Top 10 New Lactation Tidbits

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I have nothing to declare

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#1 The Zn of insufficient milk

- When your interventions do not always help increase milk production it may be genetic!
- Mutation of the protein ZnT2 which transports zinc in specific body tissues
  - Low Zn in milk
  - Reduced mammary gland development
  - Functional problems
- ZnT2 transports zinc by importing it into vesicles -- small organelles within the cell -- that then secrete zinc into the breast milk.
- Zinc is also necessary to trigger the growth of mammary glands, mammary epithelial cells and secretion pathways.
- Without functional ZnT2, zinc accumulates in the cytoplasm, becoming toxic to the cell.

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Prolactin and ZnT2 are partners

- ZnT2 is critical for mammary gland expansion and differentiation and milk secretion
- Loss of ZnT2 results in breast hypoplasia
  - Lee et al. J Biol Chem 2015;290:13064-13078
- Prolactin plays a primary role in ZnT2 activity
  - Qian et al. Am J Physiol Cell Physiol 2009; 297:C369-C377

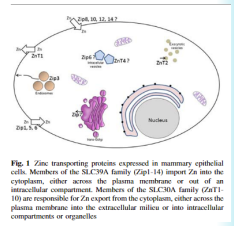

Fig. 1 Zinc transporting proteins expressed in mammary epithelial cells. Members of the SLC39A family (Zip1-14) import Zn into the cytoplasm, either across the plasma membrane or out of an intracellular compartment. Members of the SLC30A family (ZnT1-10) are responsible for Zn export from the cytoplasm, either across the plasma membrane into the extracellular milieu or into intracellular compartments or organelles

Kelleher et al. Genes & Nutrition 2009; 4:83-94

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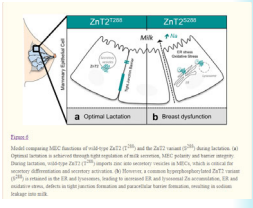
Genetic variants

- The common genetic variant S^{288} in ZnT2 causes
  - oxidative stress in the lactocyte
  - Impaired paracellular barrier function
  - Lysosomal mediated cell death
  - Increased sodium content in breastmilk



- Lee et al. Scientific Reports 2018;8:3542

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Looking for zinc

- It is possible to take a sample of saliva and sequence the gene for ZnT2 (SLC30A2) and see if there is a mutation directly
- Some companies can do this now
- Low zinc levels in mother's milk would strongly suggest a defect in a zinc transporter
- The mom's serum zinc levels are not affected because low milk zinc is caused by a defect in her breast.
- However, if the mom's serum zinc levels were low, then she would likely be suffering from another issue (inflammation, diabetes, obesity, or very low dietary intake of zinc) that my also lead to low milk zinc levels.

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What can we do?

- Most women are marginally low in zinc
- Adding a bit more of zinc to the diet would not be harmful but too much could be toxic
- Unknown if it would be therapeutic with the ZnT2 variants
- In some cases domperidone may help.
- Since ZnT2 is regulated by prolactin and depending upon the defect in ZnT2, extra prolactin may help fix the problem
- Enrich the mother's diet with antioxidants
- Most lactation defects seem to have an inflammation component
- The underlying consequence of a defect in ZnT2 may be inflammation
- So if we reduce inflammation, we can solve the problem that the defect in ZnT2 is actually causing
- Future drug that targets the particular pathway/mechanism

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#2 Massage for jaundice

- Body massage and abdominal massage
  - Increases frequency of bowel movements
  - More rapid passage of bilirubin-laden meconium (stimulates peristalsis)
  - Helps reduce bilirubin levels
  - Stimulates vagus nerve that causes insulin and gastrin secretion accelerating digestion & absorption of food and increase in defecation
- Gozen et al. J Spec Pediatr Nurs 2019;e12237
- Eghbalian et al. Infant Behav Dev 2017;49:31-36
- Chen et al. Tohoku J Exp Med 2011;223:97-102

