The Art & Science of Breastfeeding

Saturday, January 23, 2021

Program

Welcome to IABLE's third Art and Science of Breastfeeding Conference!

The vision for this conference is to highlight and celebrate the spectacular research being done in the field of breastfeeding and human lactation. The work of lactational physiologists, human milk biologists, chemists, immunologists, social science researchers, etc, is as essential as our clinical observations to the advancement of breastfeeding science and medicine.

I know that you will enjoy learning about the fascinating research being conduct by our presenters. It is a glimpse into the discovery of biologic plausibility for the theories and hunches we rely on in clinical practice. I hope it will peak your curiosity and excitement for future scientific learning in this intriguing field.

Anne Eglash MD, IBCLC, FABM

Founder, President, The Institute for the Advancement of Breastfeeding and Lactation Education

Agenda

9:45-10:00am	**Sign in**	
9:45-10:00	**Introductions**	
10:00-11:00	**Maternal Plasma Levels of Oxytocin during BF**	**Kerstin Uvnas Moberg, MD**
11:00-12:00	**Comparative Lactation**	**Laura Hernandez, PhD**
12:00-12:45	**Break**	
12:45-1:45	**Integrative Health and Breastfeeding**	**Jill Mallory, MD, IBCLC**
1:45-2:00	**Break**	
2:00-3:00	**The Effects of Exercise on Human Milk**	**Kristin Stanford, PhD**
3:00-3:15	**Break**	
3:15-4:15	**Risk of Overweight Assoc. w/ Early Rapid Weight Gain**	**Jillian Trabulsi PhD, RD**
4:15-5:15	**Bed Sharing and Breastfeeding**	**Melissa Bartick, MD, MS, FABM**

Speakers

Melissa Bartick, MD, MS, FABM

Dr. Bartick is an internist and has been Assistant Professor in Medicine at Harvard Medical School. She has numerous breastfeeding publications in peer-reviewed journals. She served as the chair of the Massachusetts Breastfeeding Coalition from 2002 to 2014, where she was also a founder of Ban the Bags. She served on the Board of Directors of the United States Breastfeeding Committee from 2009-2015. She has served on the Board of the Academy of Breastfeeding Medicine since 2019, where she has coauthored clinical protocols, including the 2020 Bedsharing and Breastfeeding protocol. She was founder of the Breastfeeding Forum of the American Public Health Association, where she served two terms as chair. She is founder and co-chair of her state's Baby-Friendly Hospital Collaborative. She has blog contributions to the Huffington Post, the WBUR CommonHealth Blog, among others. Dr. Bartick received her BA from the University of Virginia and holds an MSc in Health and Medical Sciences from University of California, Berkeley and an MD from University of California, San Francisco. She works as a hospitalist at Mount Auburn Hospital and is the mother of two grown sons. As of June 2020, she is pursuing an MPH at Harvard School of Public Health.

Laura L. Hernandez, PhD

Dr. Hernandez is an Associate Professor in the Dairy Science Department at the University of Wisconsin-Madison, she is also a member of the Endocrine and Reproductive Physiology, Interdisciplinary Graduate Program in Nutritional Sciences, and the Comparative Biosciences Graduate programs. She received her Ph.D. in 2008 from the University of Arizona under the direction of Dr. Bob Collier and completed her post-doctoral in Molecular and Cellular Physiology with Dr. Nelson Horseman and the University of Cincinnati College of Medicine. Her area of research has focused on how serotonin controls the mammary gland and various aspects of lactation. Dr. Hernandez combines basic research from the cell to whole-animal level in a variety of mammalian species to broaden the focus on the importance of the mammary gland and its contributions to and regulation of a successful lactation in dairy cattle. The outcomes of her novel research are aimed at demonstrating the presence of factors (specifically serotonin) produced within the mammary gland that can control the animal's physiology while lactating, particularly during the transition period when cows are the most metabolically and physiologically challenged. She specifically focuses on the interaction of serotonin and calcium metabolism during the transition period. Her research has determined that serotonin is an important regulator of mammary gland, maternal calcium, and maternal energy homeostasis during lactation. She has authored/co-authored, 33 peer reviewed journal articles. Her research on the coordination of maternal metabolism during lactation by the mammary gland has numerous applications to women that are breast-feeding, and is focused on improving maternal health during this time frame and in later life.

Jill Mallory, MD, IBCLC

Dr. Jill Mallory is board-certified in family medicine and has been an IBCLC for over a decade. She completed a fellowship in integrative medicine through the University of Arizona. She works at the Wildwood Family Clinic in Wisconsin, where she practices the full spectrum of family medicine, including obstetrics, newborn home-visiting, integrative medicine consultation and lactation consultation.

Speakers

Kristin Stanford, Ph.D

Dr. Stanford received her Ph.D. from the University of California, San Diego, in Biomedical Sciences, and completed her postdoctoral training in Integrative Physiology and Metabolism at the Joslin Diabetes Center / Harvard Medical School. She is currently an Associate Professor in Physiology and Cell Biology and Associate Director of the Diabetes and Metabolism Research Center at The Ohio State University. The overall focus research in her lab is to determine the novel molecular mechanisms of exercise that improve metabolic and cardiovascular health. This will be broken down into two major aspects: 1) To determine exercise-induced adaptations to white and brown adipose tissue, with a specific focus on lipids that are released from adipose tissue during exercise; and 2) to ascertain the effects of parental exercise on the metabolic and cardiovascular health of offspring.

Jillian Trabulsi, PhD RD

Dr. Trabulsi is an Associate Professor & Associate Chair of Nutrition in the Department of Behavioral Health and Nutrition at the University of Delaware in Newark, Delaware. She earned her Ph.D. in Nutritional Sciences at The University of Wisconsin – Madison and completed a post-doctoral fellowship in Pediatric Nutrition and Growth at The Children's Hospital of Philadelphia. Dr. Trabulsi has over 25 years of experience in the field of nutrition, including work in clinical, industry, and academic settings. Her scientific contributions include studies related to the effect of diet composition on health outcomes and the application of energy balance principles to assess growth and nutritional status in healthy individuals and in those with chronic disease. Her research is funded by grants from the National Institutes of Health as well as private foundations and her work is published in peer-reviewed journals.

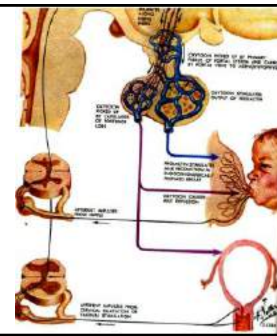
Kerstin Uvnäs Moberg

Dr. Moberg is a physician and professor of physiology with a research focus on the healing aspects of oxytocin. Her vision is to help creating healthier and happier women by expanding the knowledge about female physiology and by creating medical interventions based on oxytocin. She is a pioneer in research about oxytocin," the hormone of love and wellbeing", and was one of the first researchers to point out the behavioral, psychological and physiological effects of oxytocin during birth, breastfeeding and menopause.

Maternal Plasma Levels of Oxytocin during Breastfeeding

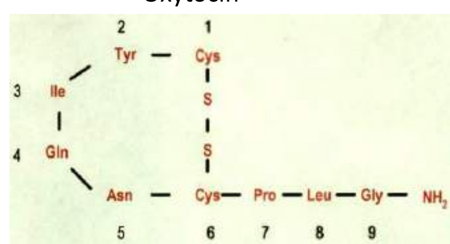
Kerstin Uvnäs Moberg
MD, PhD, Professor of Physiology

Oxytocin induces milk ejection

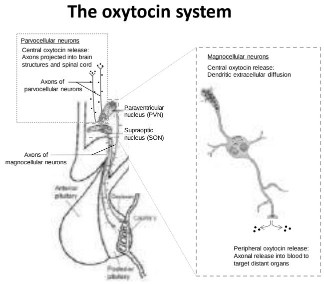


Breastfeeding is much more than giving of milk

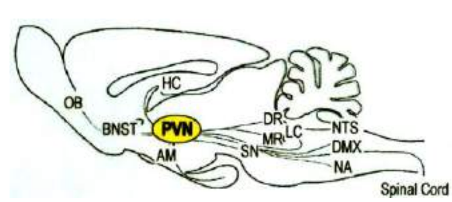
Oxytocin



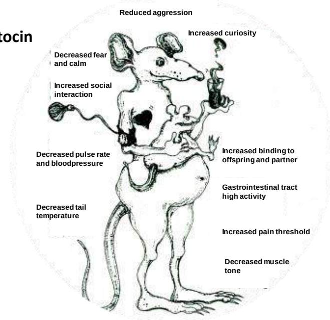
The oxytocin system



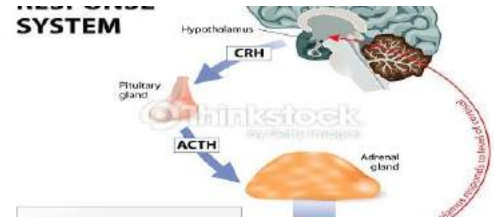
Projections of oxytocin containing nerves



Effects of oxytocin



Oxytocin counteracts all pathways involved in the release of Cortisol



Main effects of Oxytocin

Stimulates labor and milk ejection
Stimulates social behaviour
Exerts anti-stress effects
Promotes growth and restoration
Promotes health

Clinical trials with oxytocin

Autism
Social phobia
Schizophrenia
Depression
Anxiety
Stress related disorders
Substance abuse
Adjunct to psychotherapy

Different aspects of oxytocin related effects on mothers

- Giving of milk and warmth
- Caring and interaction
- Bonding
- Protection and defense
- The aggressive behavior is triggered when the environment is perceived as dangerous or unfamiliar.

Pair bonding in voles

Oxytocin linked effects involved in bonding

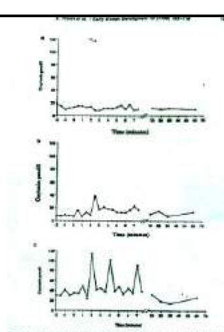
- Increases the strength of visual, auditory, tactile and olfactory stimuli
- Potentiates memory formation of these sensory cues and recognition of them
- Stimulates the release of subsances that cause wellbeing such as dopamine, endorphins and serotonin
- Decreases stress levels (HPA axis and sympathetic nervous system)
- Links the cues and memories to the neuroendocrine effects

Continous release and effects of oxytocin during:

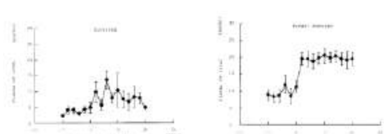
- **Pregnancy (estrogen)**
- **Labor**
- **Birth**
- **Skin-to-to skin with baby after birth**
- **Breastfeeding**

Breastfeeding

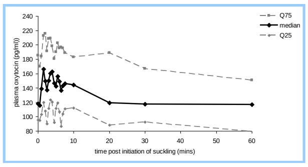
Suckling induces a peak shaped oxytocin response



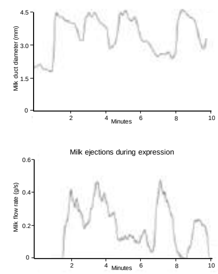
Oxytocin patterns in response to suckling and breast massage



Oxytocin levels (n=61)



Milk ejection



Milk ejection I

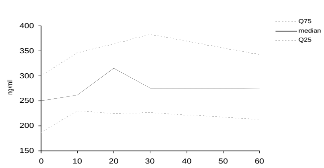
When the muscles around the milk ducts are contracted, by local neurogenic mechanisms and by a high sympathetic nervous tone, milk ejection is blocked.

Touching of the nipple during suckling opens the milk ducts by local neurogenic effects in the nipple and by a decrease of sympathetic nervous tone.

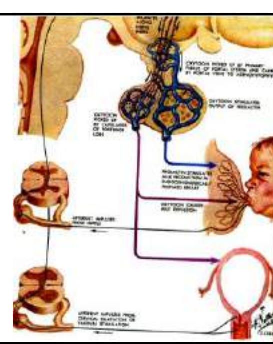
Milk ejection II

Circulating oxytocin induces contraction of myoepithelial cells in the mammary gland to eject milk

Prolactin levels



Oxytocin induces milk ejection



Prolactin stimulates milk production

Milk production l

Is stimulated by actions of Prolactin on the lactocytes in the mammary gland after being released from the anterior pituitary in response to suckling

Milkproduction ll

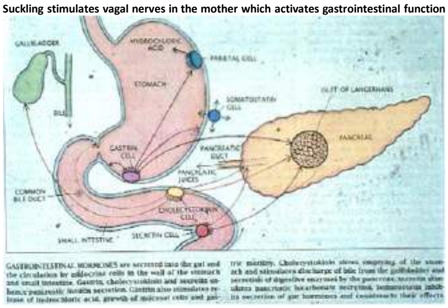
Prolactin release from the anterior pituitary is stimulated by lowered dopamin levels and increased oxytocin levels

Breastfeeding is much more than giving of milk

Breastfeeding stimulates gastrointestinal function and metabolism

The mother ”eats”lduring breastfeeding

Suckling stimulates vagal nerves in the mother which activates gastrointestinal function



Uvnäs Moberg. The gastrointestinal tract in growth and reproduction. Scientific American 1989

Stimulation of the vagal nerve in response to suckling

Growth and increased function of the gastrointestinal tract

Stimulation of insulin release and increased storing of ingested nutrients

Balance between saving and use of nutrients in response to suckling

Insulin released by activation of the vagal nerve induces storing if nutrients, which results in gain of weight

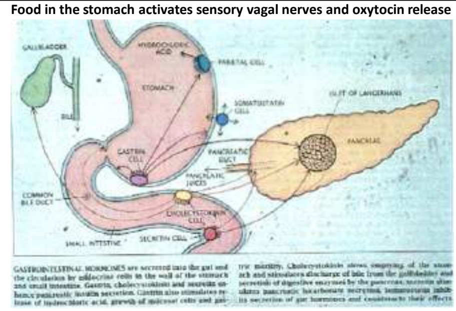
At the same time glucagon, which mobilizes nutrients, is released by the circulating oxytocin levels

As more oxytocin is released later on during breastfeeding, relatively more glucagon is released, which results in loss of weight

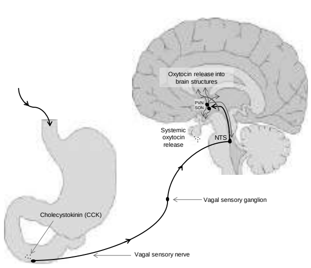
Food in the gastrointestinal tract stimulates oxytocin release via activation of the vagal nerves

Food is necessary for oxytocin release and milk production

Food in the stomach activates sensory vagal nerves and oxytocin release



Uvnäs Moberg- The gastrointetstinal tract in growth and reproduction. Scientific American 1989



Food in the intestine triggers the release of CCK leading to oxytocin release in the brain of both in mothers and babies

No food, no milk

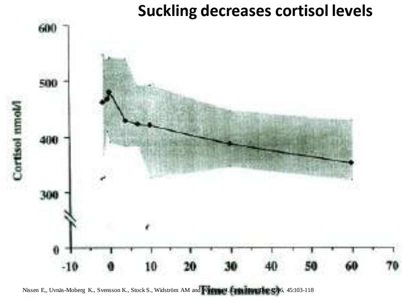
If the vagal nerves from the gastro-intestinal tract of lactating rats are cut, no oxytocin or prolactin is released in response to suckling after a few days. No milk is ejected and the rat mothers stop care for the offspring. They overeat and become fat.

Breastfeeding induces anti-stress effects

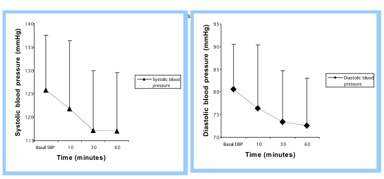
Decreased activity in the hypothalamo – pituitary-adrenal (HPA) axis

Decreased activity in the sympathetic nervous system

Suckling decreases cortisol levels



Suckling decreases blood pressure



Breastfeeding induces psychological and behavioral adaptations

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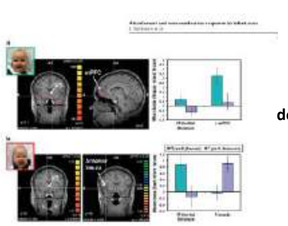
Breastfeeding and looking at a happy baby induces oxytocin release and makes the mother happy



oxytocin activates dopamine and the reward centre

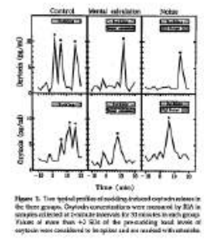
Maternal mental adaptations linked to oxytocin release in the brain during breastfeeding

Decreased levels of anxiety
Decreased detachment
Increased social interaction

(Karolinska Scales of Personality)

Influence of psychological stress on suckling-induced pulsatile oxytocin release.
Obstetrics and gynecology, 84(2), 259-262.
Ueda, T., Yokoyama, Y., Irahara, M., & Aono, T. (1994).

