

Hormones

Breastfeeding Support for Mothers with Hormone-based disorders


*I receive royalties for Making More Milk
No other disclosures of financial or conflicting interests to make.*



© 2023 Lisa Marasco MA, IBCLC, FILCA
LisalBCLC@Marasco.us


Hormonal Continuum

← Not enough Just right Too much →



Breast Development & Lactation require a proper balance of hormones and their receptors for optimal development

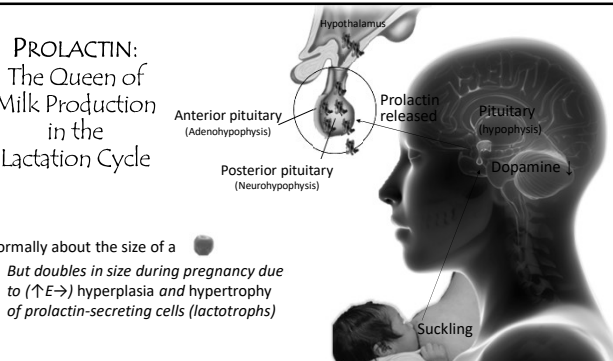
PROLACTIN: Pretest your knowledge



Prolactin is stimulated by which of the following?

- A. Androgens
- B. Estrogen
- C. Dopamine
- D. Nipple stimulation
- E. Sucking pressure
- F. Prolactinomas
- G. Domperidone, metoclopramide
- H. Acupuncture
- I. All of the above

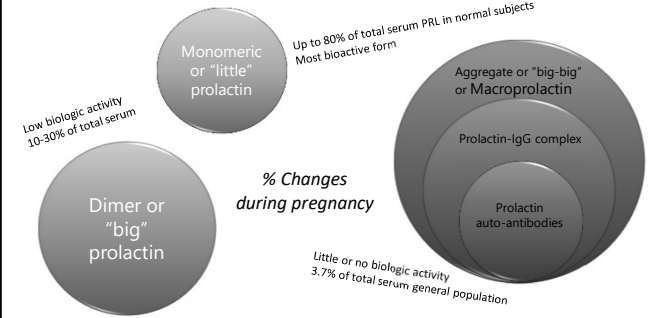
PROLACTIN: The Queen of Milk Production in the Lactation Cycle



Normally about the size of a ●
But doubles in size during pregnancy due to (↑E→) hyperplasia and hypertrophy of prolactin-secreting cells (lactotrophs)

Suckling

Multiple forms of Prolactin!



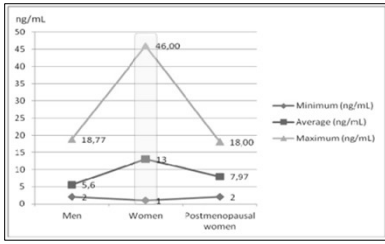
Low biologic activity 10-30% of total serum

Up to 80% of total serum PRL in normal subjects
Most bioactive form

% Changes during pregnancy

Little or no biologic activity 3.7% of total serum general population

Normal human prolactin levels



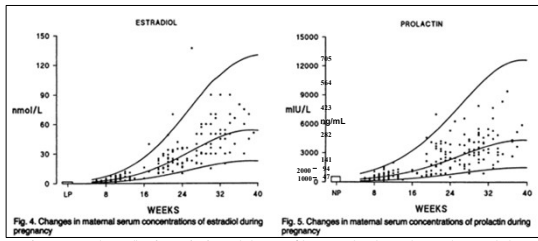
Group	Minimum (ng/mL)	Average (ng/mL)	Maximum (ng/mL)
Men	5.6	18.77	18.00
Women	2	13	46.00
Postmenopausal women	7.97	18.00	18.00

© 2013 Miguel Angel Castaño López, José Luis Robles Rodríguez and Marta Robles García. Originally published in Intech under CC BY 3.0 license. Available from <http://dx.doi.org/10.5772/56194>. The data was taken from Fuchs, F., & Kappeler A. Endocrinología de la Gestación. 1982, segunda edición. Salud Editores, S.A. Capítulo 22, Pág. 245-72.

*Conversion factor: mU/l × 0,0472 = ng/ml; ng/ml × 21,2 = mU/l.

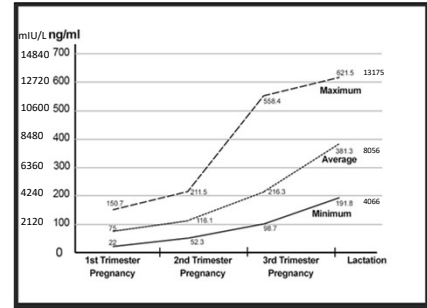
Hormones

Estrogen (E2) drives Prolactin in pregnancy



"There is clearly a need to examine those changes that occur during normal pregnancy so that unusual or unexpected trends can be identified..."

Pregnancy Prolactin range



© 2013 Miguel Angel Castaño-Díez, José Luis Robles Rodríguez and María Robles García. Originally published in Intech under CC BY 3.0 license. Available from: <http://dx.doi.org/10.5772/54758>. The article was taken from Taylor & Francis Group's Inspec. Studies of prolactin secretion in human pregnancy. Ann J Obstet Gynecol 1972;113:44-20

What happens in pregnancy if prolactin is low/suppressed?