Ahmdipour et al. Am J Perinatol 2019; doi: 10.1055/s-0039-1685493. [Epub ahead of print]

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Massage therapy for reducing bilirubin levels

- Touch therapy techniques from Tiffany Field
  - Touch Research Institute, University of Miami, Miller School of Medicine
- Vimala massage
  - Seyyedrasooli et al. J Caring Sci 2014;3:165-173

https://www.johnsonsbaby.in/baby-massage/newborn-massage-guide

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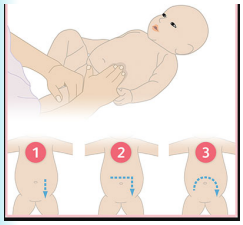
" I love you" massage pattern



Infant Massage USA
www.infantmassageusa.org

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#3 Probiotics for jaundice

- Probiotics (*Bifidobacterium, S. boulardii, C. butyricum*, probiotic oligisaccharides, *B. subtilis, Bacillus clausii*) have been shown to reduce total bilirubin, time of jaundice fading, and duration of phototherapy
- Chen et al. Frontiers in Pharmacology 2017;8:432
- Chandrasekhar et al. Pediatr Ther 2017;326
- Possible reduction in bilirubin absorption
- May correct imbalance of gut microbiota-gut dysbiosis
- Increase abundance of Bifidobacterium (involved in metabolism of bilirubin through galactose metabolic pathway)
- May suppress activity of beta-glucuronidase enzyme (reduces bilirubin back to unconjugated state)
  - Suganthi & Das. J Clin Diagnostic Res 2016;10:SC12-SC15

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Liu et al. Pak J Med Sci 2015;31:1172-1175

- Control group n=34
  - Treated with phototherapy and medication
- Treatment group n=34
  - Treated with bifid triple viable 2 g/day
  - *Lactobacillus bulgaricus*, live *Bifidobacterium, Streptococcus thermophilus*

Table-I: Serum bilirubin levels before and after treatment (X̄±s, μmol/L).

Group	Before	1 d after	4 d after	7 d after
Control (n=34)	351±48	312±41a	195±40a	108±21a
Treatment (n=34)	347±52	309±42a	155±37a	79±18a
t	0.367	0.876	2.747	5.918
P	>0.05	>0.05	0.002	0.001

Compared with the levels before treatment, aP<0.05.

Probiotics
- Facilitated growth of normal bacterial colonies
- Metabolites corrected slightly alkaline environment
- Weakened activity of beta-glucuronidase enzyme preventing it from binding and hydrolyzing bilirubin
- Enhanced liver enzymes which improved excretion and binding of bilirubin

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#4 The Bili Cam: There's an app for that!

- BiliCam is a smartphone-based non-invasive medical device that uses the on-device camera to monitor jaundice in newborns.
- It requires a color calibration card printed on special paper to reduce glare
- The technology is based on the analysis of newborns' images collected in a standardized way on the phone.
- The color data in the image are used to estimate the bilirubin level.

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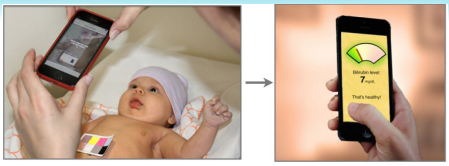

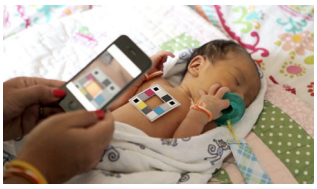

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References

- Taylor JA, Stout JW, de Greef L, et al. Use of a smartphone app to assess neonatal jaundice. Pediatrics 2017; 140:e20170312.
- de Greef L, Goel M, Seo MJ, et al. BiliCam: using mobile phones to monitor newborn jaundice. In: Proceedings of the 2014 ACM International Joint Conference on Pervasive and Ubiquitous Computing (UbiComp '14); September 13–17, 2014; Seattle, WA. 331–342.

