatment*
- **High testosterone: down-regulates prolactin and estrogen receptors**

Insufficient mammary tissue: Genetic? Hormonal?




Observations in the literature

Harold Walker (1957)

Left: Almost the whole gland is filled with alveolar tissue- little fat or fiber. Right: secreting tissue is limited to thin streak along base of the gland. There is a large central mass of fibrous tissue and much fat.

"The development of a large duct system further suggests hormonal dysfunction."



Neifert et al study

(1985): Case study of 3 women with lactation failure. Common factors: absence of typical breast changes during pregnancy, failure of pp breast engorgement, at least one abnormal breast, including less density of tissue (by light scan)

(1990) Prospective study of 319 primips. Breast exams were performed in last trimester, then the mothers were followed for outcome.


Risk factors: peri-areolar breast incisions; minimal prenatal breast enlargement; minimal post-partum breast engorgement.

Huggins study

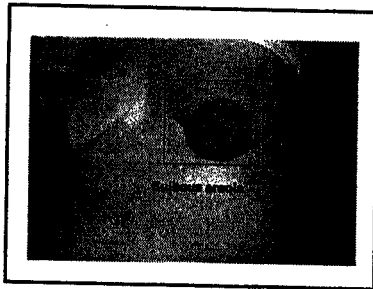
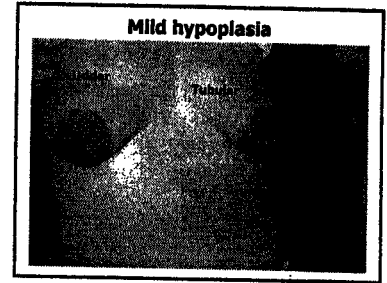
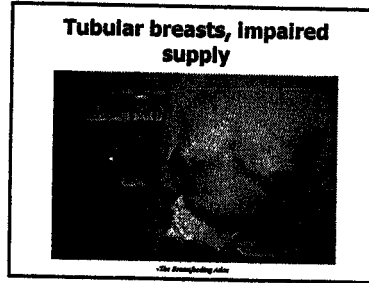
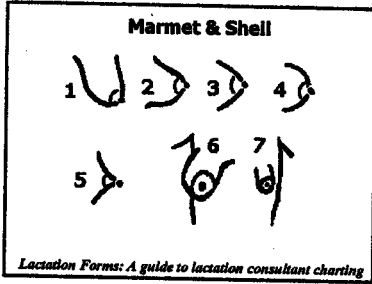
Huggins, Petok & Mireles: Enrolled women who had questionable looking breasts, categorized them by four types, then followed them for breastfeeding outcome. **Major risk factors:**

- **inframammary distance >1.5"**
- **hypoplasia types 2-4**
- **stretch marks?**

Breast Types - Huggins et al



Reprinted from Walker, Harold, "The Breast and Lactation," 1957, pp. 100-101. Copyright © 1957 by W.B. Saunders Company. All rights reserved. This book is a registered trademark of W.B. Saunders Company.



Other correlations to primary failure...

- **Obesity:** *Hilton, Rasmussen, Kjøhede*
 - "excessive fatness in the reproductive period may inhibit lactation performance in women..."
 - "Obese rats initiate lactation less successfully, produce less milk than controls, and have a higher concentration of fat but lower concentration of lactose and protein in their milk than do nonobese rats.....Studies in obese rats show that these animals remain hyperinsulinemic during transition from pregnancy to lactation, which may inhibit the delivery of nutrients to the mammary gland for milk biosynthesis"
 - Additional commentary from Rasmussen: Fat is a source for progesterone, so obese women continue to produce progesterone after the placenta is removed - "it can take them longer to develop a milk supply."

- **Hypertension?** - Nelfert in *Dr. Mom*, 1998
- **Prolactin resistance?** *Zargar et al. (2000)* Mother of 3, insufficient milk, normal prolactin secretion and reserves, normal mammary tissue development- authors theorize *resistance* to prolactin the cause of her repeated lactation failures
- **The unknown and uncharted... PCOS?**

Clues from Induced lactation

- Traditional cultures expect good supplies when inducing milk production
- In U.S. and developed countries, full supplies are rare
- Our adoptive moms are often infertility patients
- **PCOS is considered leading cause of infertility**

Two intriguing cases...