Noise and psychological stress inhibit maternal oxytocin release



A calm and safe environment, as well as warm, supportive and friendly interction facilitate oxytocin release and its many good effects

A stressful environment as well as non-supportive interaction inhibit oxytocin release and its effects

Breastfeeding gives rise to many oxytocin linked adaptive effects in the mother

Breastfeeding also gives rise to oxytocin release and oxytocin linked, adaptive effects in the baby

Breastfeeding is associated with

- Pulsatile release of oxytocin
- Milk ejection
- Release of prolactin
- Lowering of blood pressure
- Lowering of ACTH and cortisol
- Increased levels of gastrointestinal hormones
- Decreased anxiety
- Increased social interaction and bonding
- Reduced sensitivity to pain

Breastfeeding related effects become longlasting

The more breastfeeding the lower the risk of:

Stroke
Hypertension
Heart infarction
Diabetes type 2
Reumatoid arthritis

Associations with oxytocin levels

Amount of milk ejected
Higher levels of prolactin
Longer period of breastfeeding

Lower levels of somatostatin
Higher birth weight

Lower levels of ACTH
Lower blood pressure

More interaction between mother/fathers and infants
Higher levels of social interaction
Less anxiety and more calm

Factors that promote and facilitate oxytocin release and breastfeeding success

Skin-to-skin contact with baby promotes maternal oxytocin release and facilitates breastfeeding

Wqrmth
Touch
Support

Social interaction

Physical and mental support

Trust in own capability

Literature:

Maternal plasma levels of oxytocin during breastfeeding – A systematic reveiw
Uvnäs Moberg et al, PLOS ONE 2020

kerstinuvnasmoberg.com/se.

Kerstin Uvnäs Moberg
Facebook
Instagram
Books
The Oxytocin Factor
Oxytocin, the Hormone of Closeness
Oxytocin, the Biological Guide to Motherhood
Why Oxytocin Matters

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Comparative Lactation

Laura L. Hernandez, Ph.D.
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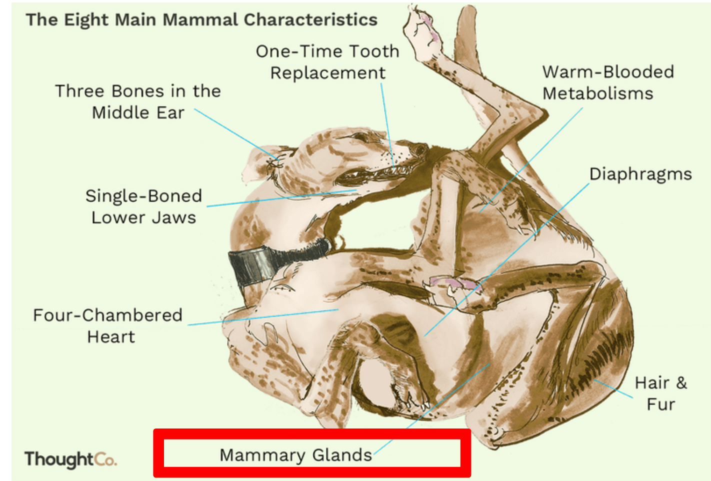
Department of Animal and Dairy Sciences


The Eight Main Mammal Characteristics
One-Time Tooth Replacement
Three Bones in the Middle Ear
Warm-Blooded Metabolisms
Diaphragms
Single-Boned Lower Jaws
Four-Chambered Heart
Hair & Fur
Mammary Glands
ThoughtCo.

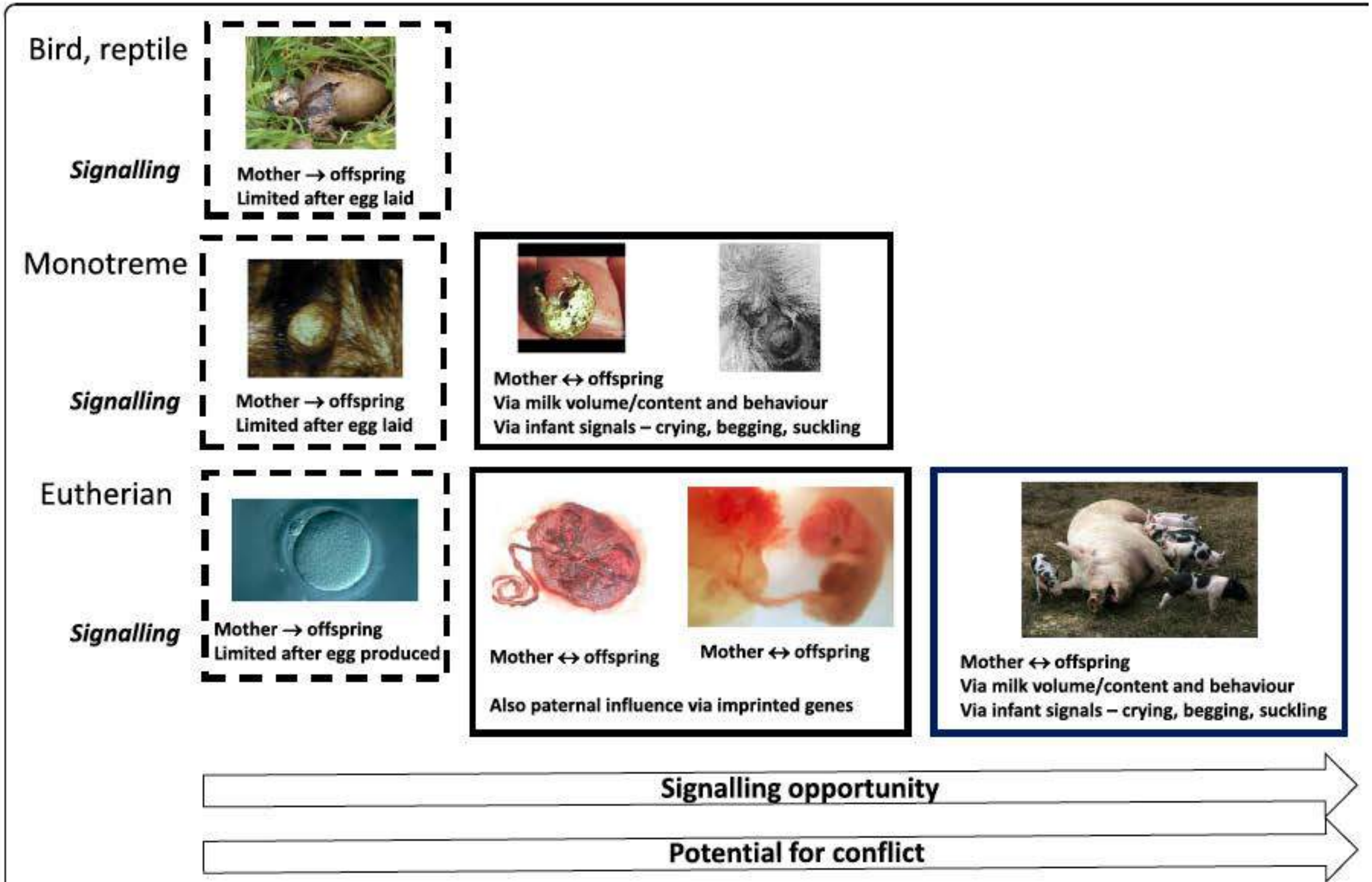
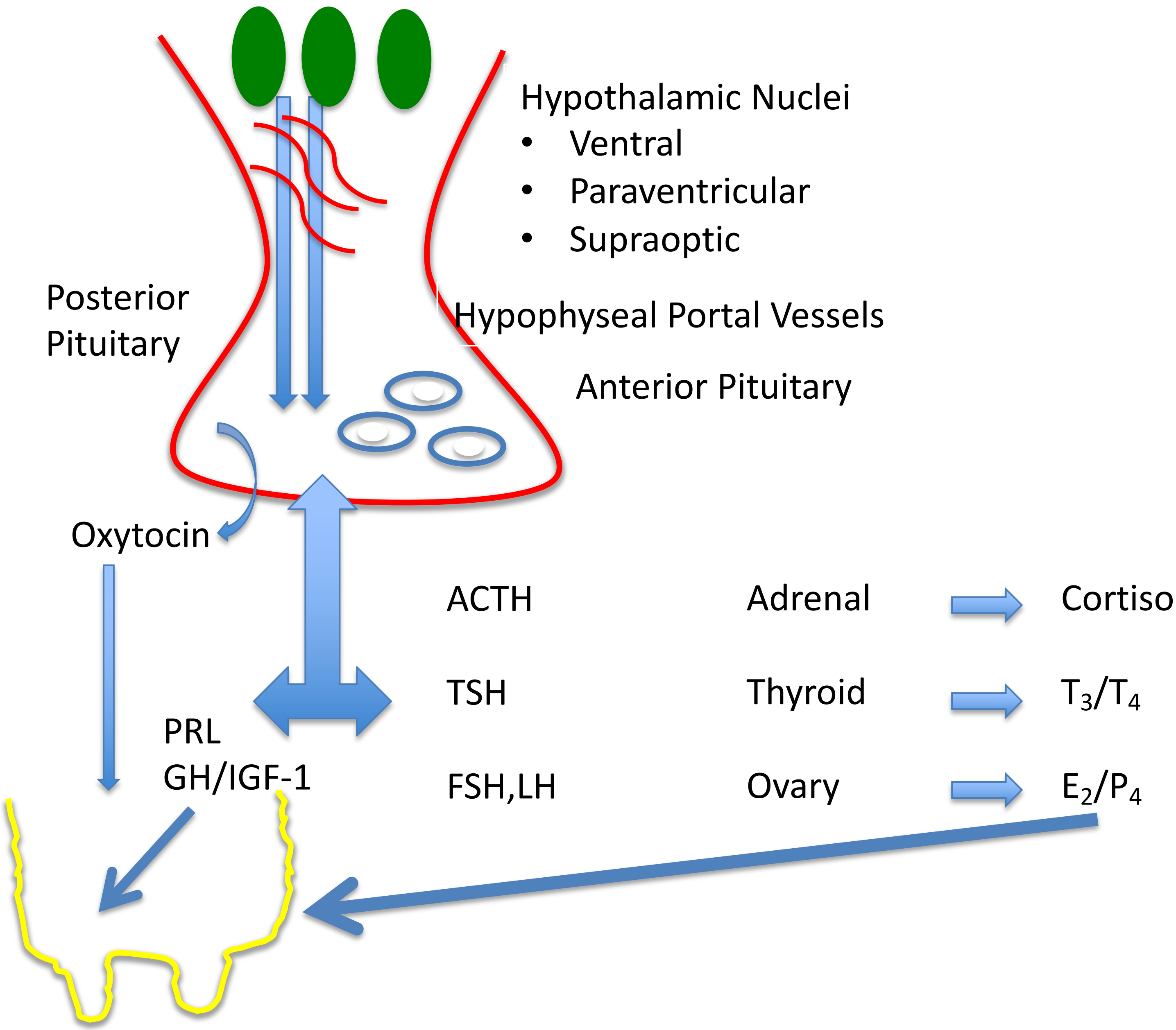


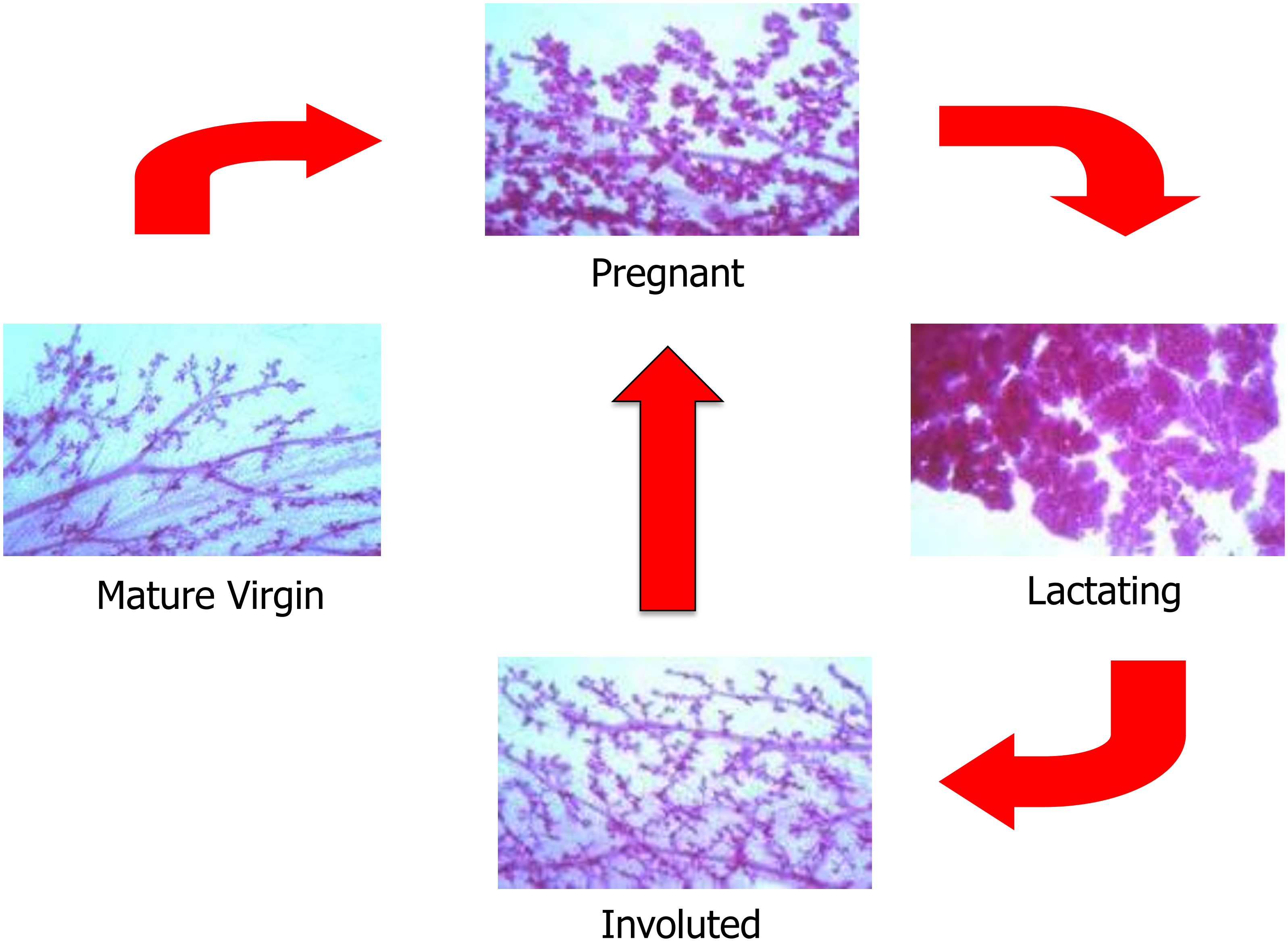
Fig. 1 Potential signalling routes between mother and offspring. These routes illustrate the different contributions made by the egg, placenta, amniotic fluid and lactation and their effects on both signalling opportunity and potential for mother–offspring conflict

