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Dr. Jen 4 Kids

www.drjen4kids.com

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- I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

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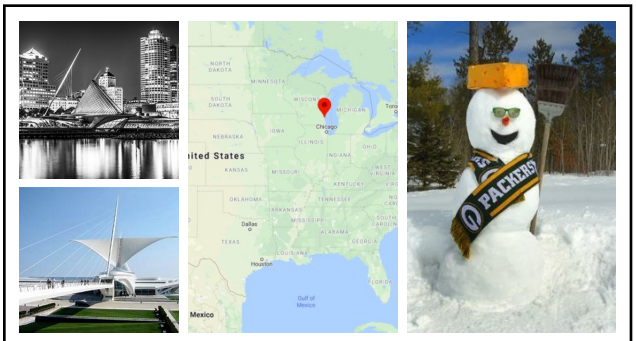

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Road Map

- Emphasizing exclusivity
- The tricky time of transitioning
- The Three Bs: Birth weight, Bilirubin and Blood sugar
- The importance of skin-to-skin
- How this all changes when the baby shows up a little early
- When should we supplement, with what and how much

5

AAP Guidelines, 2022

The American Academy of Pediatrics (AAP) recommends exclusive breastfeeding for approximately 6 months after birth. The AAP supports continued breastfeeding, along with appropriate complementary foods introduced at about 6 months, as long as mutually desired for 2 years or beyond.

Breastfeeding and the Use of Human Milk, Pediatrics 2022

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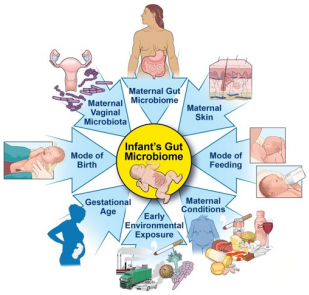
Microbiome



Kapourcheli 2020

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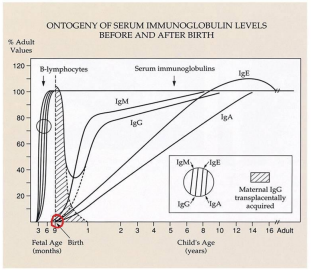

Mosby items and derived items © 2004 by Mosby, Inc.

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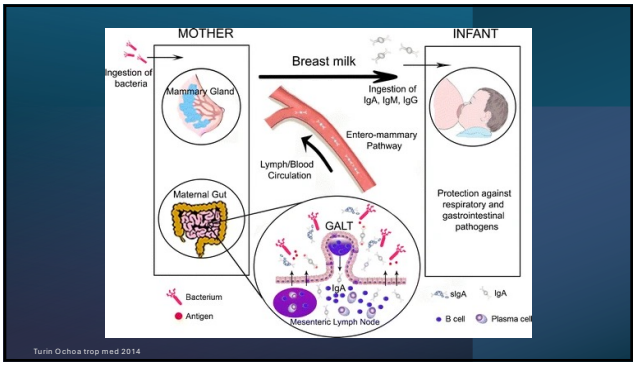

Turin Ochoa trop med 2014

9

Milk-Saliva

Retrograde inoculation

- During breastfeeding, baby saliva reacts with breastmilk to produce reactive oxygen species, while simultaneously providing growth-promoting nucleotide precursors.
- This combination produces a potent combination of stimulatory and inhibitory metabolites that regulate early oral – and hence gut – microbiota.
- Represent unique biochemical synergism which boosts early innate immunity.

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Preventing inflammation: Prebiotics

- They are non-digestible food components that beneficially affect the gut by providing food for the good bacteria that (hopefully) already inhabit it.
- In human milk, the most common prebiotics are oligosaccharides, which are also the third most common component of mature human milk.