- **Case 1:** Obese mom in mid-20's presented with second child, FTT. First baby was crisis pg when mom was a teen, with milk supply problems that mother attributed to poor information. Current baby was conceived after experiencing secondary infertility, and mom was determined to "get it right" this time. Further discussion revealed that mom had been diagnosed with Stein-Leventhal.

- **Case 2:** Moderately overweight mom presented a few days later with third baby, who was also FTT at 3 wks of age. This mom described a history of infertility and milk supply problems, but also really wanted to breastfeed this baby. Further discussion revealed that mom had been diagnosed with Polycystic Ovary Syndrome.

Common trait: infertility. Further research revealed that Stein-Leventhal and PCOS were the *same syndrome*.

Interference cont 3

THEORY: progesterone drop not sufficient to sensitize alveoli for lactogenesis II

THEORY: could PCOS-induced hypertension suppress lactation in certain affected women?

→ Supports Neifert's observation of hypertension as a risk factor for lactation failure

→ Supports Hypertension noted as risk factor for early cessation of lactation (*J Peds Nov 2002*)

Interference cont 4

THEORY: hormonal imbalances might disrupt milk production by interfering with one or more links in synthesis chain

→ sufficient lactose needed to draw water into cells for volume

→ other constituents may be missing, resulting in thin, "watery milk"

Interference cont 5

THEORY: concomitant hypothyroidism may cause problems (secondary or subclinical)

→ Supports Montoro

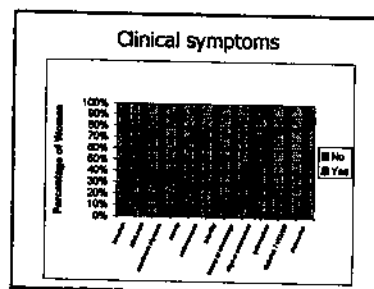
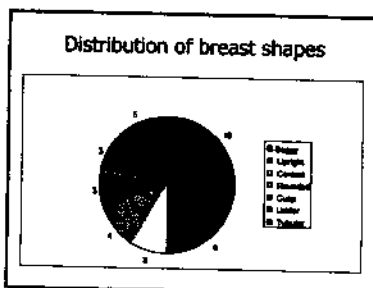
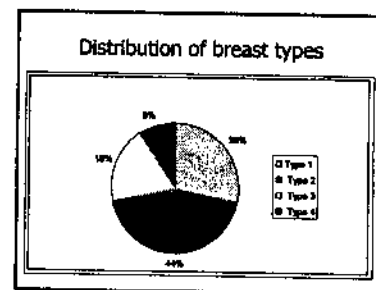
- "A hx of menstrual irregularity before pregnancy may be elicited, particularly menorrhagia, which is reported to occur frequently even in patients w/ mild hypothyroidism"
- "Secondary hypothyroidism may be seen in pituitary or hypothalamic diseases... Anemia may also be seen in hypothyroidism."

Question....

Does this mean that PCOS might cause breastfeeding problems for all affected women?

A study of lactation failure from the perspective of PCOS

Marasco 2001: enrolled women with documented supply failure and screened for common factors, looking at clinical sx, hormonal sx, family hx, breast shape, breast size, veining, intramammary distance, day milk reported in. (n=30)



Breast growth

| Breast growth | 0 | 1 | 2 | Total |
|---------------|-----|-----|-----|-------|
| Pregnancy | 12 | 8 | 10 | 30 |
| percentage | 40% | 27% | 33% | 100% |
| Postpartum | 18 | 8 | 4 | 30 |
| percentage | 60% | 27% | 13% | 100% |

Additional observations.....