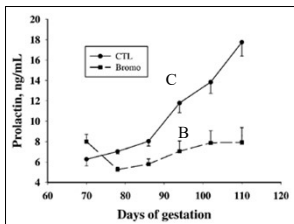


Figure 1. Prolactin concentrations in the blood of gilts (young primiparous) receiving an empty capsule (CTL) or 10 mg bromocriptine (Bromo) thrice daily from d 70 to 110 of gestation

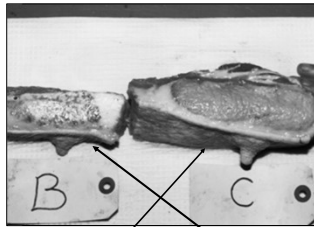


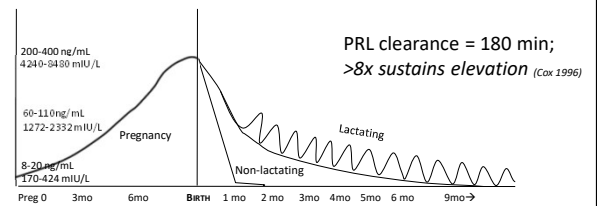
Figure 4. Transversal cut from the mammary gland of gilts receiving an empty capsule (C, placebo) or 10mg of bromocriptine (B) thrice daily from d 70 to 110 of gestation

Farmer, C., Sorensen, M. T., & Peticlerc, D. (2000). Inhibition of prolactin in the last trimester of gestation decreases mammary gland development in gilts. *J Anim Sci*, 78(5), 1303-1309.

Prolactin through the reproductive cycle

Baseline a product of surges

Influenced by frequency & quality of stimulation

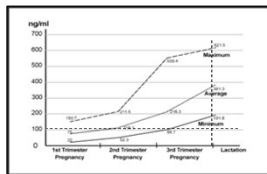


Timing of initiation matters!

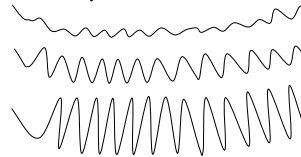
Nedkova 1995 (Bulgarian)
 Studied effect of early initiation on PRL in 90 women: All newly delivered mothers had serum PRL level over 100ng/ml, author accepted as minimum threshold

Initiation of breastfeeding	Prolactin Day 4*
< 6 hrs post-delivery	164
@ 6-12 hrs post-delivery	124
@ 72 hrs post-delivery (c-sections)	29

*Feeding frequency unknown, likely q4hrs



Amplitude matters




"Good lactators gave a prolactin response 236% above baseline after nursing whereas poor lactators showed a blunted or flat response"
 -Ostrom, 1990

"...a relatively low basal level and a moderate feeding-induced response are early indicators of...less productive lactation... In unfavourable cases, the feeding-induced PRL increases gradually disappeared and lactation stopped"
 -Godo 1988



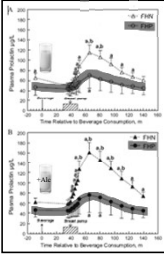
Zhang 2016: Are prolactin levels linked to suction pressure?

Hormones



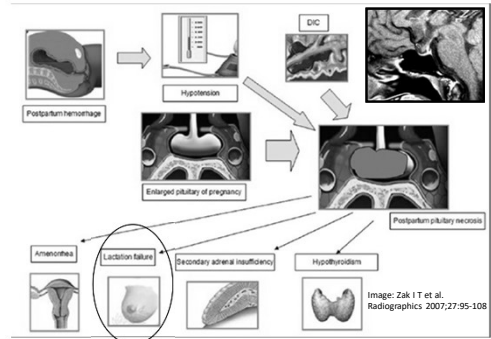
Other risk factors

- Family history of alcoholism
 - ✓ Smaller prolactin response to breast stimulation
 - ✓ Infants fed more often in late afternoon



Mennella, J. A., & Pepino, M. Y. (2010). Breastfeeding and prolactin levels in lactating women with a family history of alcoholism. *Pediatrics*

Sheehan's Syndrome



Shahzad, H., Sheikh, A., & Sheikh, L. (2012). Cabergoline therapy for Macroprolactinemia during pregnancy: A case report. *BMC Research Notes*, 5(1), 606. Used with permission.

Other risk factors

- Cranial Radiotherapy (CRT) tx at young age
 - Anterior pituitary problems- GH, PRL
 - Prolactin declines further over time*
 - High lactation failure rate
 - Follin: 6/7; Johnston: 10/12

Johnston, K., Vowels, M., Carroll, S., Neville, K., & Cohn, R. (2008). Failure to lactate: a possible late effect of cranial radiation. *Pediatr Blood Cancer*, 50(3), 721-722.
Follin et al. (2013). Prolactin insufficiency but normal thyroid hormone levels after cranial radiotherapy in long-term survivors of childhood leukaemia. *Clin Endocrinol (Oxf)*, 79(1), 71-76.

What about Hyperprolactinemia?

- Frequently caused by prolactinomas
- Often treated w/ PRL inhibitors, radiation or surgery
- Hx of galactorrhea is no guarantee of good lactation
- Sporadic information

Hyperprolactinemia is different

"big-big" or macroprolactin

10-25% of serum PRL in hyperprolactinemia vs 4%

Frequently associated with anti-PRL autoantibodies!

*Low biological activity

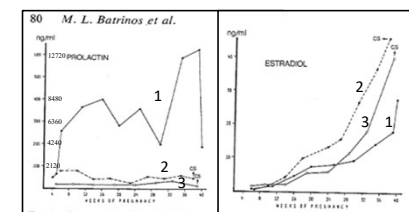
Radavelli-Bagatini, et al. (2013). Macroprolactinemia in women with hyperprolactinemia: a 10-year follow-up. *Neuro Endocrinol Lett*, Shimatsu, A., & Hattori, N. (2012). Macroprolactinemia: diagnostic, clinical, and pathogenic significance. *Clin Dev Immunol* 2012

Case study of three mothers

CASE 1: Treated w/bromocriptine prior to pregnancy; levels rose normally then extra high (~600ng/12721mIU); headache @ 39 wks for 6 hrs.

CASE 2: Treated with CRT (Cobalt Radiation Therapy) Twins

CASE 3: Tumor removed surgically. Twin pregnancy.



Batrinos, M. L., Panitsa-Falla, C., Anagnostou, M., & Pitouli, S. (1981). Prolactin and placental hormone levels during pregnancy in prolactinomas. *Int J Fertil*, 26(2), 77-85.