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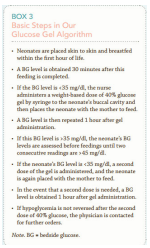
#5 Sugar Babies

- 40% glucose gel administered to buccal mucosa
  - Allows absorption rate similar to IV administration
  - More effective than feeding alone
  - Did not require NICU admission
  - Compatible with exclusive breastfeeding
  - No rebound hypoglycemia



BOX 3
Basic Steps in Our Glucose Gel Algorithm

- Neonates are placed skin to skin and breastfed within the first hour of life.
- A BG level is obtained 30 minutes after this feeding is completed.
- If the BG level is <35 mg/dl, the nurse administers a weight-based dose of 40% glucose gel by syringe to the neonate's buccal cavity and then places the neonate with the mother to feed.
- A BG level is then repeated 1 hour after gel administration.
- If this BG level is >35 mg/dl, the neonate's BG levels are assessed before feedings until two consecutive readings are >45 mg/dl.
- If the neonate's BG level is <35 mg/dl, a second dose of the gel is administered, and the neonate is again placed with the mother to feed.
- In the event that a second dose is needed, a BG level is obtained 1 hour after gel administration.
- If hypoglycemia is not reversed after the second dose of 40% glucose, the physician is contacted for further orders.

Note. BG = bedside glucose.

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Reference

- Harris, D. L., et al. (2013). Dextrose gel for neonatal hypoglycemia (the Sugar Babies Study): A randomised, double-blind, placebo-controlled trial. Lancet, 382(9910), 2077–2083.
- Bennett C, Fagan E, Chaharbakhshi E, Zamfirova I, Flicker J. Implementing a protocol using glucose gel to treat neonatal hypoglycemia. Nurs Womens Health. 2016 Feb-Mar;20(1):64-74.

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#6 What's in that tube of glucose gel?

- Evaluated 2 brands of dextrose gel
- Tested 0.5mL aliquots from top, middle, and bottom of tube
- Showed random differences in dextrose concentration, varying by up to 81% depending on where in the tube the sample came from
- Would this partially account for infants whose blood sugar failed to rise after gel treatment?

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Reference

- Solimano A, et al. Dextrose gels for neonatal transitional hypoglycemia: What are we giving our babies? *Paediatrics & Child Health* 2018; 24(2):115-118.

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#7 Probiotics to treat mastitis

- Bacteria are increasingly becoming resistant to traditional antibiotic therapy
- Orally administered probiotics *Lactobacillus fermentum, Lactobacillus salivarius,* and *Lactobacillus gasseri* have been shown to effectively treat infectious mastitis
- Recurrent mastitis was shown to be lower in group treated with probiotics compared to group treated with antibiotics

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Strain specific

- Only specific strains of probiotics have been shown to be effective in correcting or preventing mammary dysbiosis
  - *Lactobacillus salivarius* CECT5713
  - *L. gasseri* CECT5714
  - *Lactobacillus fermentum* CECT5716
  - *L. salivarius* PS2

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References

- Arroyo R, Martin V, Maldonado A, et al. Treatment of infectious mastitis during lactation: antibiotics versus oral administration of Lactobacilli isolated from breast milk. Clinical Infectious Diseases 2010; 50:1551-1558.
- Fernandez L, Arroyo R, Espinosa I, et al. Probiotics for human lactational mastitis. Beneficial Microbes 2014; 5:169-183.
- Jimenez E, Fernandez L, Maldonado A, et al. Oral administration of Lactobacillus strains isolated from breast milk as an alternative for the treatment of infectious mastitis during lactation. Applied and Environmental Microbiology 2008; 74:4650-4655.