- 4 women not diagnosed hypothyroid, yet had hx of borderline low levels. *Can subclinical levels have an impact?*
- Some women reported sensations of fullness reminiscent of engorgement
- Mother's perceptions of which day milk came in most often based on volume increase vs. color change- latter is most accurate

Significant findings

- 43% officially dx'd PCOS, 30% more likely PCOS
- 50% had signs of androgen excess: hirsutism, acne
- 50% were obese
- 57% experienced infertility
- 67% experienced irregular menstrual cycles
- 67% of women reported little or no breast changes during pregnancy
- Avg. intramammary distance 1.62 inches, with 50% greater than 1.5 inches.

Clear risk factors

- Pregnancy breast growth & shape
 - > Agrees with Nelfert et al, Huggins et al; disagrees with Cox et al
- Intramammary space > 1.5"
 - > Agrees with Huggins et al
- Non-prominent veining
 - > Agrees with Huggins et al, Cox et al

Reconciling breast growth significance

- Cox (n=8) found no relationship between milk production and breast volume or breast growth, but rather a relationship between milk production and *storage capacity*
- Nelfert, Huggins, Marasco & Cox all had different populations.
- Is it possible that some women experience growth in gland (storage capacity?) that is balanced by little or no measurable net change in volume?

reconcile can't

"...while proliferation of breast tissue is necessary for sufficient milk production to sustain an infant, the breast does not need to be enlarged above pre-conception size to continue significant milk production. *Further studies are needed to identify the proportions of different tissues in the lactating and quiescent breast.*"

Interesting observations:

- Breast growth, areolar growth, and breast volume influenced by hPL
- Nipple growth and rate of excretion of lactose related to concentration of PRL
- Rate of breast growth high until ~5 mos

What can be done for affected mothers?



Dilemma for the current baby

- **Relative lack of success for usual measures**
 - Pumping alone: little or no change
 - Pharmaceuticals: Reglan, domperidone: some effect, but not great
 - Herbs: Marginal improvement, may be due to *inappropriate targeting or inadequate dosage amounts*. Most commonly tried: fenugreek, blessed thistle, nettle, fennel, goat's rue.

targeting issues

- Lawrence: "except in extreme cases (Sheehan's), hormone depletion is rarely an issue, *but hormone release and target-organ sensitivity are...* For any hormone to exert its biological effects, specific receptors for the hormone must be present in the target tissue. Changes in serum concentration have no effect if receptors are not present in the mammary gland to bind the hormone."

Confounding treatment variables

- **Endocrine imbalances** unknown
- **Prolactin:** no direct relationship between levels and milk production, yet it matters
 - Prolactin tests often revealed either perfectly normal or borderline levels for time postpartum. Might the poor supply in the presence of adequate hormone be due to down-regulated receptors, or prolactin resistance as theorized by Zargar et al? Or is it, at this point, a matter of not enough alveoli to provide enough milk for baby?

variables...

- Thyroid: treatment may not always "cure"
- Testosterone? Intriguing theca-lutein cyst case study by Kay Hoover
- Huggins, et al: showed that continued pumping resulted in gradual increase in milk supply in many mothers; max potential may take 3 mos to know
 - Sproff: "mild deficiencies in estrogen, progesterone, thyroxine, cortisol, insulin, prolactin, GH, can be compensated for by excess prolactin."

The special case of PCOS

- Multiple problems make it difficult to determine and target the cause; exact endocrinopathy unknown
 - Prolactin- Levels often normal. Is the real issue prolactin resistance, or is it a matter of not enough stimuli to provide enough milk for baby?
 - Thyroid- deficiency may not respond to galactogogue and even treatment may not always "cure"
 - Cottrill, 1981: "The PRL response to methyprazole in women with spontaneous disease was significantly smaller than in controls"
 - Testosterone- serum levels do not always reflect clinical symptoms
 - Progesterone- if deficient for breast growth, cannot "teach" this after delivery.