Hormones

Case study of three mothers

Table I. Prolactin (PRL) and estradiol (E₂) levels in the three patients with prolactinomas before and after termination of pregnancy

	Before pregnancy Prolactin (PRL) ng/ml		Delivery		Amniotic fluid		Umbilical cord		Suckling	
			PRL ng/ml	E ₂ pg/ml	PRL ng/ml	E ₂ pg/ml	PRL ng/ml	E ₂ pg/ml	Before	After
Case I	Before treatment	200-250	182	28,000	610	17,000	262	25,000	75	88
	After bromocriptine 40-60									
Case II	92->200		47.5	46,000	625	13,600	600	20,000	12.5	12.5
	After irradiation 23-27									
Case III	After excision of adenoma 7.5-10		14.5	40,000	650	19,000	600	20,000	170	13,000

"None were able to breastfeed..."

Batrinou et al. (1981). Prolactin and placental hormone levels during pregnancy in prolactinomas. *Int J Fertil*, 26(2), 77-85.

Clinical Experiences -76 comments



"From my experience, women with a history of prolactinomas have varied lactation outcomes. Some women have hyperlactation, some have a normal supply, and some have insufficient lactation. Perhaps it is the treatment pre-pregnancy that impacts the prolactin level postpartum."

women-health-info.com/2018/08/01/prolactinoma-lactation.html

Screening for prolactin problems



- Checklist**
- Did the milk ever come in?
 - Hx of pp hemorrhage, acute hypotension?
 - Hx of pituitary problems or tumors?
 - Hx of infertility, meds like cabergoline or bromocriptine
 - Personal or family hx of autoimmune problems? Alcoholism?

Treatment quandary for low prolactin

Physical stimulation

Pharmaceutical stimulation ~Off-label~

Domperidone Sulpiride

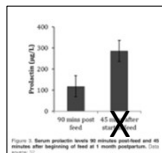
Replacement therapy N/A

Measuring prolactin



For Basal/Baseline level:
After 2-3 hours no stimulation

For Surge:
30-45 from start of nursing/pumping
OR 15-30 minutes after start of nursing/pumping

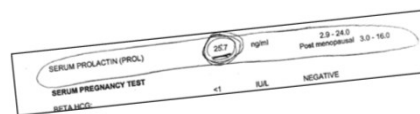


Baib, M., Gardner, H., & Hartmann, P. (2018). Normal Human Lactation during the postpartum period. *PLoS ONE*, 13(12), e0200000.

Prolactin Problems

Laboratory Measuring issues:

- Labs have no reference ranges for lactation!
- Must factor in frequency of feeding/pumping



Hormones

Prolactin Reference

Approximate Prolactin Levels for Exclusively Breastfeeding

Stage	Baseline		Level after Suckling	
	ng/mL	mIU/l	ng/mL	mIU/l
Female menstrual life	2-20	42-425		
Third trimester of pregnancy	100-550	2128-11700		
Term pregnancy	200-600	4255-12766		
First 10 days postpartum	200	4255	400	8510
1 month	100-140	2128-2978	260-310	5532-6596
2 months	100-140	2128-2978	195-240	4149-5106
4 months	60-80	1277-1702	120-155	2553-3298
6 months	50-65	1063-1383	80-100	1702-2128
7 months-1 year	30-40	638-851	45-80	957-1702

Thyroid Dysfunction

Can be primary, secondary, overt, subclinical, autoimmune

Onset can be prior to preg, during preg, post-delivery, or even later

Can also occur in conjunction with other conditions such as PCOS

Incidence much higher in women

THYROID: Pretest your knowledge

Which of the following have been associated with thyroid dysfunction?

A. Infertility

B. Autoimmunity

C. Hyperemesis

D. Anemia

E. Hypertension, pre-eclampsia

F. Changes in pregnancy breast development

G. Fast letdown

H. Delayed lactation

I. Low milk supply

J. Hyper production of milk

K. All of the above

Thyroid Hormones regulate metabolism

THYROID HORMONES:

T3 = triiodothyronine

T4 = thyroxine

FEEDBACK REGULATION:

TRH = Thyroid-releasing hormone

TSH = Thyroid-stimulating hormone, also called thyrotropin. Indicator of thyroid function.

Prolactin

Thyroid

Hypertension

Hyperemesis/Tirexsis

Reproductive Endocrinologist Perspective

RE preferred TSH range for preconception is .5-2.5, with 1.0 as ideal

2018 proposed range .3-3.5 for general & fertility (Moncayo 2017)

→Pregnancy ranges are trimester specific

Controversial- still not settled

HYPOTHYROIDISM: Not enough hormone

High TSH verified by low T3/T4

- ❖ Common symptoms may include weight gain, cold, fatigue, hair loss
- ❖ Can affect fertility
- ❖ *Hashimoto's thyroiditis*- autoimmune, most common cause

Hormones

Hypothyroidism in Pregnancy

Uncontrolled hypothyroidism can cause
 → anemia
 → pregnancy induced hypertension
 → postpartum hemorrhage

Risk factors for delayed Lact 2

Rat studies: Less mammary tissue development

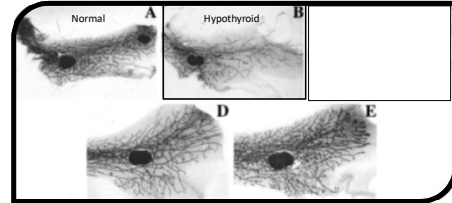
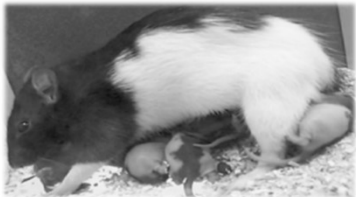


Fig. 3. The effects of thyroid hormones and progesterone (P) on tertiary branching. Whole mounts of mammary glands from mice are presented. (A) 3-month-old C3H mouse; (B) 3-month-old hypothyroid C3H mouse, after treatment with propylthiouracil for 5 weeks; (C) 3-month-old hyperthyroid C3H mouse, treated with thyroxine for 5 weeks; (D) 39-day-old BALB/c mouse (reproduced by permission of the Society for Endocrinology, SB); (E) 39-day-old intact BALB/c mouse treated with P for 15 days (reproduced by permission of the Society for Endocrinology, SB).