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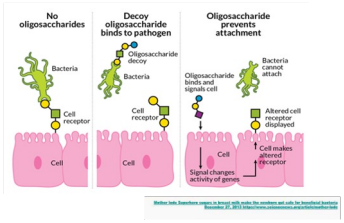
HMO as anti-adhesive antimicrobial



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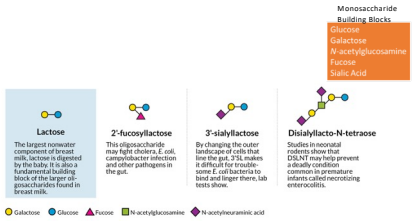

Bode L, et al. Adv Nutr 2012; 2:3(3):383S-391S

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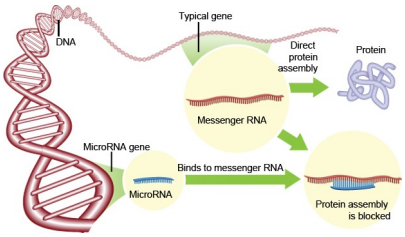

Steve Karp

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miRNA in Human milk

- Breastfed infants receive approximately **1.3 x 10^7 copies/liter/day** of miRNA
- The highest concentration of miRNA of any body fluid
- Breast milk is a major epigenetic modulator of gene expression of the milk recipient

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microRNA in Human Milk

- Epigenetic signals delivered to the infant through microRNA
- Results in more protein for the baby that can help
  - Metabolism
  - Immune system
  - Fat production
  - Muscle production
  - Bone growth

Melnik, Schmitz 2017

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Primary Prevention of Cow's Milk Sensitization and Food Allergy by Avoiding Supplementation With Cow's Milk Formula at Birth: A Randomized Clinical Trial

- Babies who received cow's milk-based formula in the first three days of life were at higher risk of cow milk protein allergy, including anaphylaxis, at age two.

Urashima JAMA peds 2019

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Infection protection

- Diarrhea
- Respiratory infections
- Otitis media
- Urinary tract infections
- Neonatal sepsis
- Coughing and wheezing
- Death

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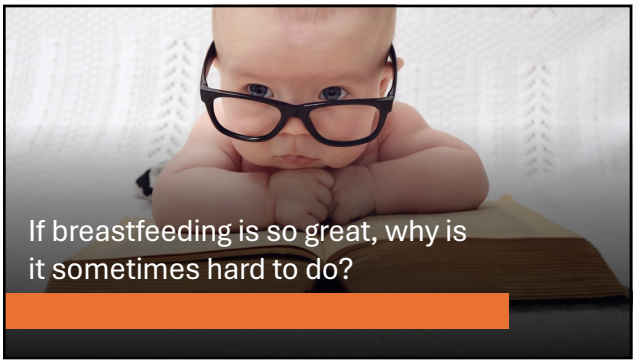

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So many reasons

- Non-evidenced based maternity care practices
- Risk factors for low supply including insulin resistance
- Other maternal and infant characteristics
- Formula marketing practices
- Misunderstanding normal newborn behavior
- Systemic bias
- Lack of paid family leave

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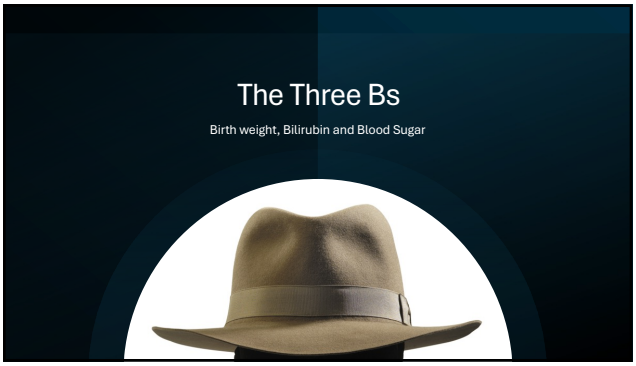

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Fetal physiology

- High pulmonary blood pressure because the lungs are not providing gas exchange, the placenta is
- Low systemic blood pressure because of the placenta
- Relatively low oxygen state because of the placenta
- A lot more red blood cells because of the low oxygen state
- Continuous flow of food from the placenta

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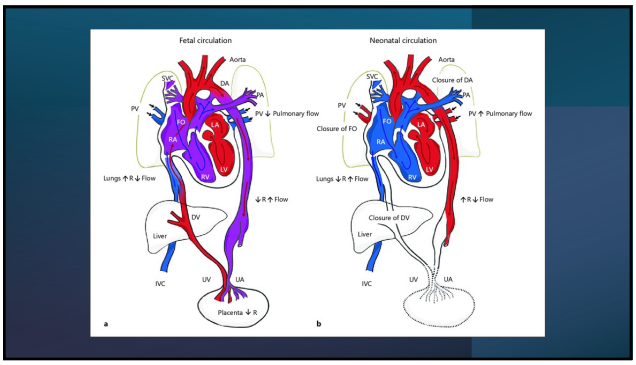