Look at the big picture

- A good maternal health history is important, including any medical conditions, allergies, history of depression, current medications
- What is the basic problem? Is there a lactogenic medication or herb that seems to target this issue?
- What is mother's comfort and philosophy regarding medications or herbs?
- Are there institutional or HCP restrictions on what can be used? *Must work carefully within framework of mother's HCPs*

Galactagogue choices for pcos

Herbal:

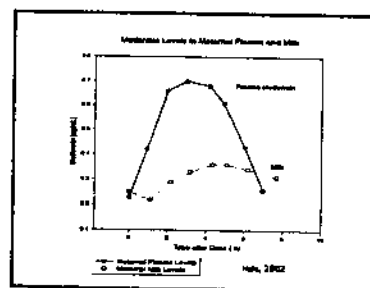
- Goat's Rue- may possibly have similar action to metformin. *Added benefit: increase needed breast tissue?*
- Fenugreek- also reputed to increase breast tissue; also a hypoglycemic. *Check for fx of hypoglycemia for fenugreek or goat's rue*
- Vitex/Chasteberry has been used to treat PCOS because of reputation for balancing hormones; could act indirectly as a galactagogue

Pharmaceutical:

- Risperin -SPECIAL CAUTION- women with PCOS appear more prone to depression. Screen history, and watch carefully if used
- Domperidone: best choice if available

pcos...

- Metformin: potential to correct multiple unknown imbalances
 - Best potential when there is moderate breast development already in place
 - Metformin improves insulin resistance, does not act directly on insulin or glucose
 - Tom Hale recently studied 5 milk samples from women taking metformin; levels in milk were extremely low. (*Diabetologia* online, 2002) Rating is being changed from L3 to L2.



Case studies with metformin

- With first case mother, researched and then started on metformin @ approx 2 mos pp. She reported that she felt her milk supply coming up..... until.....
- Moen, para 3, IBCLC, not dx'd PCOS until after recognizing sx during presentation. Had already experimented positively with vitex (2 caps qid); now added metformin 500mg SR, decreased vitex & domperidone by 50%- noted increase in baby's diaper output after 1 mo. of therapy (baby age 6 mos)

Two pcos moms w/ low supply prescribed metformin by their MD/MC- one mother's output doubled, the other came up dramatically

- Mom of 6yr & 4 mo old started back on metformin after experiencing 15lb wt gain and rebound of PCOS symptoms.
 - After 3 days of 1000mg then upping to 1500mg, she noted: "All day my breasts have been very full and my son has been gurgling himself silly! The Met is the only thing that has changed and it seems that my volume has gone way up."

Hope for future babies?

Permanent or reversible hypoplasia?

- Stein 1944, after ovarian wedge resection: "In one case of primary amenorrhea there was practically no visible breast development..... Most remarkable and rapid development after surgery..... Breasts enlarged and nipples and areolae developed noticeably in a few months. After marriage and birth of a child, lactation occurred..... Successfully."
- and "there was a notable improvement.... The breasts developed markedly, especially in those young women with primary amenorrhea and in whom the breasts were formerly immature."

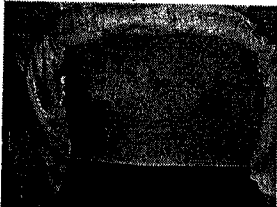
hypoplasia

- Bodley & Powers, 1999, Luteal Phase Insufficiency case
- Breast growth windows? Gigantomastia: sensitivity to prolactin... could there be under-sensitivity with hypoplasia?
- Cancer gene cell research- trying to close growth windows may lead to learning how to re-open them.

hypoplasia

- Potential relationships between obesity, diabetes, PCOS, hypoplasia. Treatments such as metformin may correct underlying problems and allow for proper growth and effective hormones
 - Latest research shows that metformin through first trimester reduces miscarriage rate from 65% to 15% and risk of GD from ~40% & ~29% to 3%
- Progesterone cream/supplement therapy during pregnancy... Katharina Dalton
 - Red raspberry leaf?

Not always successful..