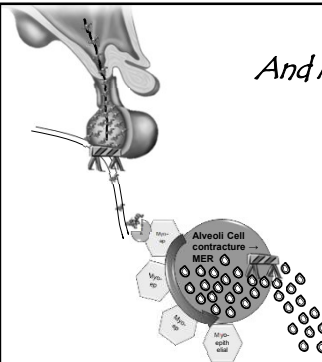
Howey, R. C., Trott, J. F., & Vonderhaar, B. K. (2002). Establishing a framework for the functional mammary gland: from endocrinology to morphology. *Mammary Gland Biol Neoplasia*, 7(1), 17-38.

Hypothyroid rats have smaller litters, longer gestations and "poorer lactation"
 (Hapon 2003, 2005)



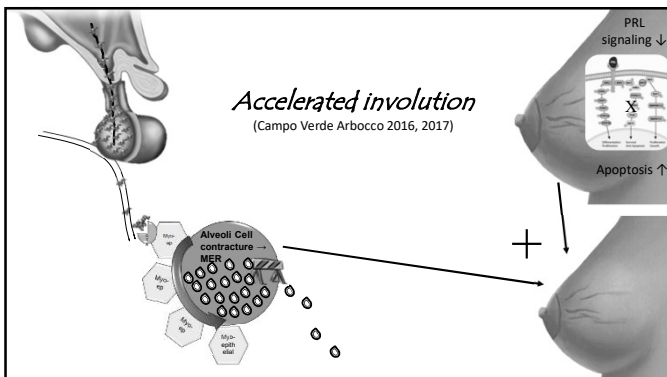
And MER problems

...a reduction in circulating Oxytocin postpartum with impaired milk ejection & lactation (Hapon 2003, 2005)



Accelerated involution

(Campo Verde Arbocco 2016, 2017)



HYPERTHYROIDISM- too much hormone!

- Low TSH verified by elevated T3/T4
- ❖ Common sx include weight loss, fast heart beat, sleep problems, nervousness, frequent BMs
- ❖ Grave's most common cause, autoimmune
- ❖ Previously thought not to affect lactation


Symptoms of HYPERTHYROIDISM

Excessive Production of thyroid hormones

T₃ T₄

Intolerance to heat
 High blood sugar
 Low serum cholesterol

Hormones

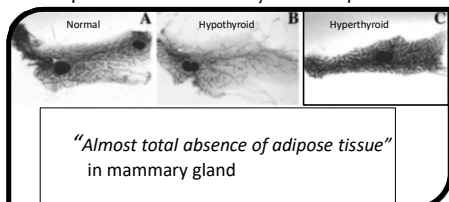


Hyperthyroidism

Sx often improve during pregnancy, but more severe HT can cause pregnancy complications such as

- Hyperemesis
- Fetal growth restriction
- Pre-eclampsia
- Preterm labor

Impact on mammary development




"Almost total absence of adipose tissue" in mammary gland

Fig. 3. The effects of thyroid hormones and progesterone (P) on tertiary branching. Whole mounts of mammary glands from mice are presented: (A) 3-month-old C3H mouse; (B) 3-month-old hypothyroid C3H mouse, after treatment with propylthiouracil for 5 weeks; (C) 3-month-old hyperthyroid C3H mouse, treated with thyroxine for 5 weeks; (D) 39-day-old BALB/c mouse (reproduced by permission of the Society for Endocrinology, 58); (E) 39-day-old intact BALB/c mouse treated with P for 15 days (reproduced by permission of the Society for Endocrinology, 58).


Howey, R. C., Trott, J. F., & Vonderhaar, B. K. (2002). Establishing a framework for the functional mammary gland: from endocrinology to morphology. / Mammary Gland Biol Neoplasia, 7(1), 17-38.

Rat studies: Hyperthyroid



Hyperthyroid rats have larger litters with earlier and *prolonged* labors.

Pregnant hyperT rats showed good mammary growth and evidence of milk production *but poor or complete lactation failure* depending on the degree of hyperT



Problem was pinpointed to oxytocin release and milk ejection (Varas 2002)

POSTPARTUM THYROIDITIS/ POSTPARTUM THYROID DYSFUNCTION

PPT occurs at a rate of ~5% of all pregnancies
Onset anytime in 1st year, but usually 1-6 mos
Now considered an autoimmune condition
Thyroid function usually normalizes by 12 mos but at high risk of failing later

Screening for thyroid problems

Checklist

→ Unexplainable sluggish milk production OR rapid onset of milk production OR hyperlactation OR change in milk output OR letdown problem

- History of thyroid problems before now?
- Thyroid function questioned during pregnancy?
- Thyroid treatment during pregnancy?
- Sudden unexplained changes in energy, mood, weight, skin, heat or cold intolerance?
- Family history of thyroid problems?
- At risk for excess or deficient iodine intake?
- Visible goiter?
- Personal/family history of autoimmune problems?

Hormones

Strategy for Thyroid & Supply: the First Step

Replacement hormone is first line of treatment for hypoT-related supply problems...

The dessicated thyroid extract debate

Reducing thyroxine is the first line of defense for hyperT- related milk supply problems

Beware of over- or under-treatment postpartum

American Thyroid Assoc weighs in (2017)

Recommendation 74:

As maternal hypothyroidism can adversely impact lactation, *women experiencing poor lactation without other identified causes should have TSH measured to assess for thyroid dysfunction.*

Alexander, E. K., Pearce, E. N., Brent, G. A., Brown, R. S., Chen, H., Dosiou, C., . . . Sullivan, S. (2017). 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid*

American Thyroid Assoc weighs in (2017)

Recommendation 75:

Given its adverse impact on milk production and letdown, *subclinical and overt hypothyroidism should be treated* in lactating women seeking to breastfeed.