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The transitioning newborn

- Breathing: initiates pulmonary gas exchange, replacing placental oxygenation.
- Cardiovascular adjustments are also critical; the foramen ovale and ductus arteriosus close, redirecting blood flow.
- Thermoregulation becomes essential as the newborn manages its own body temperature, relying on brown fat metabolism and behavioral adaptations like seeking warmth.
- Metabolism switches from placental supply to independent nutrient uptake, initiating processes for glucose regulation

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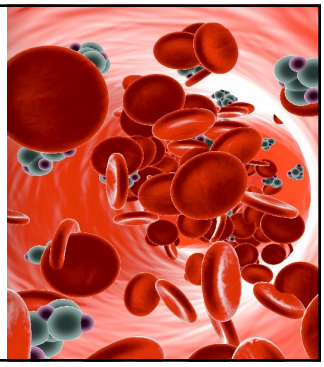
What Happens Normally

- After birth, the nutrient flow the baby received through the placenta is interrupted allowing maternal metabolism to transition to lactation.
- Glucose is the main source of energy for the brain.



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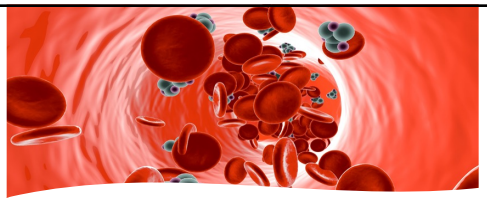

What Happens Normally

Immediately after birth and before the onset of suckling there is a time in which the newborn undergoes a unique kind of "starvation" where glucose is scarce. This normal and expected.

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Normal Glucose Regulation

The energy balance is eventually regained through human milk nutrients which supply the newborn with ketone bodies required for energy.

However, during this short period of "starvation" and scarce glucose, ketone bodies are also not available because of a delay in ketogenesis.

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Normal Glucose Homeostasis

Other metabolic fuels are used as the source of energy for the neonatal brain.

The neonatal brain can use not only glucose, but lactate, pyruvate and, ketone bodies (KBs).

These substrates are then converted into acetyl-coenzyme A, the main input for the citric acid (Krebs) cycle leading to ATP (energy production).

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Normal Glucose Homeostasis

Glucose alone, even at high concentration, cannot maintain mitochondrial respiration at the level necessary for optimal neuronal functioning.

Complementing glucose with pyruvate, lactate or ketone bodies allows energy demands to be met, allowing the neonatal brain to survive a period of low glucose with no damage to the function of the neurons.

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Definition

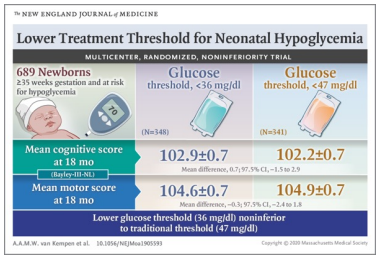
The AAP policy on this is called "Postnatal Glucose Homeostasis" because there is no specific value of glucose that has been identified which defines hypoglycemia as pathology.

Brief periods of hypoglycemia are unlikely to cause neurologic damage

32

Lower versus Traditional Treatment Threshold for Neonatal Hypoglycemia

Van Kempen, 2020 NEJM



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Symptoms are Key

Symptomatic blood sugar can show up as irritability, seizures, lethargy, cyanosis coma, temperature instability

The differential for these symptoms is more broad than just low glucose

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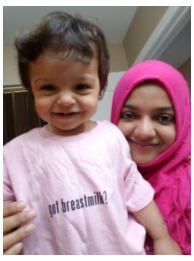
Symptoms are the Key

- Low blood sugar with no symptoms. Not an issue.
- Breast milk meets the nutritional requirements of healthy, term infants and those same healthy term exclusively breastfed infants do not develop symptomatic low blood sugar because they are not eating.
- Healthy term infants do not need to have their blood sugar screened.

35

Symptoms are the Key

- Low blood sugar with symptoms: Big problem.
- These children have some reason they can't make up for low blood sugar with other fuels.
- Those kids should be screened. Because then, the number means something.