This mom did "everything right"- metformin treatment before and during pregnancy, progesterone by good start to breastfeeding, but only drops of milk even with herbal galactagogue

One mom's experience

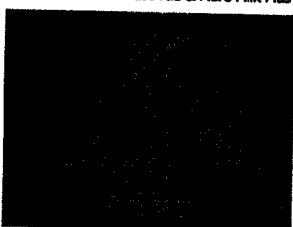
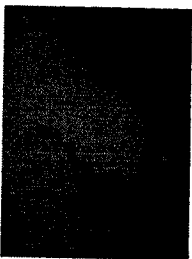
LACTATION BREW:

- Pregnancy- tea of red raspberry leaf, nettles, alfalfa, clover
- Postpartum- to the above added hops flower, blessed thistle, marshmallow root, fenugreek powder and goat's rue powder

Another mom's experience.....

- Type 2 breasts, 30ccs q 2-3 hours @ 1 wk
- Started on *More Milk Plus* & *Goat's Rue* 10-12x/24 hours
- Enhanced breast growth
- Recently added *Mother's milk* and *raspberry leaf tea*, plus eating oatmeal
- Intake @ 6wks = 104ccs
- Inconclusive but encouraging**

Significant veining and breast growth after several weeks of *Goat's rue* & *More Milk Plus*

Breasts now heavy with milk

Online resources

- Collection of lactation biology articles: <http://mammary.nih.gov/reviews>
- PCOS Pavilion on OB/GYN net: <http://www.obgyn.net/pcos/pcos.asp>
- Polycystic Ovary Syndrome Association: <http://www.pcosupport.org/>
- Herb profiles by Health World Online: <http://www.healthworld.net/clinic/therapy/herbal/herbic/herbs/>
- Brief Herb monographs: http://www.nutritionfocus.com/nutrition_supplementatio n/herbs/index.htm
- Longwood task force in-depth monographs: <http://www.mcp.edu/herbal>

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ASSESSING FOR INSUFFICIENT MILK SUPPLY

PRIMARY FACTORS

- Breast augmentation
- Breast reduction
- Breast biopsy/surgery
- Breast radiation
- Blunt trauma to chest or burn wounds
- Retained placental fragment
- Hemorrhage
- Anemia
- Hypertension
- *Hypothyroidism OR Low thyroid
- *Diabetes
- *Infertility
- *Hormonal problems
- *Insufficient mammary tissue

Insufficient mammary tissue: (p26; 45-46)

- Breast type 2, 3 or 4?
- Unusual breast shape? _____
- Distance between breasts > 1.5"? _____
- Markedly asymmetric?
- Prenatal breast growth? 0 1 2
- Postpartum breast growth? 0 1 2
- Lack of significant vascularization
(poor veining of the breast)

SECONDARY FACTORS

Mother:

- Poor latch
- Poor breast/mouth fit
- Firm, inelastic breast tissue
- Infrequent feeds (<8x/24 hrs)
- Restricted feeding times
- Scheduling
- Infrequent pumping sessions
- Medications _____
- Hormonal birth control
- Pregnancy
- Breast infection
- Herbs _____
- Delayed lactogenesis: edema, labor drugs, hypertension/mag sulfate, Diabetes, theca-lutein cyst

Baby:

- Cardiac or respiratory problems
- High or low muscle tone
- SGA/IUGR or borderline early
- Hard/soft cleft palate
- Palatal variations
- Micrognathia
- Tongue-tie
- Improper suck

*PCOS/hormonal assessment

- _____ Infertility (40) OR miscarriage (20)
- _____ Chronic anovulation OR oligo/amenorrhea (40)
- _____ Hyperandrogenism (30) OR hirsutism or acne (10 each)
- _____ Insulin resistance or skin tags or acanthosis nigricans or hyperinsulinemia (30)
OR gestational or Type 2 diabetes (15)
- _____ Polycystic ovaries (30)
- _____ Obesity (20)
- _____ Low progesterone (20)
- _____ Family history of two or more risk factors (20)
- _____ Elevated cholesterol (10)
- _____ History of heavy menstrual bleeding or endometriosis (10)
- _____ **Total Score** (>70, suspect hormonal problems/interference with lactation)