Alexander, E. K., Pearce, E. N., Brent, G. A., Brown, R. S., Chen, H., Dosiou, C., . . . Sullivan, S. (2017). 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid*

American Thyroid Assoc weighs in (2017)

Recommendation 76:

The impact of maternal hyperthyroidism upon lactation is not well understood. Therefore, no recommendation to treat maternal hyperthyroidism on the grounds of improving lactation can be made at this time. (*No recommendation, Insufficient Evidence*)

Alexander, E. K., Pearce, E. N., Brent, G. A., Brown, R. S., Chen, H., Dosiou, C., . . . Sullivan, S. (2017). 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid*

Second level help for thyroid-related problems

Oxytocin nasal spray?

Disclosure: off-label use



Other?



Cowley, K. C. (2005). Psychogenic and Pharmacologic Induction of the Let-Down Reflex Can Facilitate Blg by Tetrasyptic Women: A Report of 3 Cases. *Arch Phys Med Rehab*
 Camarillo et al. (2021). "Ski" lowering effects of metformin: a possible mechanism of action. *J Endocrinol Invest*
 Benveniga et al. (2021). The Role of Inositol in Thyroid Physiology and in Subclinical Hypothyroidism Management. *Front Endocrinol*
 Ventura, Melo, & Carrilho (2017). Selenium and Thyroid Disease: From Pathophysiology to Treatment. *International journal of endocrinology*.

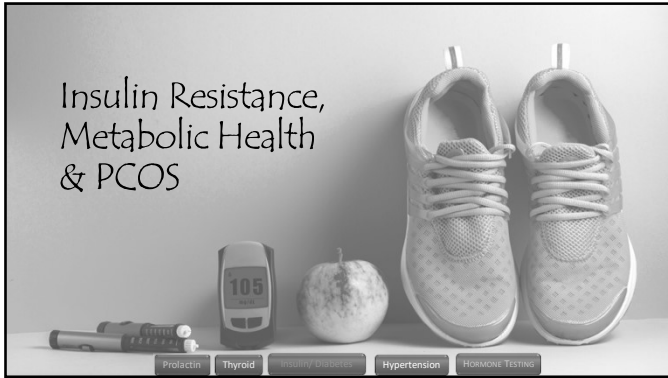
Thyroid affective galactagogue herbs

- Ashwagandha- stimulates T3
- Chickweed- supportive
- Dandelion- supportive
- Milk thistle- improves T4→T3
- Nettle- supportive/balancing
- Vervain- supportive
- Red clover- increased total & free T3 in ewes
- Malunggay? *tested for use with hyperthyroidism*
- Fenugreek- *Reduced T3 in mice & rats;*



Yarnell 2006; Tahiliani 2003; Panda 1999

Hormones

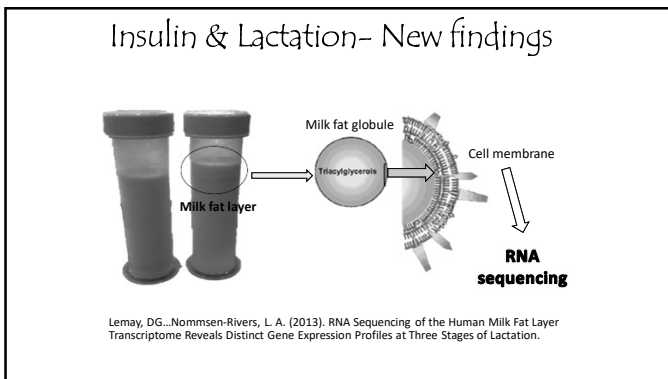
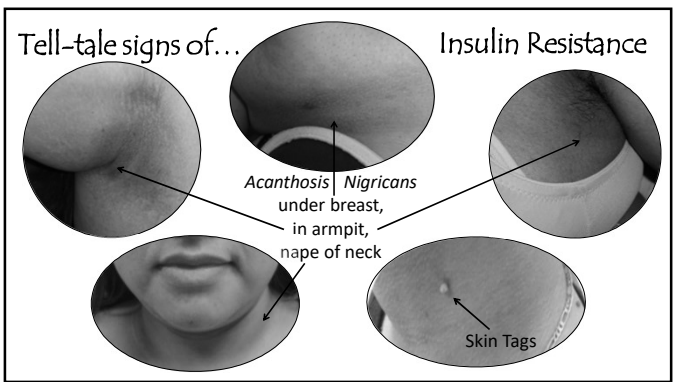
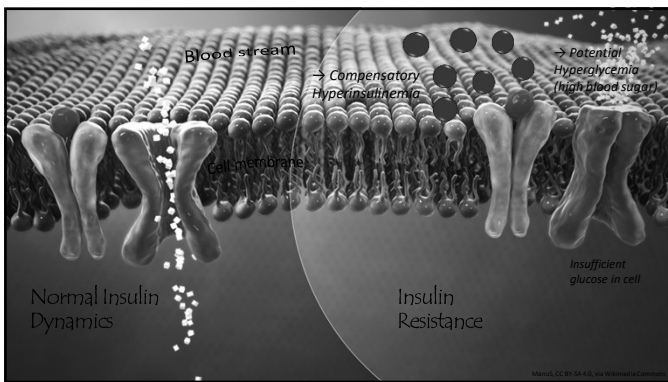


Insulin Resistance, Metabolic Health & PCOS

INSULIN:
Pretest your knowledge

Which of the following may be associated with insulin resistance?

- A. Acanthosis nigricans, Skin tags
- B. Excessive weight gain
- C. Hypothyroidism
- D. Gestational diabetes
- E. Insulin-dependent diabetes T1
- F. Persistent PTPRF levels during transition period
- G. Shorter duration of lactation
- H. Hyperinsulinemia
- I. Decreased androgens
- J. Changes in pubertal breast growth
- K. Imbalances in myo- and d-chiro-inositol
- L. All of the above



Breast insulin dynamics change with stages

Colostrum → Transitional Milk	Transitional → Mature Milk
Strong modulation of insulin signaling <i>Breast becomes sensitized to insulin</i>	Insulin signaling maintains steady-state <i>Robust expression.</i>
Up-regulation of lipogenesis, protein synthesis	Toning down of initial steep up-regulation of metabolic signals via up-regulation of PTPRF which suppresses insulin action
Inhibition of apoptosis, glycolysis and glycogenesis	
PTPRF ↑	PTPRF ↓

PTPRF = protein tyrosine phosphatase, receptor type F
(Insulin necessary for milk protein synthesis)

Lemay, et. al. (2013). RNA Sequencing of the Human Milk Fat Layer Transcriptome Reveals Distinct Gene Expression Profiles at Three Stages of Lactation.