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#8 Aripiprazole (Abilify)

- Aripiprazole (Abilify) is an atypical antipsychotic drug that is also used with other medications to treat depression
- A common adverse effect of some antipsychotic medications is hyperprolactinemia (high prolactin levels)
- Aripiprazole can be and is given to patients to reduce prolactin levels
- Breastfeeding mothers taking aripiprazole should be monitored carefully for milk sufficiency and their infants monitored for appropriate weight gain

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References

- Li X, Tang Y, Wang C. Adjunctive aripiprazole versus placebo for antipsychotic-induced hyperprolactinemia: metaanalysis of randomized controlled trials. PLoS One. 2013;8(8):e70179. doi:10.1371/journal.pone.0070179.
- Walker T, Coursey C, Duffus ALJ. Low dose of Abilify (Aripiprazole) in combination with Effexor XR (Venlafaxine HCL) resulted in cessation of lactation: A case report. *Clinical Lactation* 2019; 10:56-58.

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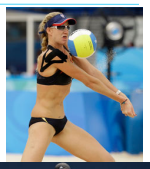
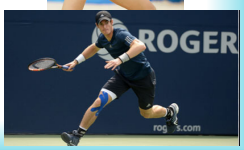
#9 Maternal therapeutic taping

- Therapeutic taping is often seen in sports medicine for use on injured athletes and as a mechanism for facilitating lymphatic drainage, increasing blood flow, decreasing inflammation, and increasing the interstitial spaces by microscopically lifting the skin.





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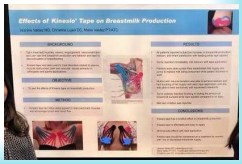
- Kinesio tape[R] was applied to the breasts using fan cuts for relaxing the pectoralis muscles and facilitating fluid movement.
- Mothers reported doubling or tripling the amount of milk they could pump after the tape was applied
- May improve milk circulation by lifting the skin, increasing the space below
- Also has been used for blocked milk ducts



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Reference

- Valdez, J., Lujan, C., & Valdez, M. (2018). Abstract 81. Effects of Kinesio Tape application on breastmilk production. *Breastfeeding Medicine, 13*(S2), S36.

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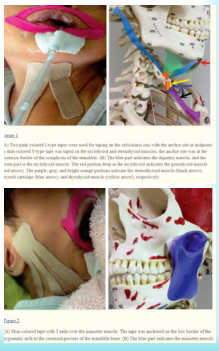
#10 Infant therapeutic taping

- Therapeutic taping is used on muscles as a mechanism to improve their function
- A case report describes how taping was used on a preterm infant to
  - facilitate lip closure of the orbicularis oris muscle
  - help with the masseter muscle for jaw movement
  - facilitate the mylohyoid muscle for hyoid bone elevation
- Significant improvement was seen in muscle power, lip closure, sucking, and swallowing



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Reference

- Lin, C-L., Wu, W-T., Chang, K-V., Lin, H-Y., & Chou, L-W. (2016). Application of Kinesio Taping method for newborn swallowing difficulty: A case report and literature review. *Medicine, 95*(31), e4458.

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Infant therapeutic taping

- Therapeutic taping to correct the muscular imbalance seen in torticollis
- A study looked at 28 infants with torticollis and found that the muscle relaxing method of taping had the greatest effect on correcting the muscular imbalance

Figure 1. Kinesiology taping showing the facilitation technique: musculus sternocleidomastoideus and the superior aspect of musculus trapezius.

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Reference

Ohman, A.M. (2012). The immediate effect of kinesiology taping on muscular imbalance for infants with congenital muscular torticollis. *Physical Medicine and Rehabilitation, 4*(7), 504-508.

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Infant therapeutic taping

- In a study of 8 infants with cleft lip, physio tape therapy was used to reduce the cleft size and facilitate surgical repair
- Reduction in cleft size ranged from 9.1mm to 36.7mm, helping with muscle elasticity and function which served to improve feeding action

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Reference

Dawjee, S.M., Julyan, J.C., & Krynauw, J.C. (2014). Lip tape therapy in patients with a cleft lip-a case report. *South African Dental Journal, 69*(2), 62-69.

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Laila's Child
R.C. Gorman

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