PCOS & Insufficient Milk Supply Bibliography

- Arthur P, Kent J, Hartmann P. Metabolites of lactose synthesis in milk from diabetic and nondiabetic women during lactogenesis II. *Journal of Pediatric Gastroenterology and Nutrition* 1994;19(1):100-8.
- Arthur PG, Smith M, Hartmann PE. Milk lactose, citrate, and glucose as markers of lactogenesis in normal and diabetic women. *Journal of Pediatric Gastroenterology and Nutrition* 1989;9(4):488-96.
- Avery, JL. FAQ: Frequently Asked Questions About Nursing Adopted Babies. Athens, TN, Lact-Aid International, Inc., 1998. Retrieved January 2, 2000 from the World Wide Web: <http://www.lact-aid.com/fagad001.htm>
- Balcar V, Silinkova-Malkova E, Matys Z. Soft tissue radiography of the female breast and pelvic peritoneum in the Stein-Leventhal Syndrome. *Acta Radiologica Diagnosis* 1972;12:353-362.
- Battaglia C, Regnani G, Mancini F, Iughetti L, Flamigni C, Venturoli S. Polycystic ovaries in childhood: a common finding in daughters of PCOS patients. A pilot study. *Human Reproduction* 2002; 17(3):771-6.
- Bingel A and Farnsworth N. Higher plants as potential sources of galactogogues. *Economic and Medicinal Plant Research* 1994; 6:1-54.
- Bodley V and Powers D. Patient with insufficient glandular tissue experiences milk supply increase attributed to progesterone treatment for luteal phase defect. *Journal of Human Lactation* 1999;15(4):339-343.
- Brumsted JR, Riddick DH. The breast during pregnancy and lactation. In: Sciarra JJ, ed. *Obstetrics and Gynecology*. Philadelphia: Lippincott, Williams and Wilkins, 1999: Volume 5, Chapter 31.
- Carmina E, Lobo R. Polycystic ovaries in hirsute women with normal menses. *American Journal of Medicine* 2001; 111:602-606.
- Carmina E, Lobo R. Do hyperandrogenic women with normal menses have polycystic ovary syndrome? *Fertility and Sterility* 1999;71(2):319-322.
- Carmina E, Lobo R. Polycystic Ovary Syndrome (PCOS): Arguably the most common endocrinopathy is associated with significant morbidity in women. *Journal of Clinical Endocrinology and Metabolism* 1999;84(6):1897-99.
- Chang RJ, Katz SE. Diagnosis of polycystic ovary syndrome. *Endocrinology and Metabolism Clinics of North America* 1999;28(2):397-408.
- Ciccarelli E; Grottoli S; Razzore P; Gaia D; Bertagna A; Cirillo S; Cammarota T; Camanni M; Camanni. Long-term treatment with cabergoline, a new long-lasting ergoline derivate, in idiopathic or tumorous hyperprolactinaemia and outcome of drug-induced pregnancy. *Journal of Endocrinological Investigation* 1997 Oct;20(9):547-51.
- Contreras P, Generini G, Michelsen H, Pumarino H, Campino C. Hyperprolactinemia and galactorrhea: spontaneous vs iatrogenic hypothyroidism. *Journal of Endocrinology Metabolism* 1981; 53(5):1036-9.
- Cox DB, Kent JC, Casey, TM, Owens, RA, Hartmann, PE. Breast growth and the urinary excretion of lactose during human pregnancy and early lactation: endocrine relationship. *Experimental Physiology* 1999, 84:421-434.
- Cresswell J, Barker D, Osmond C, Egger P, Phillips D and Fraser R. Fetal growth, length of gestation, and polycystic ovaries in adult life. *The Lancet* 1997;350(9085):1131-5.
- Fonseca AM, Souza AZ, Bagnoli VR, Celestino CA, Salvatore CA. Histologic and histometric aspects of the breast in polycystic ovary syndrome. [conference literature] *Archives of Gynecology* 1985;v.237, n. SUPPL:380-1.