Fewtrell et al., 2020



Adapted from Tucker, 1983

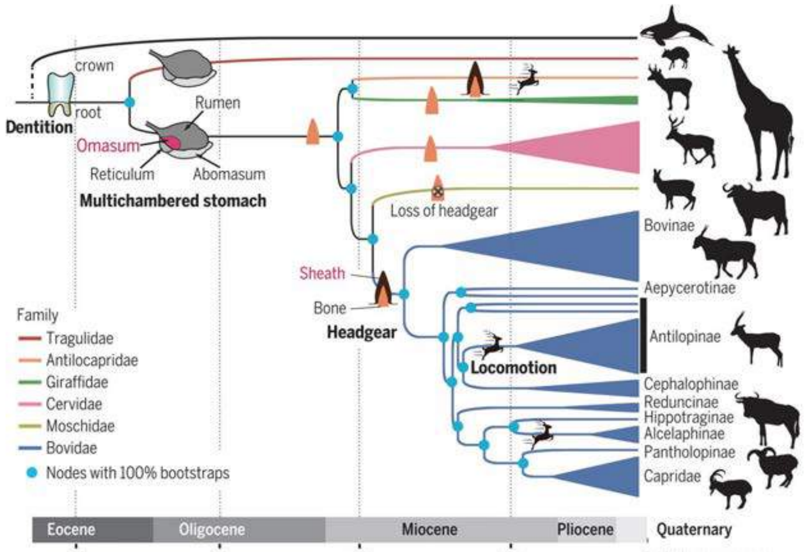
Homeostatic control of milk production



http://mammary.nih.gov/reviews/development/Development001/index.html

Humans and consumption of other milk

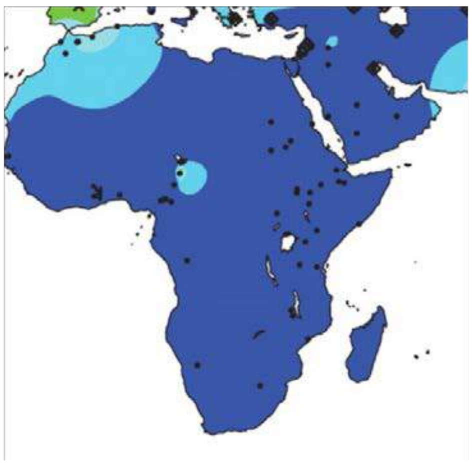
- Coevolution of humans and ruminants
  - Because of increased consumption of dairy products
  - Cows, sheep, goats have evolved from their ancestral conditions
- Cultural adaptation of humans
  - Genetics have changed and some produce lactase
- Milk is one of a few secretions that evolved to be a food
  - High quality protein, high in calcium and phosphorous
  - People in Africa, Middle East, South Asia, North-Central Europe, Britain, and Scotland have been keeping domesticated ruminants for many thousands of years



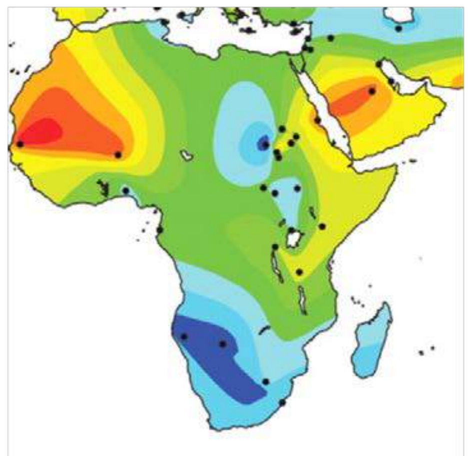
https://science.sciencemag.org/content/364/6446/eaav6202/tab-figures-data

Lactose, Lactase, Humans

Prevalence of -13910 SNP



Prevalence of Lactase Persistence



WILD TYPE: .....AAGATAA**T**GTAG**C**CC**C**TG
EUROPE: ......AAGATAA**T**GTAG**T**CC**C**TG T-13910
KENYA: ......AAGATAA**G**GTAG**C**CC**C**TG G-13915
SUDAN: ......AAGATAA**T**GTAG**C**CC**G**TG G-13907

http://www.evo-ed.com/Pages/Lactase/anthro_biogeogr.html

- Lactase required to digest the primary sugar in milk, LACTOSE
- After weaning and before adulthood, cells in the intestinal tract stop producing lactase
- Fermented milks, cheese, yogurt, and other milk products have very little lactose, if any. These were largely the products of consumption thousands of years ago
- Some populations have lactase persistence
- Developed due to pastoralism (milking livestock) in the Neolithic Revolution-10,500 year old cows in the Middle East

Origination of Dairying-Yogurt

- Dairying began in the part of the world that was not favorable for cows (Middle East, Mediterranean)
- Likely it was not originally used for feeding due to instability
- Initially made into some other type of food for stability reasons
- Ancient Assyrians boiled milk to keep it "fresh"
  - Scum on the pot
- Butter
  - Made by shaking cream in a goatskin and salted
- Yogurt
  - Boiled in a pot and wrapped in cloth and cooled slow
  - Yogurt Drinks
    - Doogh (Iran)
    - Lassi (India)
    - Laban (Arab world)

Cheese

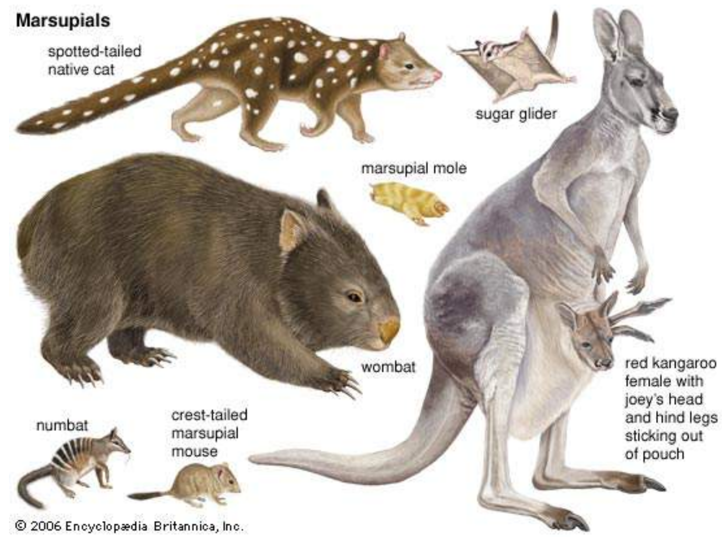
- Mesopotamians and Hitties made cow, goat, and sheep's milk cheese
- Ancient Egyptians
- Ancient Romans
  - Rennet from figs
  - De Agricultura: Oldest surviving book of Latin prose
  - Marcus Porcius Cato 234-149 BC
  - Mustacei: soft fresh cheese made with lard and unfermented must
  - Placenta: a kind of cheesecake made for religious ritual
- Greeks
  - Feta-one of oldest cheeses in the world
  - Rennet from figs
- Hippocrates was one of the early people to warn that cheese can be bad from some people (5^{th} century BC, father of medicine

Crop Milk

- **3 lineages of birds**
- Closest to mammalian adaptation of milk
- Parental feeding strategy including feeding a secretion to the chicks
- Pigeons and Doves
  - Males and females
  - 60% fat 35% protein
  - IgGs, transferrin, microbes
- Flamingos
  - Glands along whole upper intestinal tract
- Male Emperor Penguins
  - From the esophageal lining (limited, short duration)

Marsupials

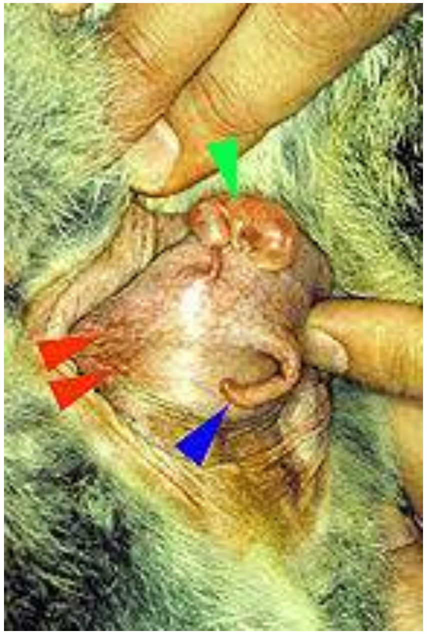
- Evolved over 80 MYA (mid-Cretaceous Period) from ancestral therian mammals (give birth to live young, no true placenta)
- 250 species
- Neonate born extremely early in development (most weight < 0.01% of mother’s body weight at birth)



Family	Types Represented	Approx. # of Species
Didelphidae	Opposums	70
Microbiotheriidae	Monito del monte	1
Caenolestidae	Shrew-opposum	7
Dasyuridae	Native cat, marsupial mice, tasmanian devil	49
Myrmecodiidae	Numbat	1
Thylacinidae	Tasmanian tiger	1
Notorytctidae	Marsupial mole	1
Peramelidae	Bandicoots	16
Thylacomyidae	Rabbit-eared bandicoots	2
Phalangeridae	Phalangers	11
Burramyidae	Pigmy Phalangers	7
Macropodidae	Kangaroos	56
Phasocolarctidae	Koala	1
Vombatidae	Wombats	3
Tarsipedidae	Honey opposum	1

Marsupial Neonate Development

- **Tammar Wallaby**
  - 28 days of gestation born
  - 350-450 mg in weight
  - Remains permanently attached to teat until **100 days of lactation** (rapid brain development)
  - **140 days lactation**: eyes are open and underfur visible
  - **Day 160**: Joey can stand unaided, kidney development completed
  - **Day 180**: thyroid function developed (body temp. regulation)
  - **Day 190**: 1st trip of out pouch
  - **Day 240**: Peak milk intake
  - **Day 250**: leaves the pouch permanently
  - **Day 300-350**: Joey ceases to suck
- Mother mates right after first joey is born and new embryo stays dormant until first joey leaves the pouch



Mammary Gland

Newborn Joey

Marsupial Lactation

- Development occurs during pregnancy, (d 10 LA pattern is evident in all 4 glands
- Oxytocin stimulates milk ejection and declines as lactation progresses
- **3 Phases**
  - **Phase 2a**: Comparable to mammary development in eutherian mammals
    - Lactogenesis is transition from Phase 1 to Phase 2 (all 4 glands; regulated by Prolactin)
    - Milk secretion starts 24 hr post-partum
    - Progesterone is NOT inhibitory to lactogenesis but necessary for mammogenesis
    - Solids about 10% of fresh weight of milk
  - **Phase 2b**: Early period of milk secretion when Joey is still in pouch
    - 3 glands regress because Joey only attaches to 1
    - Gland continues to develop as joey increases in body size (more secretory alveoli, teat gets longer)
  - **Phase 3**: Coincides with Joey leaving the pouch
    - Shift in milk composition
    - Rapid increase in growth of gland
    - Increase in total milk secretion
    - Tissue looks like that of eutherian mammals

Marsupial Milk Composition

- Lots of changes in milk composition during lactation
- Phase 2 lactation: **CHO** is high (50% of total solids) and lipid is low (~15% of total solids)
- Transition from Phase 2 to 3: **CHO** is reduced to very low concentration, lipid content may exceed 60%
- Lactose is synthesized at lactogenesis, by day 7 post-partum a second galactosyltransferase appears and adds additional galactoses to lactose (tri to penta-saccharides)
- **Milk fat** is primarily in TG form and uniform in fat in that both short and long chain fatty acids found in eutherian milk is not present
  Saturated and unsaturated fats range from C12-C20
  - Early milk is primarily palmitic acid (lung development)
  - Days 50-70: oleic acid increases
- Total **milk protein** is relatively constant (25% of solids)
  - Whey proteins are 50 to 85% of proteins during phase 2 (different than eutherians)
  - Casein secretion in phase 3

Marsupial Vitamin and Mineral Composition

- Calcium, phosphorous, magnesium, and zinc are relative similar in ranges to those observed in eutherians
  - Ca and P increase over lactation
- Copper and iron is higher in marsupials (early stage especially)
- Dam can concentrate iron in the milk about 7-9x found in blood while young are in the pouch (pouch period is similar to time in utero in eutherians)
- Na levels start high and then decline over lactation
- K levels start low and increase over lactation
- Vitamins vary widely
  - Riboflavin increases over lactation
  - Nicotinic acid decreases over lactation
  - Pantothenic acid stayed consistent

Pinniped Lactation

- Seals, sea lions, fur seals, and walruses
- Slightly higher AA than terrestrial mammals
- Traces of lactose (or none), need to conserve water
- Reside on land and sea
  - Pups are vulnerable to terrestrial predators
  - Pups need to buildup insulative layer against heat loss
  - Supply enough energy to pup to sustain itself during fasting period

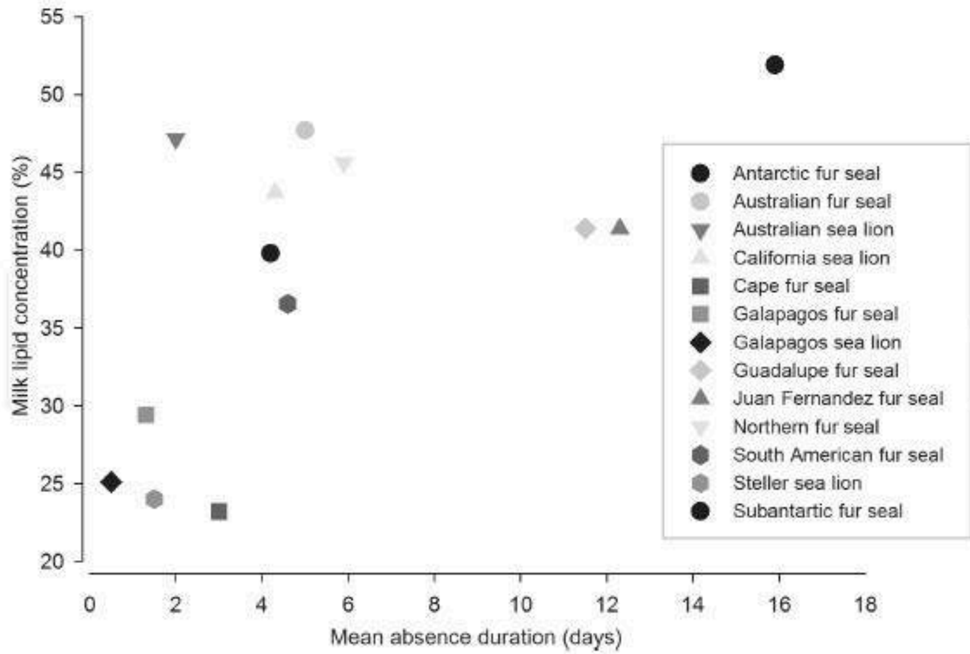
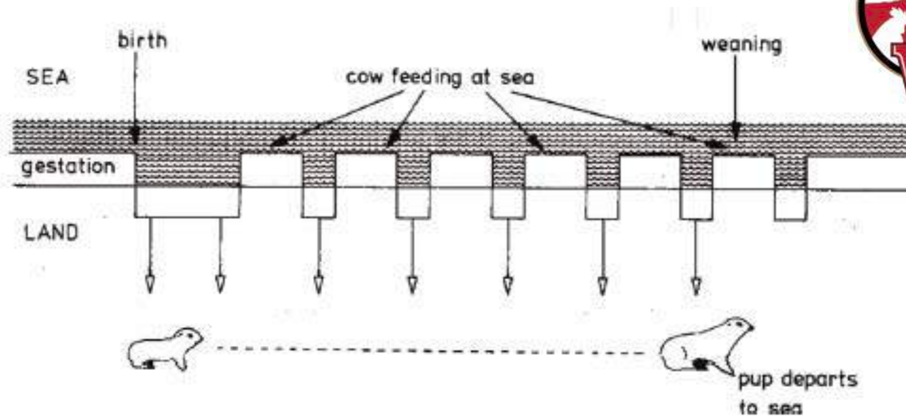