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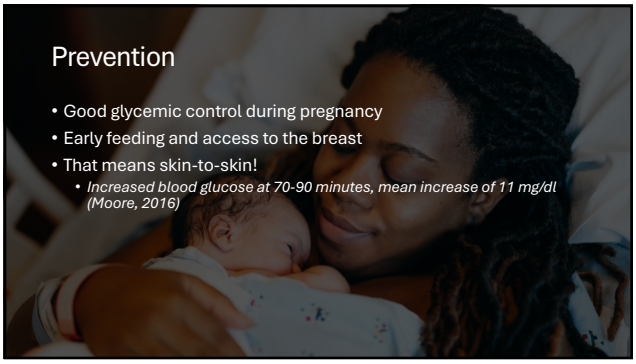

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Glucose Gel

Sugar Babies Study (Lancet December 2013) 514 babies in New Zealand, from 35-42 weeks gestation at risk for hypoglycemia. Randomized, double-blinded, placebo- controlled study.

Treatment with dextrose gel is inexpensive and simple to administer.

Dextrose gel should be considered for first-line treatment to manage hypoglycemia in the late preterm and term babies in the first 48 hours after birth.

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Another Non-Formula Therapies

Donor milk for those of you lucky enough to get it for term newborns

DAME study: There is no harm in advising women with diabetes in pregnancy at low risk of complications to express breastmilk from 36 weeks' gestation. (Forster, Lancet, 2017)

39

Screening and Management of Postnatal Glucose Homeostasis in Late Preterm and Term SGA, IDM/LGA Infants

[(LPT) Infants 34 – 36$^{6/7}$ weeks and SGA (screen 0-24 hrs); IDM and LGA ≥34 weeks (screen 0-12 hrs)]

Symptomatic and <40 mg/dL ⟶ IV glucose — 2.22

ASYMPTOMATIC

Birth to 4 hours of age		4 to 24 hours of age		
INITIAL FEED WITHIN 1 hour Screen glucose 30 minutes after 1st feed		Continue feeds q 2-3 hours Screen glucose prior to each feed		
Initial screen <25 mg/dL		Screen <35 mg/dL		
Feed and check in 1 hour		Feed and check in 1 hour		
<25 mg/dL ↓ IV glucose*	25-40 mg/dL ↓ Refeed/IV glucose* as needed	<35 mg/dL ↓ IV glucose*	35 – 45 mg/dL ↓ Refeed/IV glucose* as needed	

1.38 — 1.94 — 2.49

Target glucose screen ≥45 mg/dL prior to routine feeds

* Glucose dose = 200 mg/kg (dextrose 10% at 2 mL/kg) and/or IV infusion at 5–8 mg/kg per min (80–100 mL/kg per d). Achieve plasma glucose level of 40-50 mg/dL.

Symptoms of hypoglycemia include: irritability, tremors, jitteriness, exaggerated Moro reflex, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, poor feeding.

PEDIATRICS Vol. 127 No. 3 March 1, 2011 pp. 575 -579

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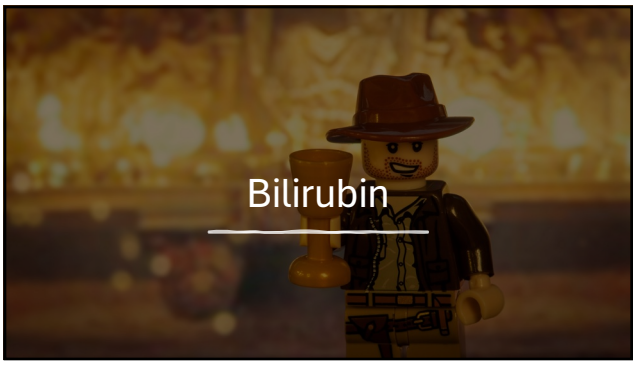

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Adaptation or Disease?

- Current view: bilirubin is a toxin and jaundice is a disease
- But what if hyperbilirubinemia of the newborn is part of normal newborn adaptation to postnatal life for most infants and represents pathology only for a few?

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Adaptation or Disease?

All normal babies will have bilirubin levels above those of an adult because there are physiologic mechanisms that produce and maintain higher levels

Bilirubin serves as an antioxidant in newborns, prior to the maturation of primary antioxidant enzyme systems, serving as an elegant bridge from in utero to extrauterine life.