- Gabay M. Galactagogues: Medications that induce lactation. *Journal of Human Lactation* 2002; 18(3):274-779.
- Glueck CJ, Wang P, Goldenberg N, Sieve-Smith L. Pregnancy outcomes among women with polycystic ovary syndrome treated with metformin. *Human Reproduction* 2002; 17(11):2858-64.
- Glueck CJ, Koyabashi S, Sieve-Smith L, Want P. Metformin reduces gestational diabetes from 29% to 2.4% in women with polycystic ovary syndrome. Cholesterol Center, Jewish Hospital, Cincinnati OH. Presented, Clinical Research, Baltimore MD, 4/10-13, 2002. *Journal of Investigative Medicine* 2002; 50:175A
- Glueck CJ, Wang P, Fontaine R, Tracy T, Sieve-Smith L. Metformin-induced resumption of normal menses in 39 of 43 (91%) previously amenorrheic women with polycystic ovary syndrome. *Metabolism* 1999; 48(4):511-519.
- Gordon C. Menstrual disorders in adolescents. *Pediatric Clinics of North America* 1999;46(3):519-42.
- Hale T, Kristensen J, Hackett L, Kohan R, Ilett K. Transfer of metformin into human milk. *Diabetologia* 2002, 45:1509-1514. Available: <http://neonatal.ttohsc.edu/lact/Metformin.pdf>
- Hildebrandt H. Maternal perception of lactogenesis time: A clinical report. *Journal of Human Lactation* 1999; 15(4):317-323.
- Hilson J, Rasmussen K, Kjolhede C. Maternal Obesity and breastfeeding success in a rural population of white women. *American Journal of Clinical Nutrition* 1997;66:1371-8
- Hokken-Koelega AC. Timing of puberty and fetal growth. *Best Practice Research. Clinical Endocrinology and Metabolism*. 2002 Mar;16(1):65-71.
- Hoover K, Platia . Delayed lactogenesis II secondary to gestational ovarian theca lutein cysts in two normal singleton pregnancies. *Journal of Human Lactation* 2002; 18(3):264-8.
- Huggins K, Petok E, Mireles O. Markers of Lactation Insufficiency: A Study of 34 Mothers. *Current Issues in Clinical Lactation* 2000, 25-35.
- Ingram JC, Woolridge MW, Greenwood RJ, McGrath L. Maternal predictors of early breast milk output. *Acta Paediatrica*. 1999 May;88(5):493-9.
- Kelly PA, Bachelot A, Kedzia C, Hennighausen L, Ormandy CJ, Kopchick JJ, Binart N. The role of prolactin and growth hormone in mammary gland development. *Molecular and Cellular Endocrinology*. 2002 Nov 29;197(1-2):127-31.
- Kent JC, Metoulas L, Cox DB, Owens RA, Hartmann PE. Breast volume and milk production during extended lactation in women. *Experimental Physiology* 1999, 84:435-447.
- Lawrence, R. *Breastfeeding: A Guide for the Medical Profession*. St. Louis, MO: Mosby; 1999.
- Legro R, Spielman R, Urbanek M, Driscoll D, Strauss J, Dunaif A. Phenotype and genotype in polycystic ovary syndrome. *Recent Progress in Hormone Research* 1998;53:217-56.
- Livingstone C, Collison M. Sex steroids and insulin resistance. *Clinical Science (London)* 2002. 102(2):151-66.
- Lo-carb diets help PCOS. *Lo Carb Living Online*. Retrieved from the World Wide Web February 6, 2003: <http://www.tryalowcarbdiet.com/article2.htm>
- Marasco L, Marmet C, Shell E. Polycystic Ovary Syndrome: A connection to insufficient milk supply? *Journal of Human Lactation* 2000;16(2):143-148.
- Marmet C, Shell E. *Lactation Charts and Forms: A Guide to Lactation Consultant Charting*. Encino, CA: Lactation Institute; 1993:5-3.
- Miyake A; Tahara M; Koike K; Tanizawa O. Decrease in neonatal suckled milk volume in diabetic women. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 1989;33(1):49-53.
- Neifert, M. *Dr.Mom's Guide to Breastfeeding*. New York, NY: Penguin Putnam; 1998, 321-2.
- Neifert M, DeMarzo S, Seacat J, Young D, Leff M, Orleans M. Influence of breast surgery, breast appearance, and pregnancy-induced breast changes on lactation sufficiency as measured by infant weight gain. *Birth* 1990;17(1):31-8.
- Neifert M, McDonough S, Neville M. Failure of lactogenesis associated with placental retention. *American Journal of Obstetrics and Gynecology* 1981;140(4):477-8.