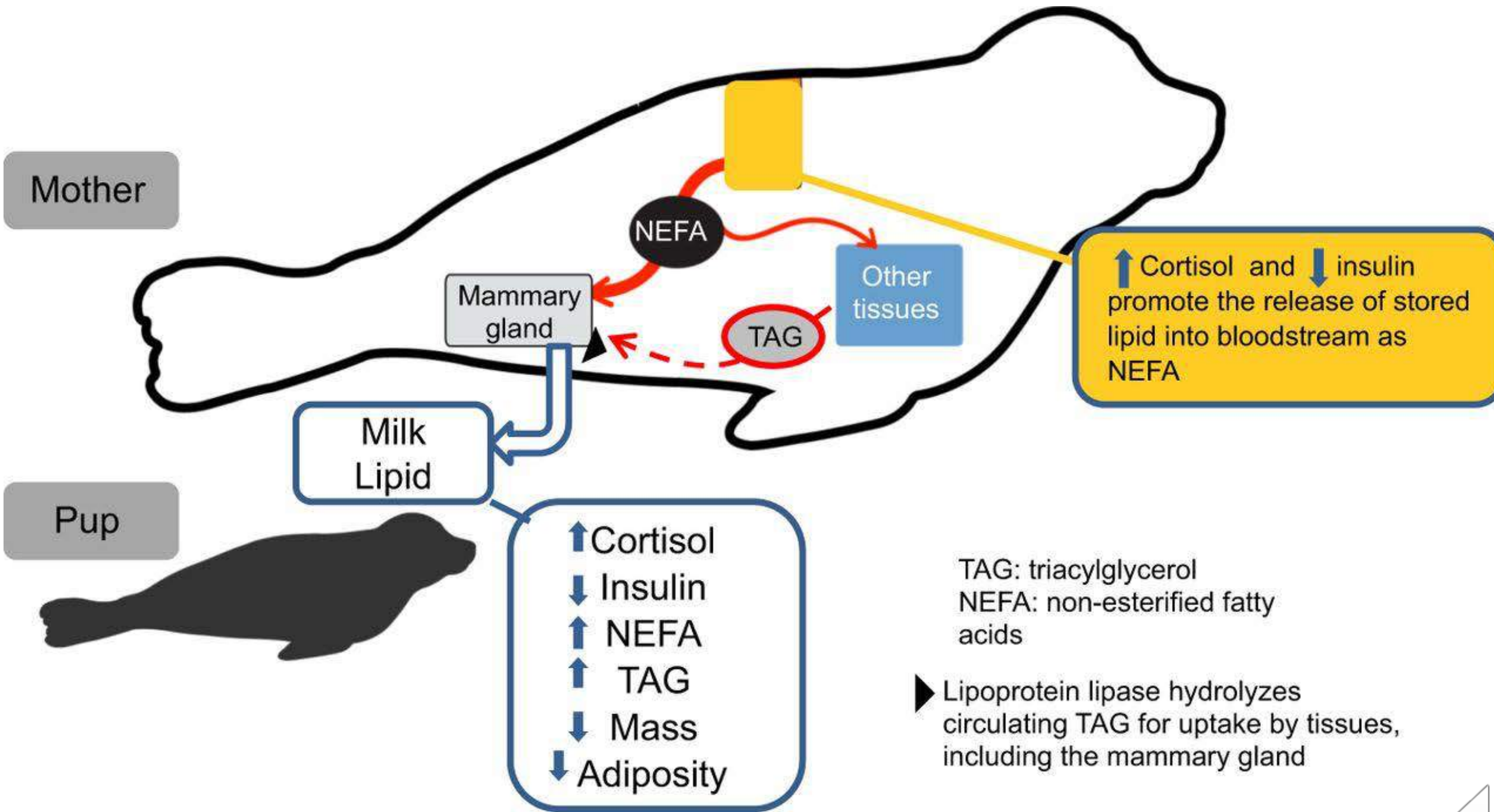
Figure 4.
The relationship between foraging trip duration (mean absence duration in days) and milk lipid concentration in 13 species of otariids (data from sources in ***Tables 4*** *and* ***6****). SL = sea lions, FS = fur seals.*

Otariids



- Sea lions and fur seals
- 4 month-3 year long lactation
- Duration of lactation: seasonal availability, predictability of food sources
- Dependent on location (northern v. southern hemisphere
- Northern fur seals: 6-8 days of attendance, 36 h-2.5 days foraging
- Subantarctic fur seals: 8 d nursing, foraging 11-23 d

Milk synthesis in a seal



Swine

- Mammary Anatomy
  - 6-20 mammary gland (3-10 pairs)
  - Arranged in 2 parallel rows on each side of ventral median line (pectoral to inguinal region)
  - Each gland is separate from adjacent glands
  - Blood supply
    - 2 branches of arterial system: common carotid supplies anterior glands, branch of abdominal aorta supplies posterior glands
    - Anastomosis of anterior and posterior mammary arteries and veins between 2nd and 4th inguinal glands so blood supplying inguinal glands may pass forward and blood supplying anterior gland may pass posterior

Swine Mammary Development

- **Mammogenesis**
  - LA development begins 45 d after conception
  - Alveoli remain small during gestation and distend ~4 d before parturition
  - DNA/RNA increases ~100 d gestation, along with estrogen
  - Require E2, P4, PRL, GH, corticosteroids for LA growth
- **Lactogenesis**
  - Lactose increases abruptly near parturition
  - Occurs ~ 2d prior to parturition, milk is expressed
  - Colostrum timing is critical to piglet survival (must be given within first hours of birth)
- **Suckling/Milk Ejection**
  - Milk flow is 10-20 seconds
  - Avg. nursing interval < 1 h (approx. 24 feeding/day)
  - Teat order is est. by 4-6 h after birth and is highly developed in pig
  - Piglet will go to same teat after 3-7 days of age
  - Milk ejection can only be induced by rubbing front teats, not back

Sow Colostrum

- Largely synthesized prior to parturition (range 1-6.0 kg)
- Prolactin concentrations have a high association with colostrum yield
- High in IgG (51.9 ng/ml) at 0 h
- Piglets are devoid of thermogenic brown adipose tissue and overall lipid content is low compared to other mammals
- Hepatic and muscle glycogen are main stores of heat producing nutrients
  - Drained by 12-17 h post birth without colostrum intake
  - Colostrum is necessary to provide energy
  - Take 3-4 weeks to have immune system develop
    - IgG provides systemic immunity
    - IgA protects intestinal mucosa from pathogens
    - Digestive enzymes
    - Stimulation of energy metabolism

Milk Synthesis in the Pig

- 4 stages:
  - Colostral
  - Ascending (17-35 nursing/day; d 2-10) and varies in length from 14-28 d: 5-10 kg/d on average
  - Plateau: sows typically weaned here
  - Descending
- Milk is not available continuously, only in milk ejection phase (10-15 seconds)
- Nursing intervals are 36-40 min
- MG use half the total circulating glucose in circulation to make **lactose** (18% of energy content of milk)
- Major source of **fatty acids** is plasma triglycerides (60% of total energy content of milk)
- **Essential and non-essential amino acids** are derived from plasma (22% of total energy content of milk)
- Reach peak MY at ~21 d lactation
- MY varies based on parity, litter size, body size, nutrition (1st lactation sow nursing 10 piglets may produce ~10-12 kg milk/day)
- Breed affects MY: 0.27 heritability for daughter-dam regression
- Number of piglets is a major determinant in MY (Litter bearing species); suckling intensity has a direct effect on MY

Piglet Protection

- Colostral Igg's must accumulate rapidly during last 2 d of gestation (IgA major immunoglobulin)
- 1L of sow's colostrum contains 1/3 blood pool IgG
- Rapidly absorbed across small intestine and max. serum concentrations are reach 12-24 h after birth
- Piglets also require external energy source during first hours of life to prevent hypoglycemia (must consume 250-300 ml of colostrum to remain in energy balance)
- Post-natal mortality in piglets can be up to 12% during d0 and d7 post-partum

Horses

- Dairy Horses
- Similar lactose content to humans
- IgG main antibody in colostrum
- Only 25% of energy is from fat (cows and humans are 50% energy from fat)
  - Only 80% triglycerides, rest is free fatty acids (10%) and phospholipids
- High level of unsaturated fatty acids, lactose, and bioactive molecules
- Large casein micelles, mainly beta casein, which there is more than cow's milk allowing for more bioactive peptides to be accessed
- Forms a softer curd
- Caseins are degraded better by humans (70% caseins digested)
- High in lysozyme and lactoferrin
- Lower energy content than cow and human milk
- Koumiss: fermented alcohol containing beverage made from mare's milk
  - Lactic-alcoholic fermentation
  - High in Vitamin C

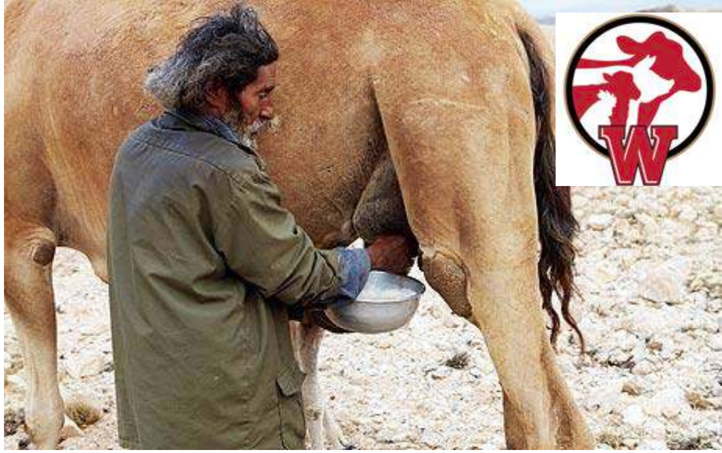
Horses

- 2-2.5 l capacity, mostly alveolar milk, with little cisternal capacity
- 30% residual milk, so oxytocin timing is critical
- Mare lives with her foal and nurses until weaning when not being milked because milk ejection and lactation persistency are directly related to behavior
- Mares are separated from foals 2-3 h prior to milking
- Peak lactation occurs within the first 3 months of lactation
- Estimated production per lactation (180 days) is approximately 2020 kg of milk and slightly more for heavy draft breeds

Horse Milk in Mongolian Culture

- Mongols lived in a milk-based society and used a lot of mare's milk
  - Key sustenance (Koumiss, dried cow's-milk curds, and powdered milk)
  - Made powered milk (1200s' it was observed)
  - Fresh mare's milk is a strong laxative
  - Made butter from it
  - Koumiss: would ferment the clear portion (whey portion of the mare's milk). Very tart and intoxicating

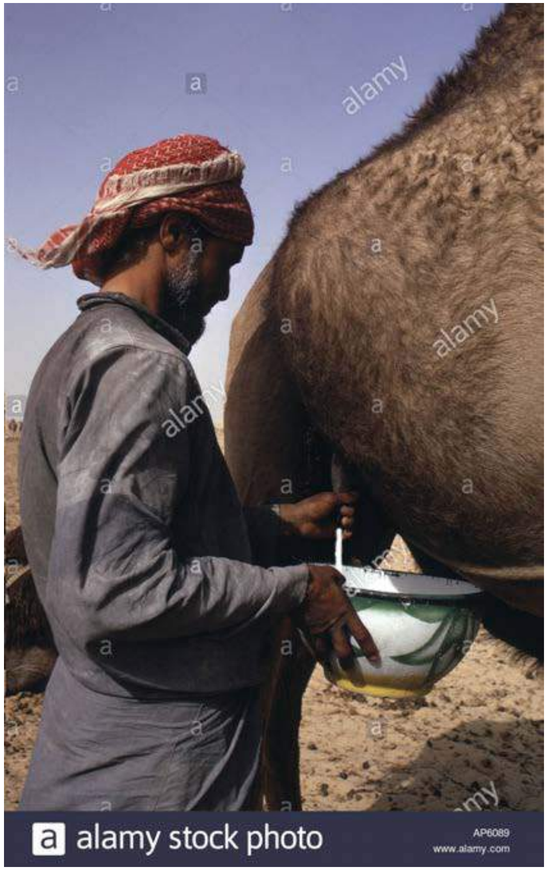
Camels



- Milk letdown is tied to the presence of the calf
- Milk yield is high in the first 7 months and then declines rapidly
- Milk is opaque-white color; sweet but sharp taste that can be salty
- Variation in taste is largely affected by the amount of readily available water and type of feed consumed by the animal
- High fat milk when water is available
- 1% fat is when water is scarce
- Higher content of Cu and Fe than cow’s milk
- Increased carnitine
- High Vitamin C compared to ruminants (similar to Mares/Donkeys)
- High Niacin concentrations
- Lower citrate which allows lactoferrin to be more effective

Camels

- Colostrum has high solids and proteins (especially whey proteins), high ash and chloride, low fat
- Economically use water
- Water content is 86% when water is readily available and 91% when water is restricted
- Maintain body temperature despite change in air temperature
- Lactate from 9-18 months depending on country
- Milk yield is high the first 7 months, then drops off rapidly (mostly a management issue)
- 80% casein-No beta-lactoglobulin
- Whey proteins: alpha lactalbumin, whey acidic protein, lactophorin (inhibitor of lipase), acidic protein (potential protease inhibitor)
- Milk fat: 98% triglycerides; small amounts of short chain fatty acids, high concentrations of C14:0, C16:0, C18:0, C16:1 is present in great proportions compared to other species



Bedouins and Arabs

- Nomadic Arabs who lived out in the desert, devout Sunni Muslims are called Bedouins
- Bedouins consumed largely milk based diet coming from camels which is more salty than cow's milk and preferred to drink milk fresh from the udder
- Muhammad and the Qur'an specified a baby would be breastfed for 2 years
- Liba: product made from colostrum
- Halum: a type of cheese using goat or sheep milk
- Iben: soured whey
- Used as therapeutic agent for stomach ulcers, liver disorders, etc
  - Kefir: fermented drink
  - Shubat: therapy for tuberculosis, chronic hepatitis, spleen inflammation (Shubat culture added to milk), national drink of Kazakstan
  - Stabilization of juvenile diabetes
  - Airag: fermented milk in Mongolia made from Bactrian camel milk
  - Susa: traditional fermented camel milk made in East Africa
  - Orom: soured cream produced from Bactrian camel milk in Mongolia

Reindeer

- Eurasia and Taiga regions
- Most intensive milking regime was developed along border of Russia, Mongolia, and China
- Traditional products:
  - Fresh milk: consumed mostly by children (often diluted with water) and used in tea and coffee
  - Stored milk: Frozen-ice cream mixed with berries; fermented-short: sour cream, cultured milk; long: stored in wooden container mixed with herbs; dried- dried in the reticulum for a longer period (winter consumption
  - Manufactured milk: cheese-curdled or dried in abomasum; butter-fresh and fermented milk; rest products-buttermilk and whey, consumed fresh and reduced and eaten as a soup

Reindeer

- Calves born at the end of the northern winter and lactation usually ends in early October
- Relatively small udders
  - Early lactation milk used for fresh consumption
  - Mid lactation milk used for cheese
  - Late lactation milk used for butter
- Peak lactation is 4 weeks, produce about 1 L per day
- Milk composition changes energetically after peak to compensate for decreased yield

Reindeer

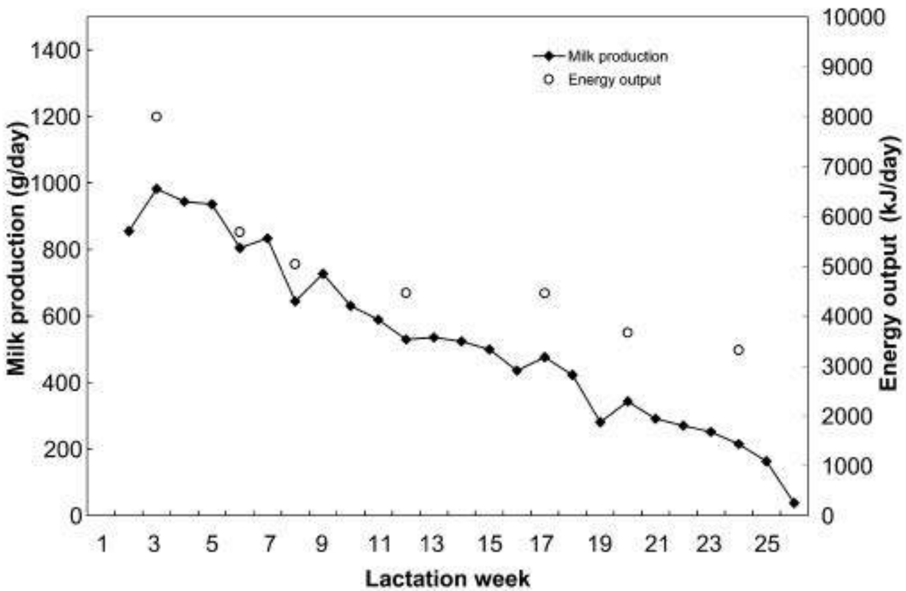


Fig. 2. Mean milk production (g/day) and total energy output (kJ/day) during lactation in reindeer (*Rangifer tarandus*). The milk production data are based on mean values from both years of the study.

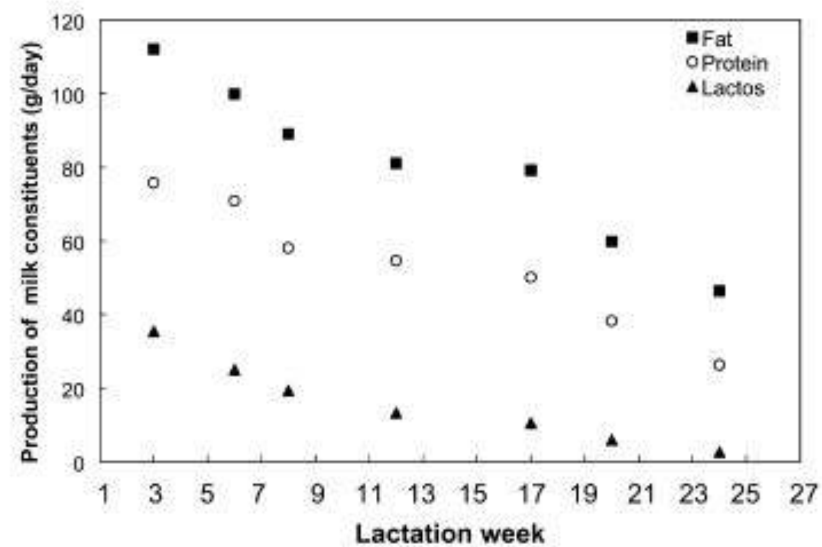


Fig. 3. Daily production (g/day) of the major milk constituents at different stages of lactation in reindeer (*Rangifer tarandus*).