Hormones

How IR can affect milk production

Markers	Mature Milk Group 1	Mature Milk Group 2
Median onset of notably fuller breasts	34 hrs	74 hrs
Insulin secretion	Above median	Below median
Insulin sensitivity	Above median	Below median
Expression of PTPRF	_baseline_	Significantly higher than Group 1 (over-expressed)
Milk Production		All reported difficulty with milk supply at either day 4 or pp week 4-6 interviews



CONCLUDING HYPOTHESIS: "Women w/ decreased insulin sensitivity (IR) will experience a more sluggish increase in milk output in response to infant demand as a result of PTPRF over-expression in the mammary gland"

Lemay, et. al. (2013). RNA Sequencing of the Human Milk Fat Layer Transcriptome Reveals Distinct Gene Expression Profiles at Three Stages of Lactation.

PTPRF as a limiter of insulin action and milk production

A limiter of insulin action and milk production

PTPRF

PTPRF as a limiter of insulin action and milk production

Insulin Resistance and low milk production

How does your insulin level affect you and your baby? When insulin levels are low, your body can't use glucose properly. This means your baby can't get the energy it needs to grow and gain weight. In addition, your body can't produce enough milk to feed your baby. This is why insulin resistance is a concern for breastfeeding mothers.

If your body produces more insulin than you need, it can lead to insulin resistance. This means your body can't use glucose properly. This means your baby can't get the energy it needs to grow and gain weight. In addition, your body can't produce enough milk to feed your baby. This is why insulin resistance is a concern for breastfeeding mothers.

What Causes Insulin Resistance?

- Obesity and Excess Weight
- Insulin Resistance
- High Cholesterol
- Diabetes

Considered high sugar levels in the blood causes diabetes.

48 mothers 1-8wks pp w/low supply

33 had signs of IR

BMI ~37

Milk production median 216 [158-332]

15 non-IR

BMI ~25

Milk production median 377 [294-598]

"Additional deficit associated w/ IR"

Nommsen-Rivers, et al. (2017). Milk Production in Mothers with and without Signs of Insulin Resistance. *The FASEB Journal*

Glover (2017). Impact of metabolic dysfunction on breastfeeding outcomes in GDM

Metabolic marker	HR (95% CI)	Insulin (µU/mL)	Significance p
Fasting glucose (mg/dL)	1.0 (0.99)	8 (21.7)	
HbA1c (%)	1.0 (1.01)	8 (22.1)	
Hemoglobin A1c (%)	1.0 (1.01)	8 (22.1)	
OGTT 1-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 2-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 3-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 4-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 5-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 6-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 7-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 8-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 9-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 10-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 11-hr (mmol/L)	1.0 (1.01)	8 (22.1)	
OGTT 12-hr (mmol/L)	1.0 (1.01)	8 (22.1)	

A1C, BMI, OGTT & subscapular were associated w/ shorter duration of lactation

not breastfeeding as long as desired

Estimated Average Glucose (eAG) (mg/dL)

127 - 153

Confirmed by Verd 2016

Compared parents with *normal* 1-hr glucose challenge tests (<7.8 mmol/L) with those who had *elevated* 1-hr test (≥ 7.8mmol/L) but *below* threshold for GDM diagnosis

Results: Mildly impaired women abandoned exclusive breastfeeding sooner than non-impaired: OR 1.65

Verd et al. (2016). The Effects of Mild Gestational Hyperglycemia on Exclusive Breastfeeding Cessation.

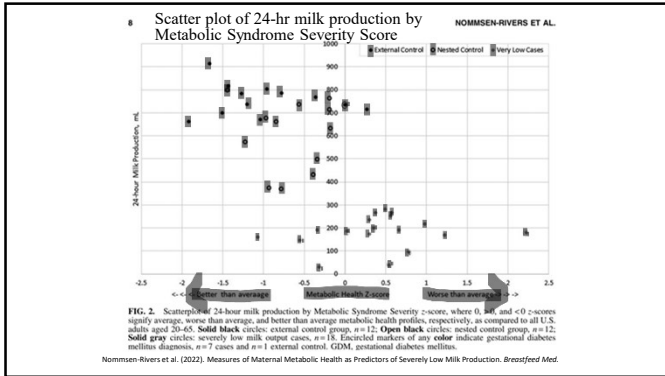
Metabolic health predicts severe low supply risk 2022

EXTERNAL CONTROL [NORMAL]	Original LMS study MODERATE LOW-NORMAL	Original LMS study SEVERELY LOW
Exclusively bfg, infant wt velocity >20g/day n=12	>300mL/24 hrs n=12	<300mL/24 hrs n=18
Normal wt 58%	Normal wt 25%	Normal wt 6%
Overweight 25%	Overweight 42%	Overweight 11%
Obese Class I (30-34.9) 0%	Obese Class I 25%	Obese Class I 37%
Obese Class II (35-39.9) 0%	Obese Class II 8%	Obese Class II 28%
Obese Class III (>40) 8%	Obese Class III 0%	Obese Class III 39%
GDM 8%	GDM 0%	GDM 39%

Severely Low Supply had significant differences in: *BMI, waist circumference, glucose, c-peptide, HOMA-IR, Elevated Triglycerides, systolic & diastolic blood pressure, metabolic syndrome risk z-score*

Nommsen-Rivers et al. (2022). Measures of Maternal Metabolic Health as Predictors of Severely Low Milk Production. *Breastfeed Med.*

Hormones



Matias 2014: GDM Risk factors for lactation problems

N=883 Racially and ethnically diverse population
 1/3 of GDM mothers experienced delayed onset of lactogenesis

Matias et al. (2014). Maternal prepregnancy obesity and insulin treatment during pregnancy are independently associated with delayed lactogenesis in women with recent gestational diabetes mellitus.