43

Adaptation or Disease?

- Bilirubin can ameliorate gram negative endotoxic shock from E.Coli
- In vitro studies suggest that physiologic jaundice may protect against early-onset sepsis from Group B strep

Hansen Sci Rep 2018

44

Measuring Bilirubin

What does it mean?

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Total Bilirubin

- The total serum bilirubin (TSB) level has not been useful as a sensitive and specific predictor of neurological outcomes.
- Laboratory and available clinical data are consistent with basic pharmacological principles in demonstrating that *free (unbound) bilirubin* rather than TSB is a critical serum factor involved in brain uptake of bilirubin and subsequent neurotoxicity.

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Free (unbound) Bilirubin

- Bilirubin-albumin binding is a function of the concentrations of bilirubin and albumin, and the binding affinity for bilirubin (strength of bilirubin binding to albumin).
- The binding affinity may be decreased in the presence of:
  - sepsis
  - acidosis
  - hypoxia
  - free fatty acids
  - various albumin-binding drugs.

Amin, S. B., & Lamola, A. A. (2011). Newborn Jaundice Technologies: Unbound Bilirubin and Bilirubin Binding Capacity in Neonates. Seminars in Perinatology, 35(3), 134-140.

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Free (unbound) Bilirubin

- Free bilirubin (Bf) can cross the intact blood–brain barrier and cause subsequent neuronal damage.
- Bf concentration determines the distribution of bilirubin between the tissues and vascular space and therefore the risk of bilirubin-induced neurotoxicity.
- No good tests

Amin, S. B., & Lamola, A. A. (2011). Newborn Jaundice Technologies: Unbound Bilirubin and Bilirubin Binding Capacity in Neonates. Seminars in Perinatology, 35(3), 134-140.

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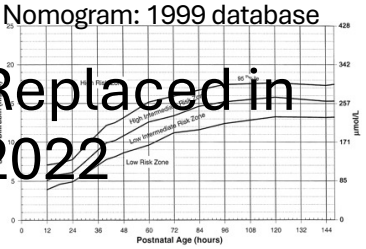
Bhutani Nomogram: 1999 database



Bhutani, V. K., Johnson, L., & Sivieri, E. M. (1999). Predictive Ability of a Predischarge Hour-specific Serum Bilirubin for Subsequent Significant Hyperbilirubinemia in Healthy Term and Near-term Newborns. Pediatrics, 103(1), 6-14.

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Risk factors for increased unbound bilirubin

Hyperbilirubinemia Neurotoxicity Risk Factors

Risk Factors
• Gestational age <38 wk and this risk increases with the degree of prematurity[8]
• Albumin <3.0 g/dL
• Isoimmune hemolytic disease (ie, positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
• Sepsis
• Significant clinical instability in the previous 24 h

50

This is why it took so long

- Although breastfeeding and human milk have many benefits, brief use of formula might lead to a more rapid decline in TSB concentrations and reduce the risk of readmission for phototherapy.
- Although insufficient data are available, supplementation using the mother's expressed milk may have similar benefits to infant formula supplementation without the potential concerns associated with formula.
- The risks to the establishment of breastfeeding and milk supply, including potential health consequences to the infant and mother unrelated to jaundice, must be weighed against any benefit of introducing infant formula supplementation for bilirubin reduction.

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Birth Weight

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Excess Weight Loss

Weight loss of >7% of birth weight suggests possible breastfeeding problems and requires further evaluation

Excess weight loss, typically defined as loss of ≥10% of birth weight, is common.

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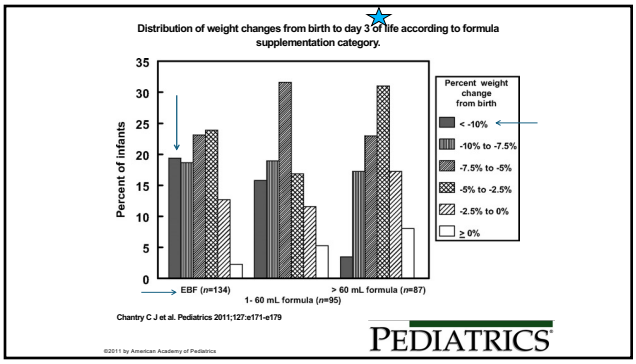