Gjostein et al., 2004

Human Milk and Lactation

	Human Milk	Bovine Milk
COMPONENT CHO		
Lactose	7.3 g/dl	4.0 g/dl
Oligosaccharides	1.2 g/dl	0.1 g/dl
PROTEINS		
Caseins	0.2 g/dl	2.7 g/dl
α-lactalbumin	0.2 g.dl	0.1 g/dl
Lactoferrin	0.2 g/dl	trace
Secretory IgA	0.2 g/dl	0.003 g/dl
β-lactoglobulin	None	0.36 g/dl
MILK LIPIDS		
Triglycerides	4.0 %	4.0 %
Phospholipids	0.04 %	0.04 %
MINERALS		
Sodium	5.0 mM	15 mM
Potassium	15.0 mM	45 mM
Chloride	15.0 mM	35 mM
Calcium	8.0 mM	30 mM
Magnesium	1.4 mM	4.0 mM

Human Lactation

- Frequent suckling, high-sugar, dilute milk
- Most similar to chimpanzees vs. baboon or macaque milk
- All mammals have unique milk but milks of closely related species are similar
- Milks of the great apes are likely the closest in composition to the australopithecine mother (Low in protein, low in fat, high in sugar and water)
- Increase in brain size
- Dietary shift that *Homo* made early was a diet higher in animal matter because it's easier to digest than plant matter to support energy demands by brain

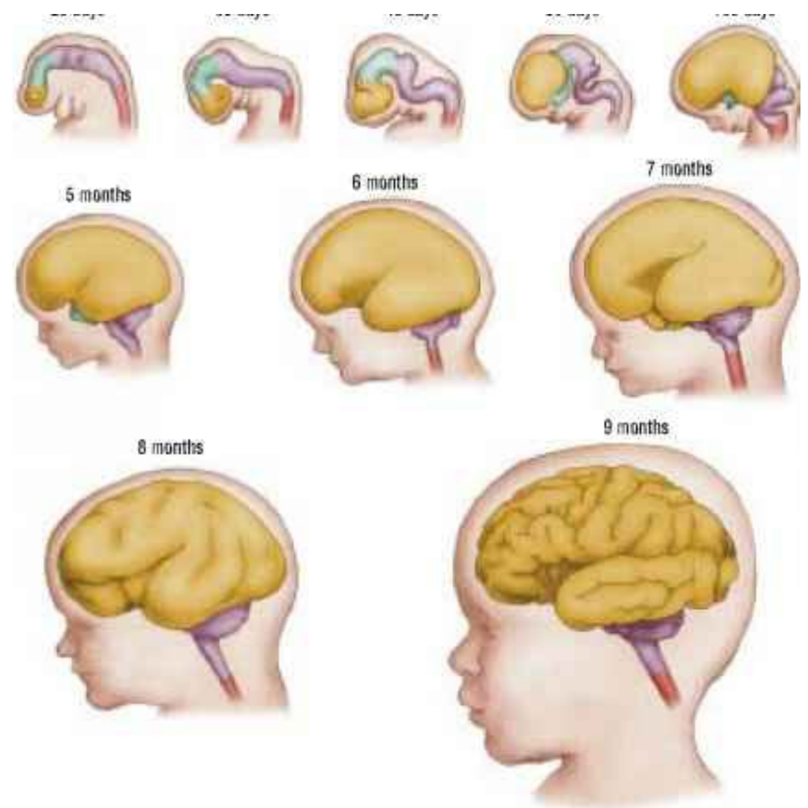
Human Lactation



- Humans begin to need solid foods around 6 months of age, unlike great apes who do not eat solid food until around 1 year of age
- May be evolutionary…..the sooner a mother can shift nutritional burden to other foods, the shorter interval between births
- **Premodern technology human lifestyle:** Interbirth intervals of 3 years
- Wild gorillas and chimpanzees do not fully wean babies until 4-5 years, with interbirth interval being greater than 5 years
- Energy output of lactating human breast is about 30% of the mother's resting energy in total

Human Brains

- Baby is born with a brain 25% the size of an adult human
- 1st 18 months of like, the human brain grows rapidly
- Most myelination occurs after birth in human brains
- Marsupial babies grow almost their entire brain on milk
- The size of a human brain and the rate of growth could be the reason behind the increase in fat of milk of *Homo*
  - LCPUFA (mother's diet)
  - DHA (mother's diet)

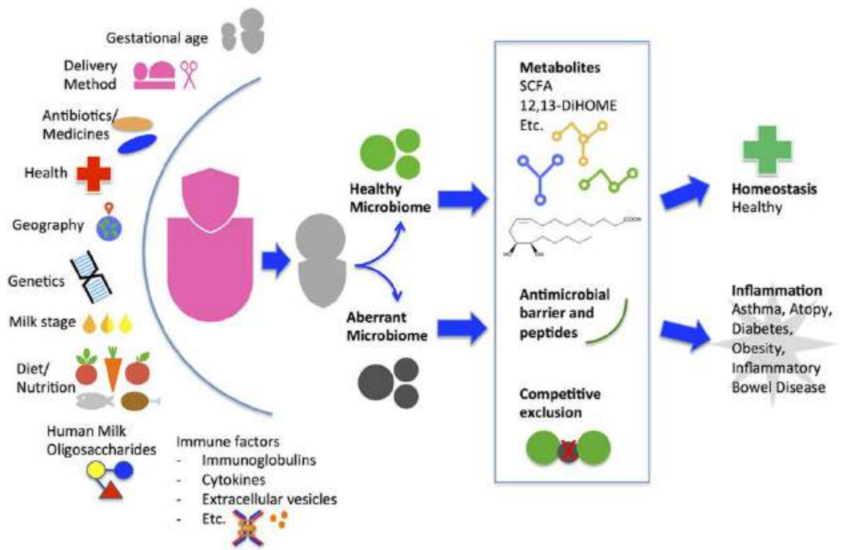


Human Milk Composition

- **CHOs**: High lactose content, provides 40% calories available to infant because baby requires glucose for the brain and because of the water demand for the baby
- **Proteins**: Low casein content, bound in micelle form with Ca and P; α-lactalbumin; Lactoferrin (iron-binding and anti-bacterial properties); IgA
  - Amino acids: High cysteine:methionine ratio and some taurine (for baby's liver and brain function)
- **Lipids**: Approx. 4% of human milk, primarily triglycerides (20% from MCFAs and 80% from plasma), also contains phospholipids and cholesterol
- **Minerals**: Small amounts of macrominerals

Increase in Milk Fat for Sugar?

- 1-2 MYA likely saw an increase in milk fat due to brain size in genus *Homo*
- Human milk has higher oligosaccharide content than lactose (20-25%), which is 4x greater than the great ape milk
- Oligosaccharides are not digestible by infant and are proposed to act as prebiotics/antibiotics, with some being metabolized by symbiotic gut microbes, or acting as decoy pathogens
- These are not readily usable as energy, so may be why milk fat is increased to provide more energy



Human Milk Oligosaccharides

- Greater diversity in humans-more immune possibilities
- Human milk also has high concentrations of sIgA
- Higher lactoferrin concentrations
- Maternal transfer of immunoglobulins is higher in humans than nonhuman primate relatives
- Potentially due to lifestyle changes: settlements became permanent, increased vectors for disease, agriculture allowed for increased population density, animals, parasites, birds, etc.

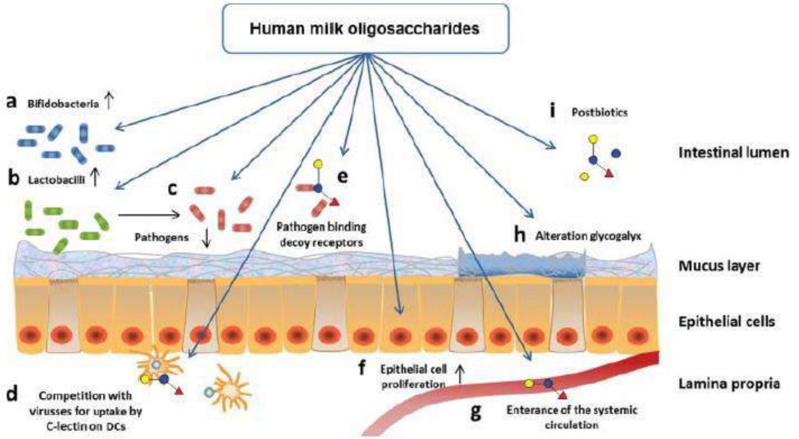
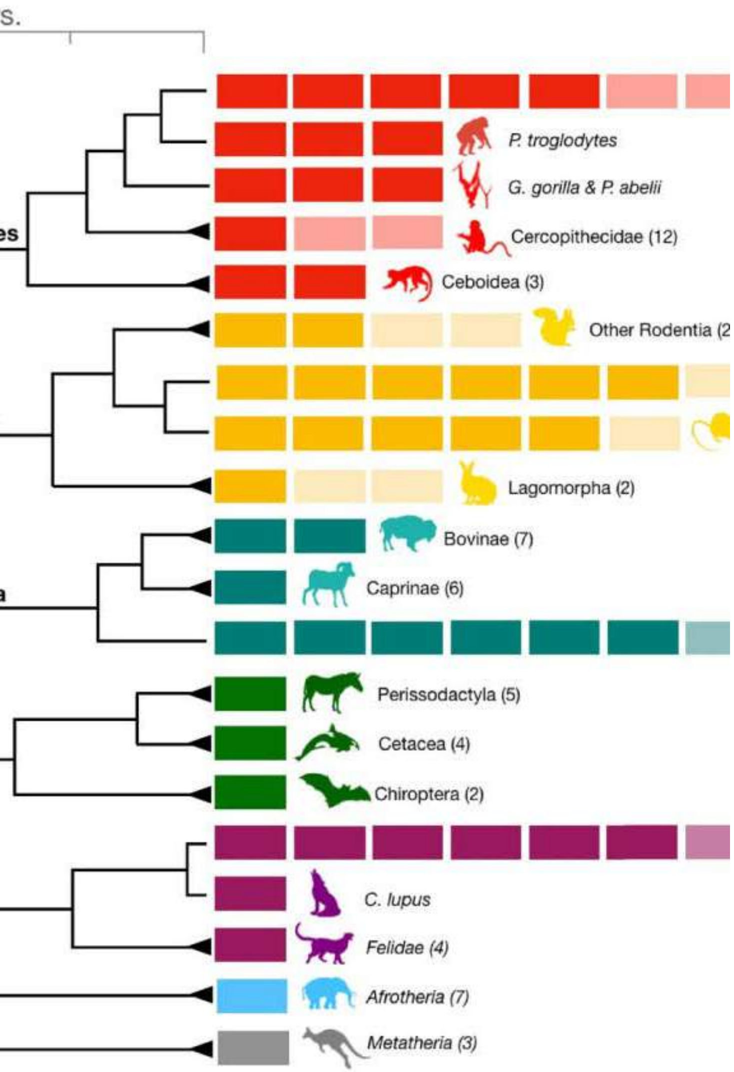


Figure 3. Beneficial effects of human milk oligosaccharides (HMOs). HMOs can specifically stimulate growth of (A) Bifidobacteria and (B) Lactobacilli, competing with and resulting in (C) a lower number of pathogens. Furthermore, HMOs can (D) compete with viruses for uptake by C-lectin receptors on dendritic cells and (E) act as pathogen binding decoy receptors to prevent binding of pathogens to glycan structures on epithelial cells. HMOs can also (F) influence epithelial cell proliferation, (G) enter the systemic circulation, (H) alter the glycogalyx and fermentation products of HMOs and (I) post-biotics for other microbiota species.

https://nzyacon.com/2018/05/17/non-digestible-carbohydrates-in-infant-formula-as-substitution-for-human-milk-oligosaccharide-functions-effects-on-microbiota-and-gut-maturation/

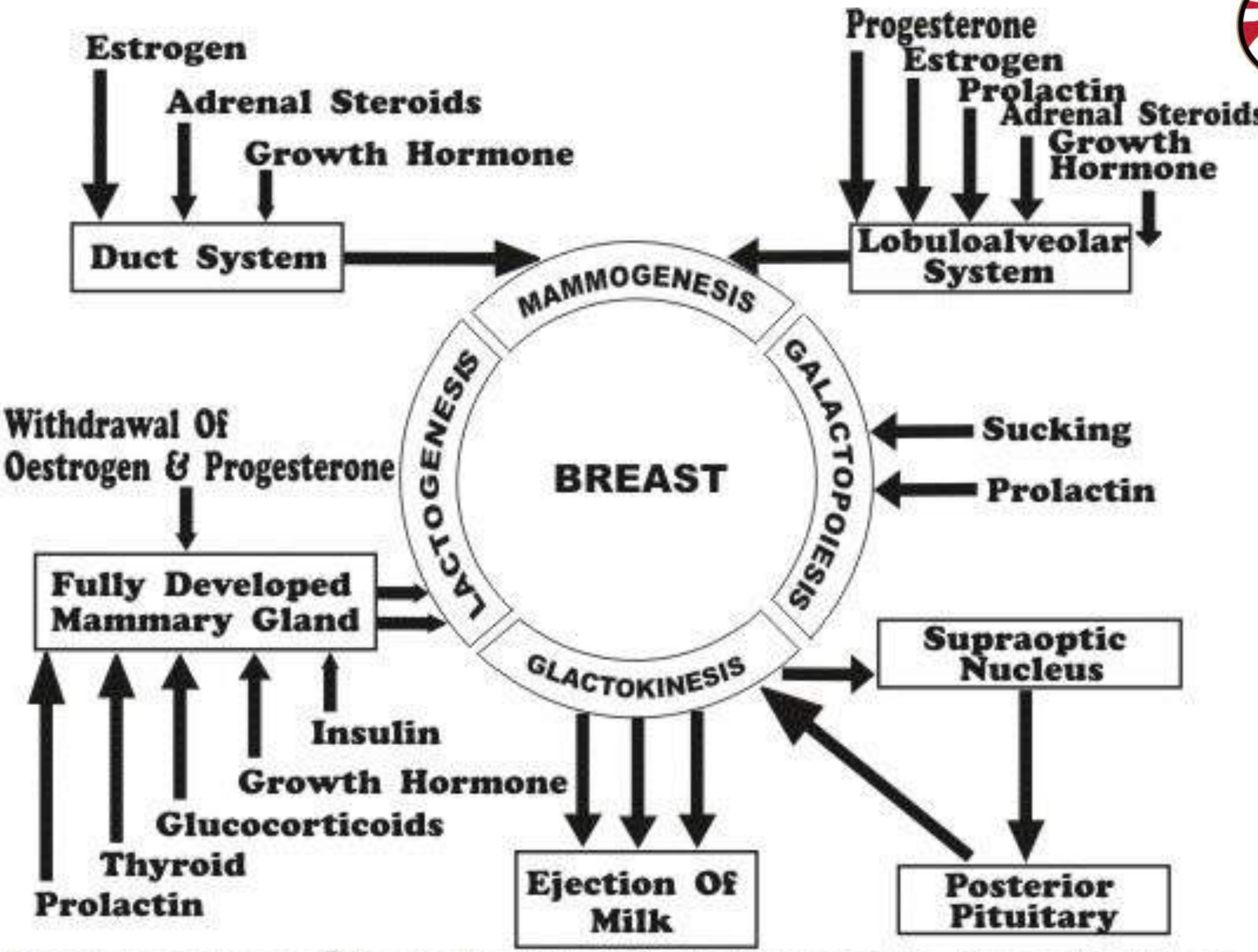
Salivary α-amylase in human milk



- Reduce starch into simple sugars
- Activity varies between individuals
- May be an adaptation to providing babies with starchy supplemental foods at a young age
- Cultural adaptations to infant survivorship, shortened time to weaning, and shortened interbirth interval
- Potentially allowed for reduced nutritional stress for mothers, able to regain condition and become fertile more quickly, improving reproductive potential
- Very little to no expression in monkey milk except in chimpanzees

Milk Secretion

- **Milk protein**: similar to those in other species
- **Milk lipids**: Triglyceride is synthesize in alveoli from free fatty acids and glycerol; fatty acids are influences by the type of diet the mother consumes; most variable component (changes from beginning of feeding to the end)
- **Immunoglobulins**: receptor on basolateral side of cell that binds and internalizes dimeric immunoglobulins from interstitial spaces and is secreted with a portion of receptor to prevent degradation in the newborn’s GI tract
- **Salts and water into milk**: cross the Golgi and apical plasma membranes of mammary alveolar cell, but how the concentrations are regulated are poorly understood