5/8 Suwaydi 2022 GDM parents had DOL; 2 had long term LMS

Suwaydi et al. (2022). Delayed secretory activation and low milk production in women with gestational diabetes: a case series. *BMC Pregnancy Childbirth*

Pregnancy complications/GDM

	Any Bfg Rate	Duration: Full Bfg	Duration: Any Bfg
Healthy = 527	86%	17 wks	
GDM all = 257	75%	9 wks	
GDM-Diet		12 wks	20 wks
GDM Insulin		4 wks	10 wks
GDM + BMI <30	80%		17 wks
GDM + BMI >30	65%		12 wks

Conclusions: Parents with GDM, especially those with insulin-dependent gestational diabetes, and obese mothers breastfed their children significantly less and for a shorter duration than healthy mothers.

Hummel et al. (2008). Breastfeeding in women with gestational diabetes.
 Wu et al. (2021). Gestational Diabetes Mellitus & Risk of Delayed Onset of Lactogenesis: A Systematic Review and Meta-Analysis. *Bfg Med*

Speaking of insulin... Herskin 2015

Diabetes type	Any bfg discharge	Full bfg discharge	Any bfg 4 mo	Full bfg 4 mo
Type 1	93%	72%	61%	49%
Type 2 (pregestational)	86%	45%	34%	23%

STANDARD PRACTICE: Insulin-controlled during pregnancy

VALIDATING RESEARCH EMERGING

Herskin et al. (2015). Low prevalence of long-term breastfeeding among women with type 2 diabetes. *J Matern Fetal Neonatal Med*
 Lee & Kelleher. (2016). Biological underpinnings of breastfeeding challenges: the role of genetics, diet, and environment on lactation physiology. *Am J Physiol Endocrinol Metab*
 Cordero et al. (2022). Exclusive breastfeeding among women with type 1 and type 2 diabetes mellitus. *BMC Pregnancy Childbirth*
 Wu et al. (2021). Gestational Diabetes Mellitus & Risk of Delayed Onset of Lactogenesis: A Systematic Review and Meta-Analysis. *Bfg Med*

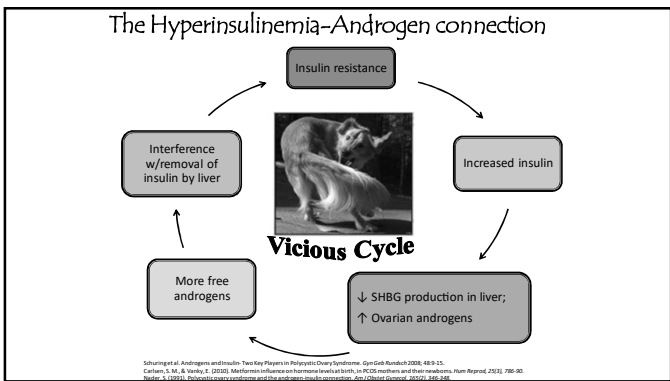
Triple Risk of Lactation Problems for insulin in pregnancy:

“Women with GDM who are on insulin therapy have a delay in the onset of lactation, which suggests that insulin treatment may have adverse effects on milk production or composition in humans.”

– Lee & Kelleher 2015

AOR 3.11

Matias et al. (2014). Maternal prepregnancy obesity and insulin treatment during pregnancy are independently associated with delayed lactogenesis in women with recent gestational diabetes mellitus.



Hormones

Androgens vs estrogens in the breast

Estrogen stimulates development of mammary tissue

Androgens slow growth of mammary tissue

Labrie F. Dehydroepiandrosterone, androgens and the mammary gland. Gynecology Endocrinology 2006; 22(3):118-30.

Clinical Symptoms of HYPERandrogenism

Facial or male-pattern hair

Acne

Acne

Excess wt w/ IR influence on pubertal mammary growth

Adult: High insulin levels soon after puberty → May reduce breast size & lactational capacity via androgens

Puberty: Insulin resistance before → Can decrease overall glandular tissue inside (IGT)

Fetal: High insulin levels before → Can increase breast size (hypertrophy)

Cesari-SM, D., & Liberato, P. (2017). Influence of adolescent and pre-pregnancy maternal weight status on lactation capability. Paper presented at the ASPA 2017 Annual Meeting, San, Amer, California, August & November-2016. (2024). Breast hypertrophy markers among women who report insufficient milk production: A retrospective online survey. Post One

What about Polycystic Ovary Syndrome (PCOS) ?

Polycystic Ovary Syndrome: A Connection to Insufficient Milk Supply?

Polycystic ovarian syndrome and low milk supply: Is insulin resistance the missing link?

PCOS

N=? Insulin Resistant


Riddle & Nommsen-Rivers 2016:
"PCOS as a risk factor for insufficient lactation may be limited to the subset of women with postpartum glucose intolerance"

Screening for Insulin problems

Checklist

- Personal or family history of diabetes?
- Failed pregnancy glucose tolerance test?
- Diagnosed with Gestational Diabetes Mellitus?
- Visible acanthosis nigricans?
- Visible skin tags? (when did they grow?)
- Onset of above symptoms?

Hormones



Case study

PCOS, breast hypoplasia and low milk supply: A case study


McGuire, E., & Rowan, M. (2015). PCOS, breast hypoplasia and low milk supply: A case study. *Breastfeeding Review*, 23(2), 29-32.

Interesting Case Study

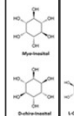
- Measured output via infant transfer = 52mls/day
- Did *not* respond to domperidone @ 30 or 60mg
- Clinical indications of insulin resistance

Metformin: Transfer increased 69% = 88mls/day

The Second M

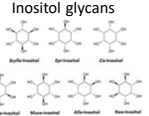


Naturally occurring nutrient, type of sugar




Myo-Inositol

Inositol glycans



Foods High in Inositol

Clements & Darnell, 1980



Small text at bottom: "Orange-Fruit-Pieces" by Evan-Amos... "Cantaloupe" by Citrus-paradise... "Kiwi" by Andrei Korovin... "Nectarine" by David J. Phillip...