- Neifert M, Seacat, J. Lactation failure due to insufficient glandular development of the breast. *Pediatrics* 1985;76:823-28.
- Neville M. Physiology of Lactation. *Clinics in Perinatology* 1999;26(2):251-279.
- Nice FJ, Coghlan RJ, and Birmingham BT: Herbs and Breastfeeding. *U.S. Pharmacist*, 25: 28, 31, 31-32, 34, 41-42, 45-46 (September) 2000. Available: <http://www.uspharmacist.com/oldformat.asp?url=newlook/files/comp/acfl1e63.htm>
- Nicholas KR, Hartmann PE. Progesterone control of the initiation of lactose synthesis in the rat. *Australian Journal of Biological Sciences* 1981;34(4):435-43
- Patel S, Korytkowski M. Polycystic Ovary Syndrome: How best to establish the diagnosis. *Women's Health in Primary Care* 2000;3(1):55-69.
- Rasgon NL, Carter MS, Elman S, Bauer M, Love M, Korenman SG. Common treatment of polycystic ovarian syndrome and major depressive disorder: case report and review. *Current Drug Targets. Immune Endocrine and Metabolic Disorders* 2002; 2(1):97-102.
- Rittmaster R. Antiandrogen treatment of polycystic ovary syndrome. *Endocrinology and Metabolism Clinics of North America* 1999;28(2):409-421.
- Schmidt D, Wallace K. How to diagnose hypopituitarism: Learning the features of secondary hormonal deficiencies. *Postgraduate Medicine* 1998; 104(7). Retrieved Feb. 6, 2003 from the World Wide Web: http://www.postgradmed.com/issues/1998/07_98/schmidt.htm.
- Shahshahani MN, Wong ET. Primary hypothyroidism, amenorrhea, and galactorrhea. *Archives of Internal Medicine* 1978;138(9):1411-2.
- Siegel J. Local doctor finds mother's milk contains insulin. *The Jerusalem Post*, September 6, 2000.
- Speroff L, Glass R, Kase N. *Clinical Gynecologic Endocrinology and Infertility* (4th edition). Baltimore, MD: Williams & Wilkins; 1989, 285.
- Sridhar G, Nagamani G. Hypothyroidism presenting with polycystic ovary syndrome. *The Journal of the Association of Physicians of India* 1993;41(11):761-2.
- Stein I. Bilateral Polycystic Ovaries. *American Journal of Obstetrics and Gynecology* 1945;50:385-396.
- Stein I, Cohen M, and Elson R. Results of bilateral ovarian wedge resection in 47 cases of sterility. *American Journal of Obstetrics and Gynecology* 1949;58:267-74.
- Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *American Journal of Obstetric Gynecology* 1935; 29:181-191.
- Weed S. *Wise Woman Herbal Childbearing Year*. Woodstock New York: Ash Tree Publishing, 1986.
- Williams, N. Supporting the mother coming to terms with persistent insufficient milk supply: The role of the lactation consultant. *Journal of Human Lactation* 2002;18(3):262-3.
- Willis, C and Livingston, V: Infant insufficient milk syndrome associated with maternal postpartum hemorrhage, *Journal of Human Lactation* 1995;11(2):123-6.