Endocrine Glands In Relation To Lactation

Human Mammogenesis

- Commences at puberty with onset of estrogen secretion by ovaries (causes enlargement of the mammary fat pad)
- Estrogen stimulates mammary growth and acts through local effects on tissue and stimulation of pituitary growth factors
- Progesterone stimulates partial development of alveoli so that by age 20 a woman who has not been pregnant has a fat pad with 10-15 branching ducts with some alveoli
- Full LA development takes place during pregnancy from estrogen, progesterone and rising levels of prolactin and placental lactogen; fat pad diminishes and is replaced by developing ducts and alveoli

Human Lactogenesis

- Onset of copious milk secretion, delayed after parturition (40-48 h) due to the delay in the fall of progesterone levels
- 3 factors necessary for successful lactogenesis
  - Developed mammary epithelium
  - High plasma PRL levels
  - Decreased P4 and E2
- Abrupt increase in milk volume secretion (50 ml on d 2 post-partum to 500 ml/day on d 4, then volume increases gradually to ~850 ml/day by 3 months post-partum)
- Milk composition changes during 1st 10 days post-partum (due to closure of tight junctions and changes from colostrum to mature milk)
- Delayed lactogenesis (stage II): >72 hr post-partum

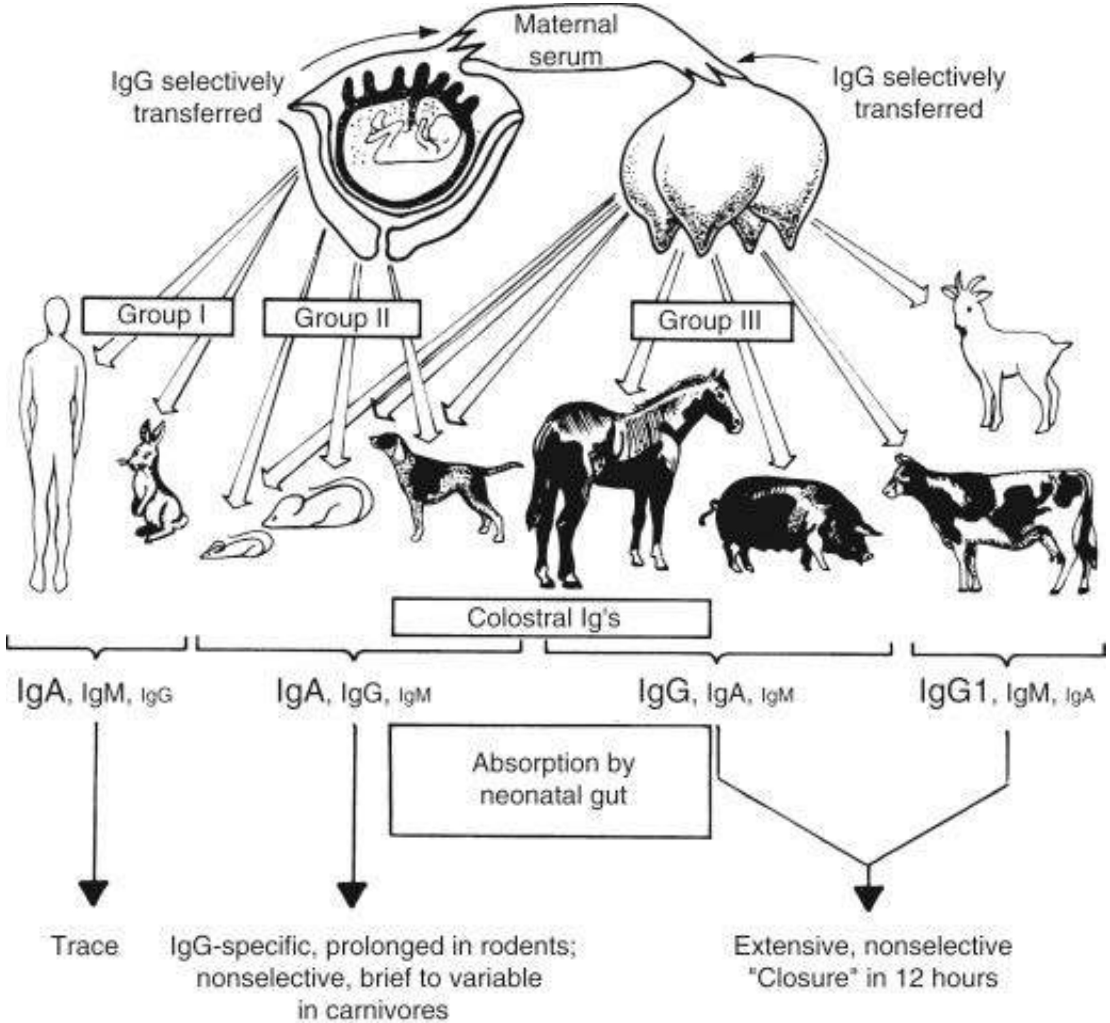
Human Lactation

- Milk production continues in response to demand (baby suckling at least once a day)
  - During weaning, rate of milk production decreases in proportion to the amount of supplementary food taken in by the infant
- Oxytocin and Prolactin
  - OXY: milk ejection reflex; higher centers of the brain regulate this
  - PRL: Also promoted by afferent nerve impulses sent to hypothalamus, but secretion is dependent on strength and duration of suckling stimulus
- Local factors
  - No direct relationship between rate of milk production and PRL levels
  - Milk contains factors that inhibit milk production (serotonin, among others) if the milk in the gland is not removed frequenetly enough

Human Involution

- Changes in the mammary gland that occur after complete cessation of lactation
- Gradual replacement of ducts and alveoli with stromal and fat tissue
- Reversion of mammary alveolar cells to less differentiated state
- Loss of epithelial cells (apoptosis)
- Complete regression of the gland to virgin state only occurs after menopause and loss of sex steroid hormones

Colostrum Transfer In Various Species



Butler et al., 2015

Integrative Health and Breastfeeding

Jill Mallory, MD, IBCLC
Wildwood Family Clinic
Madison, WI

1

I have no conflicts of interest

2

Objectives

1. Define integrative medicine as a general class of approaches
2. How might you create a healing environment?
3. Describe two therapies that involve touch and how they might be used?

3

Objectives

4. What might acupuncture be beneficial for?
5. When might you suggest chiropractic manipulation?
6. List 2 benefits of craniosacral therapy for the nursing dyad.
7. What is the purpose of remedial co-bathing?

4

Objectives

8. Why is homeopathy considered safe in breastfeeding dyads?
9. List two herbs you can use safely in lactating mothers?

5

What is Integrative Medicine?

- From the Andrew Weil Center for Integrative Medicine:
  - Integrative Medicine is healing-oriented medicine that takes account of the whole person, including all aspects of lifestyle.
  - It emphasizes the therapeutic relationship between practitioner and patient, is informed by evidence, and makes use of all appropriate therapies.

6

Why do we need to understand Integrative Medicine?

- Surveys show that a significant percentage of Americans are using alternative therapies.
- Women are more likely than men to seek alternative health care and often use alternative therapies for childbirth-related concerns.

Ayers JF. The use of alternative therapies in the support of breastfeeding. J Hum Lact. 2000 Feb;16(1):52-6.

7

IBCLC Clinical Competencies

"Provide evidence-based information regarding complementary and alternative therapies during lactation and their impact on milk production and the effect on the child. " (IBLCE, 2018)

8

The Sliding Scale of Evidence

9

Environment

- Oxytocin
- The hormone of love, safety and relaxation

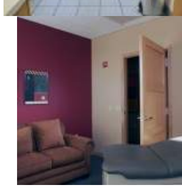
10

Environment

- Light
- Color
- Sound
- Temperature
- Smell
- Privacy
- Attitude of the practitioner

11

Home and Office



12

Hospital Rooms

- A new mother is interrupted an average of 54 times in 12 hours of hospital stay
- Half of her time alone with her infant is in intervals of 9 minutes or less

Morrison, Ludington-Hoe, & Anderson, 2006

13

Hospital Rooms

- Calm yourself first
- Close the door
- Dim the lights
- Draw the curtains
- Turn off the TV

14

Feng Shui

- The art of arranging and decorating space
- Chinese astronomy
- 4000 BC

15

The Power of Touch

16

Touch Therapies

- Skin-to-skin
- Remedial co-bathing
- Massage
- Acupuncture
- Chiropractic
- Osteopathy
- Craniosacral therapy

17

Touch

"As the most ancient and largest sense organ of the body, the skin enables the organism to learn about its environment. It is the medium by which the external world is perceived. "

Ashley Montague, 1986

18

Mother the Mother

Research done in South Africa showed that women who were talked to, smiled at, and stroked themselves were more likely to talk to, smile at, and stroke their newborns.

Sosa, Kennell, Klaus, Robertson, & Urrutia 1980

19

Breastfeeding Success

When newborns spend time skin-to-skin with their mothers, they are more likely to be breastfed, and typically are breastfed longer.

Moore ER, Bergman N, Anderson GC, Medley N. Early skin-to-skin contact for mothers and their healthy newborn infants. Cochrane Database Syst Rev. 2016 Nov 25;11(11)

20

The Power of Touch

21

The First Step

You can start nearly all lactation sessions with mother and babies in skin-to-skin contact.

22

Birth Trauma

- Torticollis
- Mandibular asymmetry
- Muscular spams
- Spinal malalignment
- TMJ dysfunction
- Cranial trauma
- Emotional trauma

23

Massage

24

Massage at Birth

- The infant crawl and maternal bleeding
- Infant massage of the breast increases oxytocin levels

Matthiesen AS, Ransjö-Arvidson AB, Nissen E, Uvnäs-Moberg K. Postpartum maternal oxytocin release by newborns: effects of infant hand massage and sucking. Birth. 2001 Mar;28(1):13-9.

25

What Does Massage Do in Infants?

- Increased vagal tone
- Increases gastric motility
- Increases insulin and IGF-1 levels
- Decreases cortisol
- Reduces metabolic demand through reduced crying

Field T. Massage therapy research review. Complement Ther Clin Pract. 2014;20(4):224-229.

26

Infant Massage

- Preterm infants in the NICU:
  - Shorter length of stay
  - Reduced pain
  - Improved weight gain
  - Improved feeding tolerance
  - Improved neurodevelopment

Pados BF, McGlothen-Bell K. Benefits of Infant Massage for Infants and Parents in the NICU. Nurs Womens Health. 2019 Jun;23(3):265-271.

27

Infant Massage

- Preterm infants in the NICU:
  - Parents who performed massage with their infants in the NICU reported experiencing less stress, anxiety, and depression.

Pados BF, McGlothen-Bell K. Benefits of Infant Massage for Infants and Parents in the NICU. Nurs Womens Health. 2019 Jun;23(3):265-271.

28

Infant Massage

- Infants receiving phototherapy:
  - Reduce bilirubin levels
  - Increase defecation frequency

Eghbalian F, Rafienezhad H, Farmal J. The lowering of bilirubin levels in patients with neonatal jaundice using massage therapy: A randomized, double-blind clinical trial. Infant Behav Dev. 2017 Nov;49:31-36.

Lin CH, Yang HC, Cheng CS, Yen CE. Effects of infant massage on jaundiced neonates undergoing phototherapy. Ital J Pediatr. 2015 Nov 25;41:94.

29

Maternal Massage

- Lowers stress hormones and blood pressure for mothers too
- Improved maternal-infant attachment

Shoghi M, Sohrabi S, Rasouli M. The Effects of Massage by Mothers on Mother-Infant Attachment. Altern Ther Health Med. 2018 May;24(3):34-39.

Liao IC, Chen SL, Wang MY, Tsai PS. Effects of Massage on Blood Pressure in Patients With Hypertension and Prehypertension: A Meta-analysis of Randomized Controlled Trials. J Cardiovasc Nurs. 2016 Jan-Feb;31(1):73-83.

Field T. Massage therapy research review. Complement Ther Clin Pract. 2016 Aug;24:19-31.

30

Maternal Massage

31

Breast Massage

- Cultural tradition
  - Oketani massage - Japan
  - Russian mammology
  - Gua-Sha – China
  - Tuina - China

32

Breast Massage

- Therapeutic breast massage may be helpful for
  - Engorgement
  - Plugged ducts
  - Mastitis
  - Breast pain
- Optimal technique is unknown

Anderson L, Kynoch K, Kildea S, Lee N. Effectiveness of breast massage for the treatment of women with breastfeeding problems: a systematic review. JBI Database System Rev Implement Rep. 2019 Aug;17(8):1668-1694.

33

Breast Massage

- DiSandro massage for recurrent mastitis
  - Bag of marbles technique
  - Gentle Kneading motion
  - Perform several times a day
  - Moves lymph

The Womanly Art of Breastfeeding, 8th edition, 2010

34

Breast Massage

- Therapeutic Breast Massage in Lactation (TBML)
  - Breastfeeding Medicine of NE Ohio
  - Mastitis, plugged ducts, engorgement
  - Immediate improvement in pain
  - 65% of women found it helpful
  - https://bfmedneo.com/resources/videos/

Witt AM, Bolman M, Kredit S, Vanic A. Therapeutic Breast Massage in Lactation for the Management of Engorgement, Plugged Ducts, and Mastitis. J Hum Lact. 2016 Feb;32(1):123-31. doi: 10.1177/0890334415619439. Epub 2015 Dec 7. PMID: 26644422.

35

Breast Massage

- Accupoint-Tuina
  - Ancient form of medical massage in Chinese medicine
  - RCT 80 women
  - 15 min/breast x 2 days

Lu P, Ye ZQ, Qiu J, Wang XY, Zheng JJ. Acupoint-tuina therapy promotes lactation in postpartum women with insufficient milk production who underwent caesarean sections. Medicine (Baltimore). 2019;98(35):e16456.

36

Breast Massage

- Accupoint-Tuina
  - Significantly increased the milk production when compared to the control group, 13-10 x that in the control group on the 3rd and 4th postpartum days.
  - Increased serum PRL level
  - Accelerated the post-surgery recovery of uterus.

Lu P, Ye ZQ, Qiu J, Wang XY, Zheng JJ. Acupoint-tuina therapy promotes lactation in postpartum women with insufficient milk production who underwent caesarean sections. Medicine (Baltimore). 2019;98(35):e16456.

37

Massage Resources

- www.lovingtouch.com
- www.infantmassageusa.org
- www.iaim.net

38

Acupuncture

39

Acupuncture

- Over 5000 years old
- Fine needles placed along meridians
- Part of TCM
- PET scan research
- Anesthesia
- Acupressure

40

Acupuncture

- NIH endorses for
  - Labor pains
  - Fertility
  - Hyperemesis gravidarium

41

Acupuncture

- Used for 1000's of years for low milk supply in China
  - Research is mixed
  - Extreme difficulty in double-blinding and placebo-controlling acupuncture studies

Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Acupuncture. 2020 Nov 16.

42

Acupuncture

Electroacupuncture increased serum prolactin, infant weight and maternal perception of milk production more than domperidone alone.

Maged AM, Hassanin ME, Kamal WM, et al. Effect of low-level laser therapy versus electroacupuncture on postnatal scanty milk secretion: A randomized controlled trial. Am J Perinatol. 2020;37:1243–9.

43

Acupuncture

- May reduce symptoms of mastitis

Kvist LJ, Hall-Lord ML, Rydhstroem H, Larsson BW. A randomised-controlled trial in Sweden of acupuncture and care interventions for the relief of inflammatory symptoms of the breast during lactation. Midwifery. 2007 Jun;23(2):184-95.

- May increase breastfeeding duration

Neri I, Allais G, Vaccaro V, Minniti S, Airola G, Schiapparelli P, Benedetto C, Facchinetti F. Acupuncture treatment as breastfeeding support: preliminary data. J Altern Complement Med. 2011 Feb;17(2):133-7.