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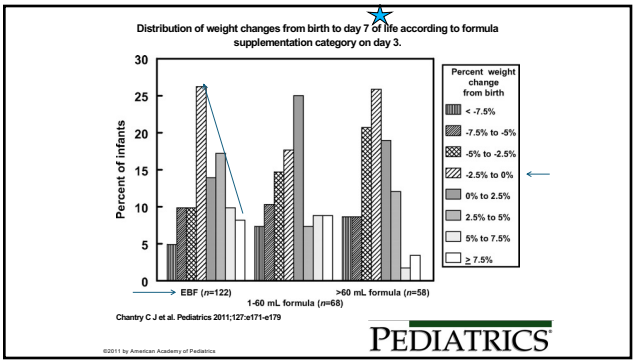

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Characteristics of Breastfed Infants With and Without EWL

Variable	Infants Without EWL (N = 188)	Infants With EWL (N = 41)	P
Net hourly intrapartum fluid balance, mean ± SD, mL/h	153 ± 128	219 ± 131	.0042[a]
Net intrapartum fluid total, mean ± SD, mL	2442 ± 1368	2964 ± 1681	.29[a]
Length of labor, mean ± SD, h	21.2 ± 17.8	17.5 ± 9.7	.32[a]
Onset of lactogenesis, mean ± SD, h	67.1 ± 21.7	84.2 ± 25.1	.0002[b]
Blood loss of >500 mL, *n* (%)	38 (24)	11 (32)	.30[c]
Birth weight, mean ± SD, kg	3.34 ± 0.38	3.53 ± 0.43	.0040[c]
Formula supplementation, *n* (%)			.48[c]
None (EBF)	108 (57)	26 (63)	
1–60 mL of formula	80 (43)	15 (37)	
Postpartum maternal edema, *n* (%)	94 (51)	30 (73)	.0084[c]

The table includes data for infants who were EBF and those who received ≤60 mL total before day 3.

Noel-Weiss, Intl Breastfeeding Journal, 2011

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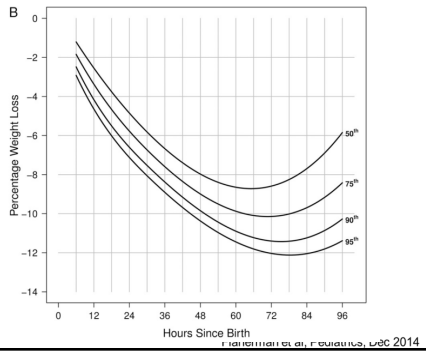

Flaherman et al, Pediatrics, Dec 2014

58

24 hour weight

Overall supplementation rate decreased from 43.6% pre- to 27.4% post-intervention and in first-time mothers from 51.9% to 31.0%.

Among infants losing ≥10% of BW, the supplementation rate decreased from 63.9% to 26.2%. There was no significant increase in maximum weight loss, peak TcB level, or LoS overall or in those with ≥10% weight loss from birth.

CONCLUSION: Routine use of 24HW as the reference for newborn weight loss calculation reduced supplementation and did not increase untoward effects during the hospital stay.

Deng, Breastfeeding Medicine, 2018

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What We Can Do

- Stool is better to watch than urine in the first few days.
- Goal is to clear meconium by day 4 for vaginal deliveries and day 5 after a C-section
- Use the Newborn Weight Loss Tool (NEWT). Assess if in the 75%.

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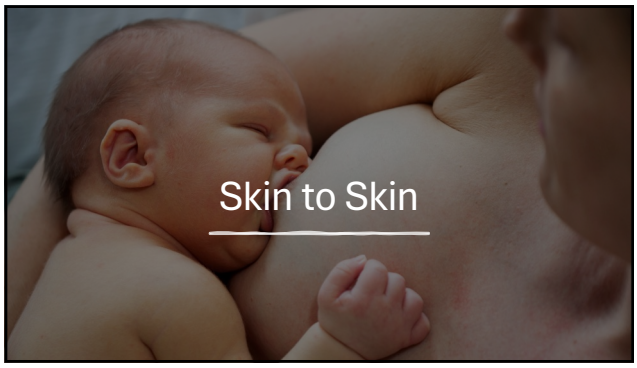

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Skin to Skin

- Temperature regulation
  - Allows the baby to preserve energy
- Decreased heart rate and increased oxygenation
- Decreased need for glucose
- Allows for instinctual feeding behaviors

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Olfactory System

The areola of the breast contains Montgomery's glands; glands which secrete a substance, the odor of which is important to the latching behavior of newborns.