Myo-inositol vs D-chiro-inositol

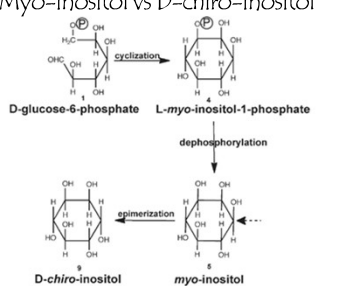


Figure 5. Conversion of D-glucose-6-phosphate to myo-inositol-1-phosphate by cyclization. Myo-inositol-1-phosphate is then dephosphorylated to myo-inositol, which then is converted by epimerization of the C3 hydroxyl (dashed left arrow) to DCI.


Larner 2010

Larner 2010	
Groups	Myo/D-chiro
Control	2.5
Type II diabetes patients	20.4
Nondiabetic relatives of type II diabetic patients	13.2
Type I diabetes patients	13.6

Insulin resistance is frequently associated with an imbalance of Myo-I to D-chiro-I

→ Caused by

- 1) impaired conversion and/or
- 2) increased urinary clearance of D-chiro-I




Larner, Brautigan & Thorne. (2010). D-chiro-inositol glycans in insulin signaling and insulin resistance. *Molecular Medicine*

Another option?

40:1

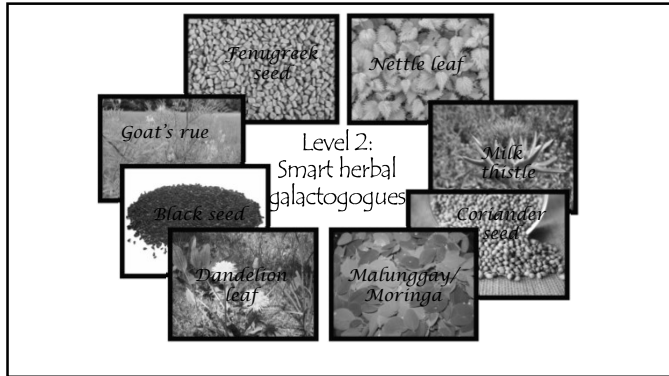
Myo D-chiro

Virtually no side-effects



Unfer 2014; Kalra 2016; Tahir 2019

Hormones



INSULIN:
Now what do you think?

Which of the following may be associated with insulin resistance?

- A. Acanthosis nigricans, Skin tags
- B. Excessive weight gain
- C. Hypothyroidism
- D. Gestational diabetes
- E. Insulin-dependent diabetes T1
- F. Persistent PTPRF levels during transition period
- G. Shorter duration of lactation
- H. Hyperinsulinemia
- I. Decreased androgens
- J. Changes in pubertal breast growth
- K. Imbalances in myo- & d-chiro-inositol
- L. All of the above

HYPERTENSION:
Pretest your knowledge

Which of the following problems might occur with hypertension and related conditions?

- A. Delayed onset of lactation
- B. Shorter duration of lactation
- C. Impaired placental function/hormones
- D. Lower prolactin
- E. Impaired myoepithelial cell contraction (milk ejection)
- F. All of the above

HYPERTENSION: fallout from metabolic issues

PIH associated with delayed lactogenesis (Salahudeen 2013)

Birth parents with gestational hypertension have more difficulties maintaining exclusive bfg and shorter duration after 6 mos (Strapasson 2018)

Women with hypertensive disease of pregnancy bfd significantly less often, esp. w/HELLP (Leeners, 2005)

Variable clinical presentations... may include both primary (disease itself) and secondary (tx fallout) factors (Demirci 2018)

✓ PLACENTA

Potential calcifications, reduced PTHrP, impaired function → could affect mammary gland development

Nahar et al. 2013; Goswami 2012; Majumdar 2005; Wild64 2003

✓ PROLACTIN

PREGNANCY	32-35 weeks	36-39 weeks	40-42 weeks
Normotensive N=121	225ng/mL 70-566	205ng/mL 65-584	229ng/mL 64-496
Pre-eclampsia	155ng/mL 27-465	183ng/mL 47-414	178ng/mL 63-326
Essential (primary) hypertension	180ng/mL 85-444	171ng/mL 52-420	149ng/mL 104-219
Mean and range			

Yuen, B. H., Cannon, W., Woolley, S., & Charles, E. (1978). Maternal plasma and amniotic fluid prolactin levels in normal and hypertensive pregnancy.

✓ OXYTOCIN

Impaired contraction response to oxytocin, possibly due to decreased OT receptor expression in the mammary gland

Akashshi et al. (2019). Pre-eclampsia-Like Features and Partial Lactation Failure in Mice Lacking Cystathionine gamma-lyase: An Animal Model of Cystathioninuria.

And what about magnesium tx?

CLUE:
MgSO4= Calcium antagonist, relaxes smooth muscle, leads to increased OT requirements for uterine toning during c-section (Hasanein 2015)

- ✓ Birth parents who took it >4wks before delivery were less likely to discharge fully bfg (Anderson 2017; Drugs that suppress lactation, Part 1)
- ✓ Postpartum tx assoc w/impaired MER, delayed Lact 2, infant lethargy (& > wt loss)
- ✓ Strategy: anticipatory guidance
 - ✓ Early frequency breast stim
 - ✓ Patience
- ✓ Magnesium suppl should be balanced- Mag with CA better

One hospital's keen observation & experience

Hormones

Hormone testing: The Next Step?

Remember: *We Know Not Because We Ask Not*

Is it really WNL?

*Or did we just
assume this?*



How do I know what is normal?



- Look at lab ranges
- Is this a hormone that is affected by pregnancy or lactation?
- Develop your expert contact network