44

Acupuncture

- A meta-analysis concluded:
  - Women who received acupuncture were less likely to develop an abscess
  - Had less severe mastitis symptoms on day five
  - Had a lower rate of fever than women in the usual care group

Mangesi L, Zakarija-Grkovic I. Treatments for breast engorgement during lactation. Cochrane Database Syst Rev. 2016;6:CD006946

45

Acupunture

- Safe
- May be beneficial
- Licensure varies from state-to-state
- Cost can be an issue
- Some insurances do cover

46

Acupunture

- Resources

https://www.nccih.nih.gov/health/acupuncture-in-depth
https://medicalacupuncture.org
https://www.asacu.org
https://www.nccaom.org

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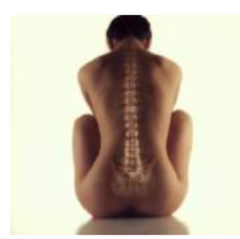
Chiropractic



48

Chiropractic

- Founded by Dr. David Palmer in 1895
- Defined by the American Chiropractic Association:
  "a healthcare profession that focuses on disorders of the musculoskeletal and nervous systems, primarily the spine, and seeks to restore the healthy relationship between the body's structure and function."

49

Chiropractic

- Adjustment
  - Restore joint mobility and alignment by application of controlled force
  - Vertebral subluxation

50

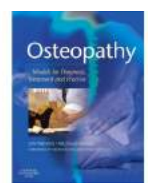
Chiropractic

- A Doctor of Chiropractic
  - 4 year post-baccalaureate degree
  - Pass a state licensing exam
- Covered by most insurances
- Evidence for effectiveness is lacking, other than for low back pain

51

Chiropractic vs. Osteopathy

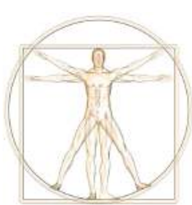
- Osteopath (DO) attends a 4 year medical school similar to MD's
- Also learn manipulation
- Most do not use this in practice



52

History of Mistrust

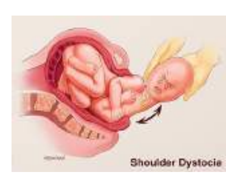
- 11 years of law suits
- AMA



53

Chiropractic

- Birth injury
  - Stiff neck
  - Jaw alignment
  - Torticollis



54

Chiropractic

- Reasons mother's may seek care for baby
  - Poor latch
  - Poor milk transfer
  - Can nurse only in one position
  - Poorly coordinated suck-swallow
  - Very fussy and difficult to settle
  - Vacuum extraction

55

Chiropractic

- Reasons lactating mother's may seek care for themselves
  - Neck pain
  - Back pain
  - Birth recovery
  - Low milk supply

56

Chiropractic

- Little published evidence
- Case series of 114 babies with sucking difficulties
  - 78% showed improvement with 4 tx and were able to exclusively breastfeed

Miller JE, Miller L, Sulesund AK, Yevtushenko A. Contribution of chiropractic therapy to resolving suboptimal breastfeeding: a case series of 114 infants. J Manipulative Physiol Ther. 2009 Oct;32(8):670-4.

57

Chiropractic

- Colic or abdominal distress
  - Can lead to premature weaning
  - Reduced crying hours seen in babies who had chiropractic or osteopathy
  - High risk of performance bias

Dobson D, Lucassen PL, Miller JJ, Vlieger AM, Prescott P, Lewith G. Manipulative therapies for infantile colic. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004796.

58

Chiropractic

- One case report of 6 months old whose sucking dysfunction resolved with chiropractic

Holtrop DP. Resolution of suckling intolerance in a 6-month-old chiropractic patient. J Manipulative Physiol Ther. 2000 Nov-Dec;23(9):615-8.

59

Chiropractic

- Lit review for adverse event cases
  - Serious adverse events in infants and children receiving chiropractic, osteopathic, physiotherapy, or manual medical therapy are rare.
  - 3 deaths reported associated with various manual therapists; however, no deaths associated with chiropractic care

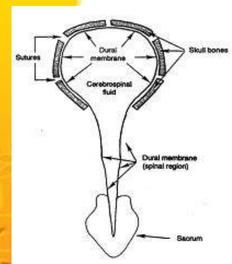
Todd AJ, Carroll MT, Robinson A, Mitchell EKL. Adverse Events Due to Chiropractic and Other Manual Therapies for Infants and Children: A Review of the Literature. J Manipulative Physiol Ther. 2015 Nov-Dec;38(9):699-712.

60

Craniosacral Therapy

61

Craniosacral



- Dr. John Upledger, an osteopath
- Gentle, non-invasive, hands-on technique
- Evaluation of the membranes and CSF
- OT's, PT's, Chiropractors, IBCLC's

62

Craniosacral

- Indications for baby
  - Torticollis
  - Colic and irritability
  - Infant feeding or sucking difficulties
  - Restriction in movement
  - Irregular head shape/asymmetries
  - Tongue mobility issues
  - Traumatic delivery, cesarean section, forceps or vacuum

63

Craniosacral

- Indications for baby
  - Post frenotomy
- Indications for mothers
  - Pain
  - Anxiety
  - Pelvic tension
  - Birth trauma

64

Craniosacral Tips

- Consider cost
- Usually 3-4 sessions
- Response arises over time
- Expect to see changes in postural states
- Suck changes may not come till after the second visit

www.upledger.com

65

Craniosacral

May reduce crying hours in colic

Castejón-Castejón M, Murcia-González MA, Martínez Gil JL, Todri J, Suárez Rancel M, Lena O, Chillón-Martínez R. Effectiveness of craniosacral therapy in the treatment of infantile colic. A randomized controlled trial. Complement Ther Med. 2019 Dec;47:102164.

66

Craniosacral

- Evidence is lacking
- Difficult to blind or sham
- Considered safe

Jäkel A, von Hauenschild P. Therapeutic effects of cranial osteopathic manipulative medicine: a systematic review. J Am Osteopath Assoc. 2011 Dec;111(12):685-93.

67

Remedial Co-Bathing

68

Remedial Co-Bathing

- No research
- All theory
- Presented by Australian midwife Heather Harris at ILCA 1994
- Combines skin-to-skin time with warm water tub immersion

69

Remedial Co-bathing

- Calm relaxing time for mother and baby together
- Dyad may or may not feed during the bath
- Present it as something new and fun to do with baby

70

Remedial Co-Bathing

- When to consider it
  - Breast refusal
  - Mom wants to breastfeed, but can't
  - Mom is not happy and not having fun with her baby
  - Offset the pressure of a rigorous lactation regimen
  - Mother is otherwise resistant to skin-to-skin

71

Remedial Co-Bathing Tips

- Low light
- Privacy
- Warmth (98-102F)
- Cup to drizzle water
- Cool wet washcloth
- Drink for mother
- Baby on torso
- Have help nearby

72

Homeopathy

73

Homeopathy

- Over 200 years old
- Founded by Samuel Hahnemann in Germany in 1790
- Theory: ultra low-doses of a substance stimulate the body's immune system to react to the disease or condition

74

Homeopathy

- "Like cures like"
- For example, ipecac in pharmaceutical doses causes nausea and vomiting
- Ipecaucanha used to relieve nausea and vomiting
- Constitutional vs. acute

75

Homeopathy

- Plant, mineral, animal, food
- Alcohol/water for 1 month
- Serial dilutions and successions
- 6X potency = diluted 610 times
- The more dilutions, the stronger the remedy
- No pharmacologic activity

76

Homeopathy

- Sometimes blended with lactose or sucrose
- Melted under the tongue
- Dissolved in water or human milk
- Cheap
- Easy to find
- No adverse effects

77

Homeopathy

- Used by just over 2% of the U.S. population.
- 19% of users in the United States see a provider.
- Research is little and mixed
- Is it just placebo?

Dossett ML, Yeh GY. Homeopathy Use in the United States and Implications for Public Health: A Review. Homeopathy. 2018 Feb;107(1):3-9.

78

Homeopathy

- Placebo effect?
  - Expectation is one of the main mechanisms
  - Reward circuit is the nucleus accumbens
  - US population 30-50%

Chi GYH, Li Y, Liu Y, Lewin D, Lim P. On clinical trials with a high placebo response rate. Contemp Clin Trials Commun. 2015;2:34-53. Published 2015 Nov 18.

Jilch S, Sel R, Shariat SF. Medical practice and placebo response: an inseparable bond?. Wien Klin Wochenschr. 2020;132(9-10):228-231. doi:10.1007/s00508-020-01626-9

79

Homeopathy

- No research in lactation
- Common uses
  - Phytolacca 30 C for early mastitis or plugged ducts
  - Conium for breast pain
  - Chamomilla for teething
  - Byronia for engorgement
  - Pulsatilla for oversupply

80

Homeopathy

- Reducing the milk supply:
  - lac caninum 30C
  - Pulsatilla 30C
  - Ricinus communis 30C
  - The typical dose is five pellets sublingually 2-3 times a day, until a decrease in milk supply is noticed, then as needed.

Eglash A. Treatment of maternal hypergalactia. Breastfeed Med. 2014 Nov;9(9):423-5.

81

Herbs

82

Herbs to Avoid

- Aloe vera latex (not juice) (*Aloe* spp.)
- Black cohosh (*Actaea racemosa*)
- Bladderwrack (*Fucus vesiculosus*)
- Blue cohosh (*Caulophyllum thalictroides*)
- Borage (*Borago officinalis*)
- Buckthorn fruit (*Rhamnus cathartica*)
- Bugleweed leaf (*Lycopus* spp)
- Cinchona bark (*Cinchona* spp)
- Cola seeds (*Cola nitida*)
- Coltsfoot leaf (*Tussilago farfara*)
- Comfrey leaf/root (*Symphytum officinale*)

83

Herbs to Avoid

- Ephedra (*Ephedra* spp.)
- Guarana (*Paullinia cupana*)
- Jasmine flowers (*Jasminum pubescens*)
- Kava (*Piper methysticum*)
- Madder root (*Rubia tinctorum*)
- Ma Huang (*Ephedra sinica*)
- Pulsatilla (*Anemone pulsatilla*)
- Queen of the Meadow root/herb (*Eupatorium purpureum*)
- Senecio (*Senecio aureus*)
- Wormwood herb (*Artemesia absinthium*)

(List courtesy of Dr. T. LowDog)

84

Galactagogues

- Fenugreek (*Trigonella foenum-graecum*)
  - FDA lists it as GRAS (generally recognized as safe).
  - 1-4 capsules (580-610mg) 3-4 times daily
  - It can also be taken as a tea of ¼ tsp seeds steeped in 8oz of water for 10 minutes, taken 3 times daily.
  - Fiber -> GI upset
  - Maple syrup smell
  - Lowers blood sugar

85

Galactagogues

- Fenugreek (*Trigonella foenum-graecum*)
  - Cross-allergy with ragweed
  - Available studies are poor quality, and there is likely significant placebo effect
  - Not generally recommended

Brodribb W. ABM Clinical Protocol #9: Use of Galactogogues in Initiating or Augmenting Maternal Milk Production, Second Revision 2018. Breastfeed Med. 2018 Jun;13(5):307-314.

86

Galactagogues

- Goat's Rue (*Glaega officinalis*)
  - Widely used as a galactagogue in Europe based on the observation that it increased milk supply in cattle in the early 1900's.
  - No human trials for effectiveness have been done
  - May cause hypoglycemia

Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Goat's Rue. 2020 Aug 17.

87

Galactagogues

- Goat's Rue (*Glaega officinalis*)
  - Usually used as a tea. 1 tsp dried leaves steeped in 8oz of water for 10 minutes taken 2-3 times daily.
  - Also available in tincture or capsule form

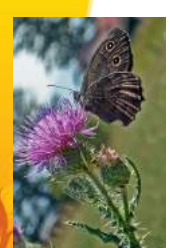
88

Galactagogues

- Blessed Thistle (*Cnicus benedictus*)
  - Tincture of leaves, twenty drops 2-4 times daily
- Borage leaves *(Borago officinalis)*:
  - Do not use!
  - pyrrolizidine alkaloids
  - hepatotoxins, which readily Pass into the breastmilk

89

Galactagogues



- Milk Thistle (*Silybum marianum*)
  - Best known for its liver-protecting effects, has been used for lactation for centuries.
  - Research on effectiveness is inconclusive
  - CYP2C9 inhibitor, so may increase drug levels
  - Cross-allergy aster family, such as daisies, artichokes, common thistle, and kiwi

90

Galactagogues

- Milk Thistle (*Silybum marianum*)
  - The tea is prepared by simmering one teaspoon crushed seeds in 8 oz of water for 10 minutes.
  - The dose is 1-3 cups daily or 1-3 grams of the ground seeds in capsule form.
  - (Note that this is not the standardized extract typically used for liver disorders.)

Brodribb W. ABM Clinical Protocol #9: Use of Galactogogues in Initiating or Augmenting Maternal Milk Production, Second Revision 2018. Breastfeed Med. 2018 Jun;13(5):307-314.

91

Galactagogues

- Wild Asparagus (*Asparagus racemosus*)
  - Roots, also known as shatavari
  - Ayurvedic tradition to increase milk production in lactating women.
  - Shatavari Kalpa, a combination of wild asparagus root and cardamom.
  - RCT of A. racemosus in women with insufficient milk supply failed to find any effect on milk production or prolactin levels.

Sharma S, Ramji S, Kumari S, Bapna JS. Randomized controlled trial of Asparagus racemosus (Shatavari) as a lactogogue in lactational inadequacy. Indian Pediatr. 1996 Aug;33(8):675-7.

92

Galactagogues

- Wild Asparagus (*Asparagus racemosus*)
  - Generally recognized as safe (GRAS) by the US FDA
  - The dose is 1 gram powdered root per day taken in milk or juice.

93

Galactagogues

- Moringa (*Moringa oleifera*)
  - From Philippines where it is called malunggay
  - Used as a food
  - Anti-inflammatory
  - May have galactagogue effect per two small studies
  - Dosed as 2 capsules three times daily

Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Moringa. 2018 Dec 3.

94

Galactagogues

- Torbangun (*Plectranthus amboinicus*)
  - Indonesia
  - “Boob food”
  - One study showed positive benefits

Rizal Damanik, Mark L Wahlqvist, and N. Wattanapenpaiboon (2006). “Lactagogue effects of Torbangun, a Bataknese traditional cuisine”. Asian Pacific Journal of Clinical Nutrition. Vol. 15 (2):267-274.

95

Galactagogues

- Fennel/Barley Water
- Steel cut oats
- Hops: Beer is a convenient source. Can also use tea or infusion. GRAS. Data is mixed.

Drugs and Lactation Database (LactMed) [Internet]. Bethesda (MD): National Library of Medicine (US); 2006–. Hops. 2018 Dec 3.

96

Hyperlactation

- Sage (*Salvia officinalis*)
  - Steeping 1–3 g of dried sage leaves in a cup of hot water.
  - Repeat every 12 hrs for 3 days if tolerated
  - Side effects in high doses, including nausea, vomiting, and dizziness

Eglash A. Treatment of maternal hypergalactia. Breastfeed Med. 2014;9(9):423-425. doi:10.1089/bfm.2014.0133

97

Hyperlactation

- Other plants that may reduce supply:
  - Peppermint
  - Parsely
  - Jasmine
  - Chastetree Berry (doses >150 mg)

Eglash A. Treatment of maternal hypergalactia. Breastfeed Med. 2014;9(9):423-425. doi:10.1089/bfm.2014.0133

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Thank You

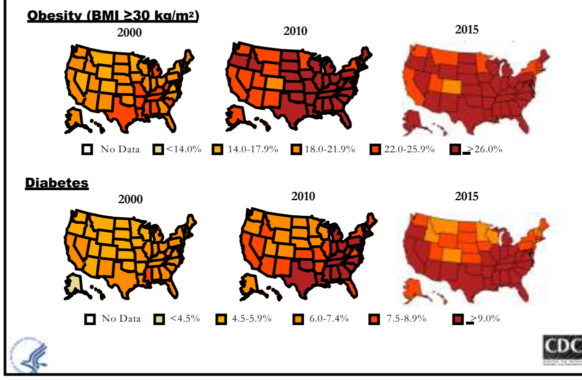
99

The Effects of Exercise on Human Milk

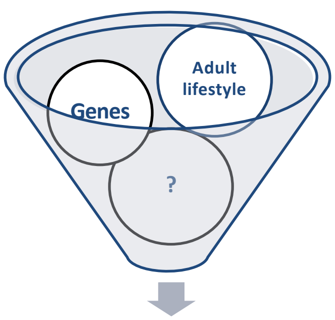
Kristin I. Stanford, Ph.D.
January 23, 2021

The Ohio State University
Wexner Medical Center

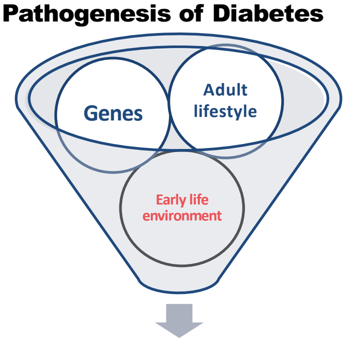
Age-Adjusted Prevalence of Obesity and Diagnosed Diabetes Among U.S. Adults Aged 18 Years or older



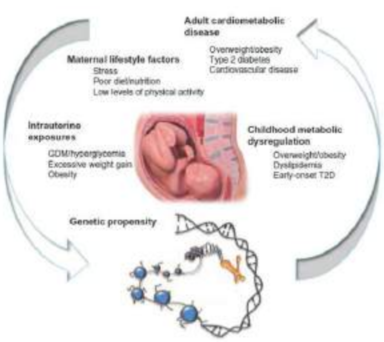
Pathogenesis of Diabetes



Pathogenesis of Diabetes

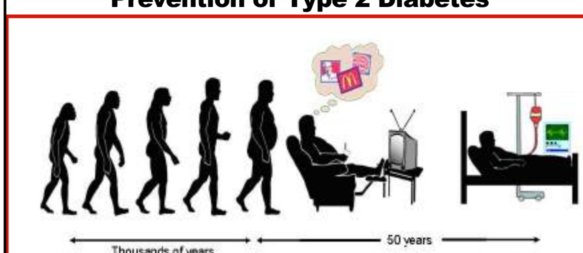


Early Life Environment



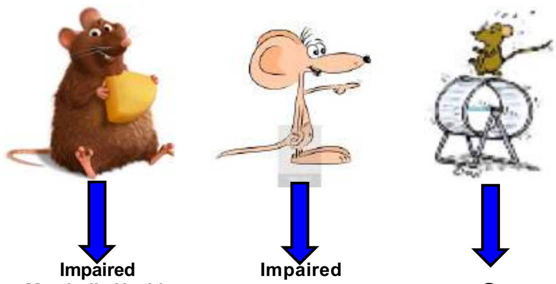
Venu L, et al. Obesity , 2008; 16:1270-1276.