Doucet S, Soussignan R, Sagot P, Schaal B. The Secretion of Areolar (Montgomery's) Glands from Lactating Women Elicits Selective, Unconditional Responses in Neonates. Hausberger M, ed. PLoS ONE. 2009;4(10):e7579.

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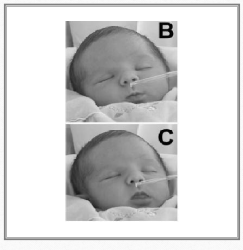

Olfactory System

The composition is similar to that of amniotic fluid and both act as "chemosignals" that help the baby figure out who mom is and how to respond to her.

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Olfactory System

- Newborns respond to the secretions of Montgomery's glands with increased oral behaviors and changing autonomic responses.
- When babies smell the odor from the glands, they increase mouthing behaviors, like licking.
- Their respiratory rate increases, perhaps to help them breathe in the odor better.
- This signaling even works when they sleep.

Doucet 2009

- Consultant. 2016;56(4):375

67

From Skin-to-skin to Latch

Brimdyr Mat Child Nutrition 2020

TABLE 2

Number of babies reported in each behavioural phase during skin-to-skin contact in the United States, Japan, Italy and Sweden studies

	United States ($n = 11$)	Japan ($n = 13$)	Italy ($n = 17$)	Sweden ($n = 28$)
Birth Cry	11	13	17	28
Relaxation	11	13	13	24
Awakening	11	13	17 (head movement)	28 (head movement)
Activity	10	13	17	28
Resting	8	5	17	25
Crawling	9	7	16	21
Familiarization	6	4	11	18
Suckling	5	2	7	15
Sleeping	1	0	10	28

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TABLE 1. The individual aspects of the guideline received rated recommendations from the Expert Panel meeting.

Guideline recommendation	Rating
All mothers	A
All babies	A
Immediately after birth	A
Skin-to-skin contact	A
All births	A
Postpone routine care	A
Uninterrupted	B
Continuous	A
Safe	A
Instinctive behaviour	B

Brimdyr, Skin-to-skin contact after birth: Developing a research and practice guideline, 2023

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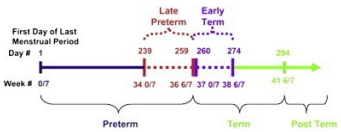
What is a "Late Preterm" Infant?



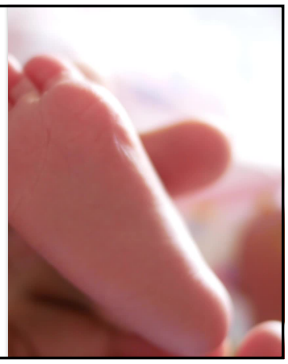
- According to the National Institute of Child Health and Human Development they are infants born between 34 0/7 weeks to 36 6/7 weeks.
- Emphasizes the fact that these infants are truly preterm, not "almost term."

From Engle WA, Kominiarek MA. Late preterm infants, early term infants, and timing of elective deliveries. Clinics in Perinatology 2008;35:325)

71

Complications: Brain development

- 5-fold increase of white matter in last weeks of gestation
- Late-preterm infants are born with only 65% of the brain volume of a full-term infant; the remaining growth occurs after birth
- Rapid development of brain tissues and peak synaptogenesis of the medulla occurs between 34 and 36 weeks postconceptional age



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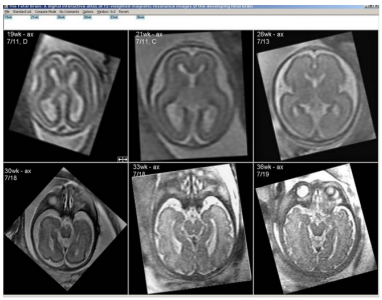

Digital atlas of fetal brain MRI.
Chapman T, Matesan M, Weinberger E, Bulas DI.

73

Complications: Feeding Behaviors

- One third of brain growth occurs in the last 6-8 weeks of gestation. The development of coordinated oral feeding appears to follow a chronological, predictable pattern in preterm neonates.
- Nervous system maturity occurs between 35 and 38 weeks gestation, during which time coordination of the functions necessary to breastfeed improve
- This suggests that *neurodevelopmental maturation*, *rather than experience or learned behavior*, is largely responsible for feeding behaviors.

Hallowell SG, Spatz DL, J Pediatr Nurs. 2012 Apr;27(2):154-62. Epub 2011 Mar

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Which is easier for the Preterm infant?

Bottle Feeding or Breastfeeding?

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Bottle and Breast

- "Oxygen saturation and body temperature of the preterm infants were significantly higher when they were directly breastfed. There were 2 episodes of apnea (breath pause more than 20 seconds) and 20 episodes of oxygen desaturation (PaO2 < 90%) during bottle-feeding and none during breastfeeding.
- We conclude that breastfeeding is a more physiological feeding method for the preterm infant and bottle-feeding may be more stressful."

Chen, C.-H., Wang, T.-M., Chang, H.-M., & Chi, C.-S. (2000). The Effect of Breast-and Bottle-Feeding on Oxygen Saturation and Body Temperature in Preterm Infants. Journal of Human Lactation, 16(1), 21-27

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Bottle and Breast

Oxygenation and ventilation

- During continuous sucking, ventilation decreases as a result of decreased breathing frequency.
- During continuous sucking, there is a minimal closure where no respiration occurs.
- That means, that during continuous sucking, healthy, bottle -feeding infants are holding their breath

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Bottle and breast

- That is thought to be fine when you are healthy and term
- Preterm infants do not handle this well: breathing pattern and ventilation during bottle feeding is associated with significant decreases in oxygenation.
- Preterm infants can have a persistent decrease in their oxygen levels 10 minutes after a feeding.
- Breastfeeding does not cause compromised oxygenation and after breastfeeding, oxygen levels remained at baseline.

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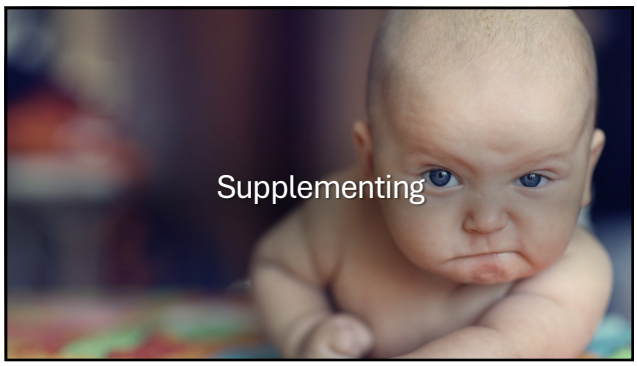

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Indications for Supplementing the Term, Healthy Infant

- Significant dehydration: clinical and laboratory evidence that is not improved with skilled assessment and proper management of breastfeeding
- Delayed bowel movements or meconium stools on day 5
- Insufficient intake despite and adequate milk supply (poor milk transfer)
- Hyperbilirubinemia- associated with starvation

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Indications for Supplementing the Term, Healthy Infant

- Maternal illness resulting in separation of infant and mother
- Infant with inborn error of metabolism (galactosemia)
- Infant who is unable to feed at the breast (congenital malformation, illness)
- Maternal medication contraindicated in breastfeeding
- Breast pathology or prior breast surgery resulting in poor milk production
- Intolerable pain during feeding unrelieved by interventions

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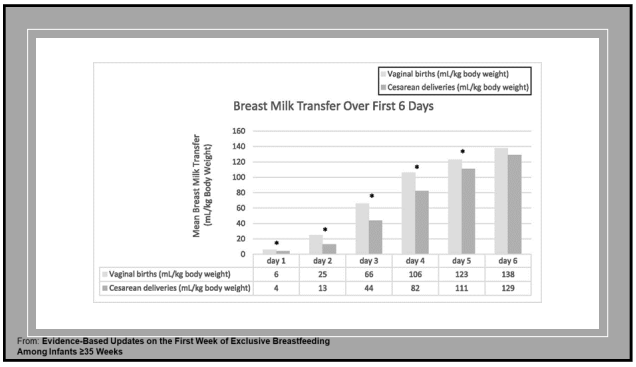

From: **Evidence-Based Updates on the First Week of Exclusive Breastfeeding Among Infants ≥35 Weeks**

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