Exercise is Critical in the Prevention of Type 2 Diabetes



- Inactivity is a major factor leading to increased rates of type 2 diabetes and obesity.
- Physical exercise is essential in the treatment and prevention of type 2 diabetes and obesity.

Maternal Lifestyle Affects Offspring Metabolic Health



Overall Hypothesis:

- Maternal physical activity before and during pregnancy will improve the metabolic phenotype of offspring.

Outline

- Maternal exercise before and during pregnancy improves the metabolic health of male and female offspring.
- Which tissue is responsible for improvements in metabolic health of offspring after maternal exercise?
- Maternal exercise improves metabolic health of offspring through adaptations to milk.

Outline

- Maternal exercise before and during pregnancy improves the metabolic health of male and female offspring.
- Which tissue is responsible for improvements in metabolic health of offspring after maternal exercise?
- Maternal exercise improves metabolic health of offspring through adaptations to milk.

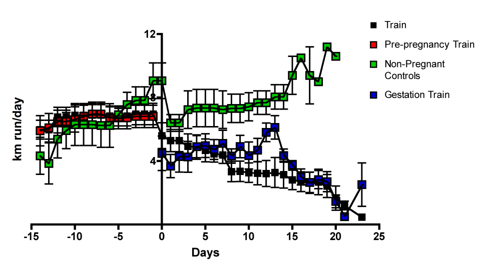
Maternal Training Paradigm

	Pre-Conception (2 wks)	Breeding (3 days)	Gestation (3 wks)
Sedentary	Sedentary	Breeding	Sedentary
Train	Train	Breeding	Train
Pre-Pregnancy Train	Train	Breeding	Sedentary
Gestation Train	Sedentary	Breeding	Train

- All dams were C57BL/6 virgin females.
- All dams were chow fed (20% kcal from fat).
- All sires were sedentary and chow-fed.

Stanford et. al, *Diabetes*, 2015

Effects of Pregnancy of Wheel Running Distance



Stanford et al. *Diabetes* 2015

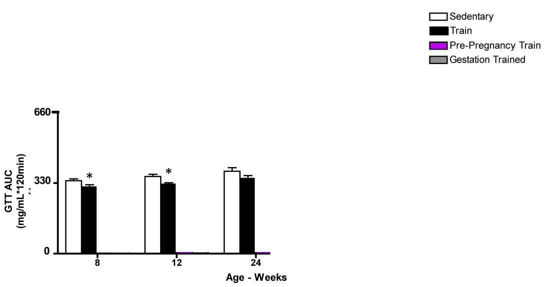
What is the effect of maternal exercise on metabolic health of offspring?

Does the timing of maternal exercise play a role in metabolic health of offspring?

Experimental Design

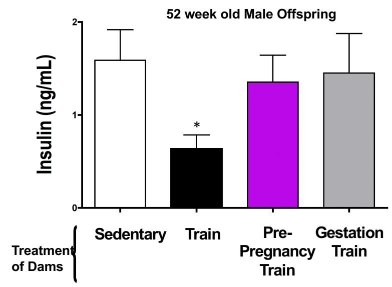
- Offspring were sedentary and chow-fed
- Offspring metabolic health monitored at 8, 12, 24, 36, and 52 weeks of age
- Data presented in male and female offspring

Maternal Exercise Improves Glucose Tolerance in Adult *Male* Offspring



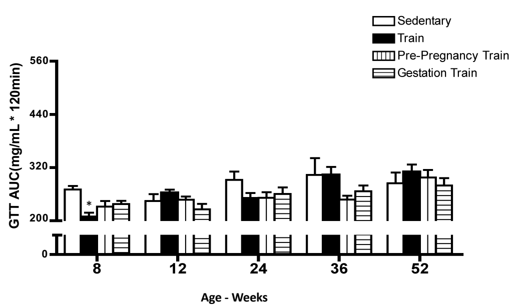
Stanford et al. *Diabetes* 2015

Male Offspring from Trained Dams Have Decreased Plasma Insulin Concentrations



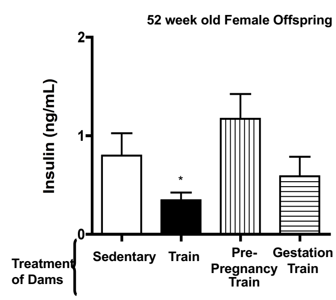
Stanford et al. *Diabetes* 2015

Maternal Exercise Does Not Alter Glucose Tolerance in Adult *Female* Offspring



Stanford et. al, *Diabetes*, 2017

Female Offspring of Trained Dams Have Decreased Plasma Insulin Concentrations



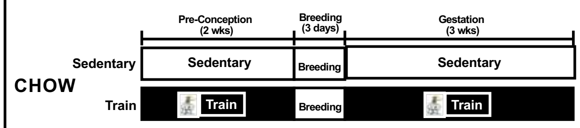
Stanford et. al, *Diabetes*, 2017

Maternal Exercise Before and During Pregnancy Improves Whole-Body Glucose Homeostasis in Offspring

- Improved glucose tolerance in male offspring
- Decreased fasting insulin in male and female offspring
- Critical to exercise both before AND during pregnancy.

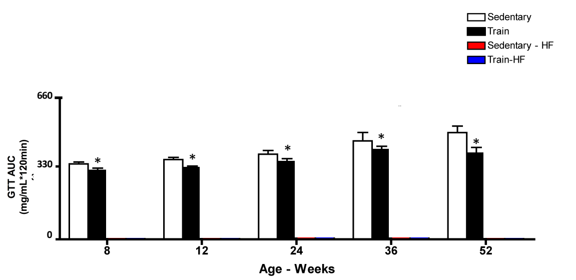
Does maternal exercise protect against the detrimental effects of a maternal high fat diet?

Maternal Training Paradigm



- Dams were either chow (20% kcal from fat) or high-fat (60% kcal from fat) fed
- Offspring were sedentary and chow-fed

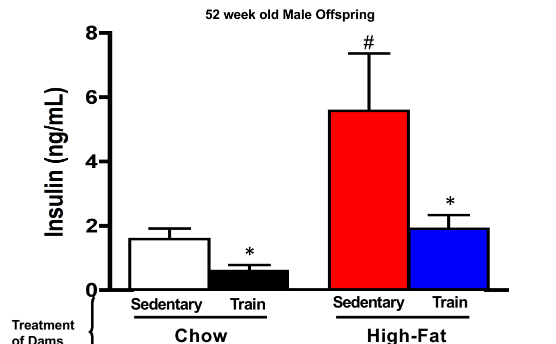
Maternal Exercise Improves Glucose Tolerance in Adult *Male* Offspring



- Maternal exercise negates the detrimental effects of a maternal high-fat diet.

Stanford et al. *Diabetes* 2015

Maternal Exercise Decreases Fasting Insulin in Adult Male Offspring

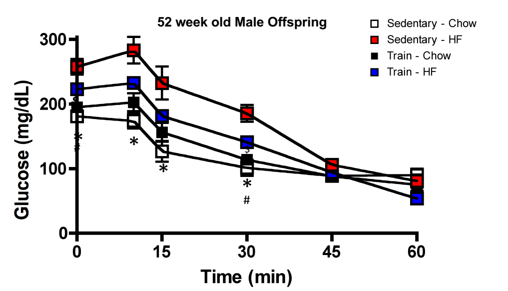


Stanford et al. *Diabetes* 2015

Maternal Exercise Decreases Body Weight in *Male* Offspring

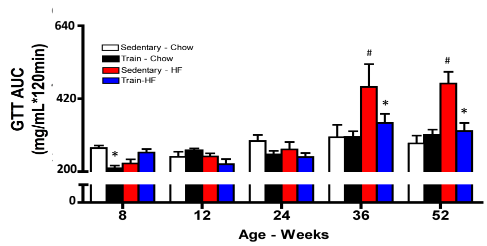
Stanford et al. *Diabetes* 2015

Maternal Exercise Negates the Effects of a Maternal High-Fat Diet on Insulin Tolerance in Male Offspring



Stanford et al. *Diabetes* 2015

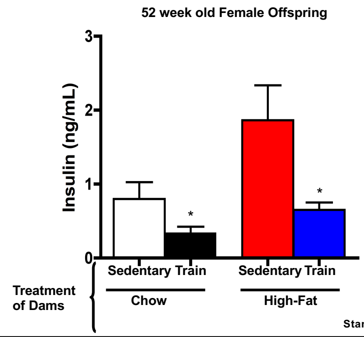
Maternal Exercise Improves Glucose Tolerance in Adult *Female* Offspring



- Maternal exercise negates the detrimental effects of a maternal high-fat diet.

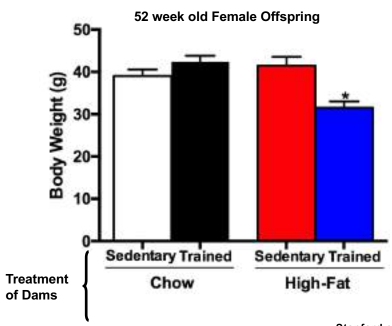
Stanford et al. *Diabetes* 2017

Maternal Exercise Decreases Fasting Insulin in Adult Female Offspring



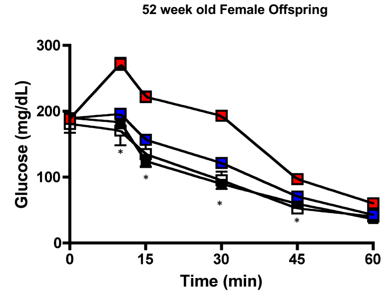
Stanford et al. *Diabetes* 2017

Maternal Exercise Decreases Body Weight in Adult Female Offspring



Stanford et al. *Diabetes* 2017

Maternal Exercise Negates the Effects of a Maternal High-Fat Diet on Insulin Tolerance in Female Offspring



Stanford et al. *Diabetes* 2017

No Effect of Maternal Exercise on Serum Lipid Concentrations Among Offspring

- Serum triglyceride
- Serum cholesterol
- Serum FFA
- Food intake in offspring (months 6-12)

Summary I: Maternal Exercise Improves Whole-Body Glucose Homeostasis in Adult Offspring

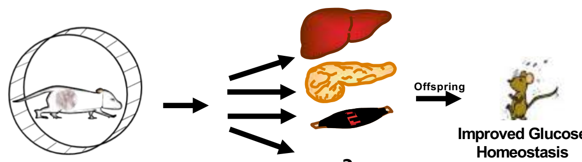
- Improved glucose tolerance
- Decreased fasting insulin
- Decreased body weight
- Decreased % body fat
- Improved insulin sensitivity
- Necessary to exercise before and during pregnancy to observe metabolic improvements
- In female offspring, exercise-induced improvements only present in when dams are fed a high-fat diet.
- Maternal exercise negates the detrimental effects of a maternal high-fat diet

What is the mechanism for this improvement?

Outline

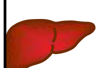
- Maternal exercise before and during pregnancy improves the metabolic health of male and female offspring.
- **Which tissue is responsible for improvements in metabolic health of offspring after maternal exercise?**
- Maternal exercise improves metabolic health of offspring through adaptations to milk.

Which Tissue is Responsible for Improved Glucose Homeostasis in Offspring after Maternal Exercise?



Which Tissue is Responsible for Improved Glucose Homeostasis in Offspring after Maternal Exercise?

- Tissue most likely to be affected by exercise is skeletal muscle.
- Previous studies have indicated that maternal exercise improves skeletal muscle insulin sensitivity and PGC1α expression. (Carter et al, MSSE 2013; Laker et al., Diabetes 2014)



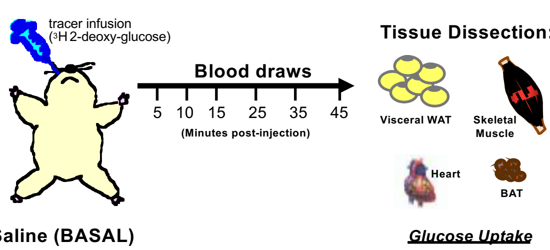
- Previous studies have shown that a maternal high-fat diet results in fatty liver in the offspring and increased expression of gluconeogenic genes (in rodents and non-human primates). (McCurdy et al, JCI, 2009)

- Decreased circulating insulin in offspring from exercise-trained dams, regardless of maternal diet.

What Tissue is Responsible for Improved Glucose Homeostasis in Offspring after Maternal Exercise?

- *In vivo* glucose uptake
- Metabolic characterization of the liver
- Physiological measurements of pancreas

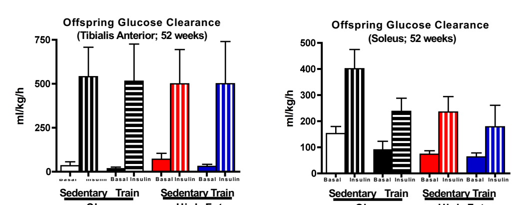
Glucose Uptake in Multiple Tissues *in vivo*



Saline (BASAL)
Insulin (16.6 units/kg BW)

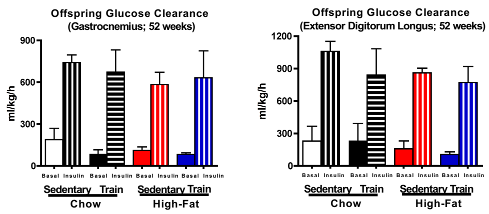
- These experiments were performed in male mice.

Maternal Exercise Did Not Alter Skeletal Muscle Glucose Clearance



Stanford et al. *Diabetes* 2015

Maternal Exercise Did Not Alter Skeletal Muscle Glucose Clearance

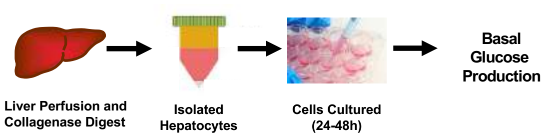


- Maternal exercise does not affect skeletal muscle glucose uptake in offspring

Stanford et al. *Diabetes* 2015

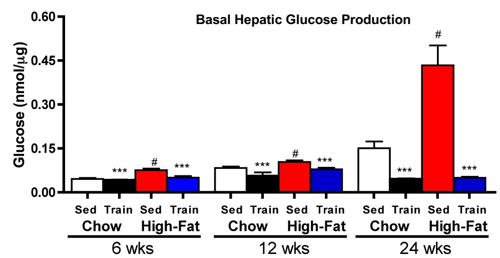
Does Maternal Exercise Affect Hepatic Glucose Production?

Glucose Production in Isolated Hepatocytes



- This was performed at 6, 12, and 24wks of age.

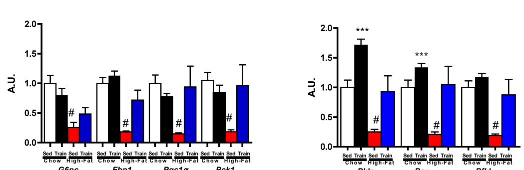
Maternal Exercise Decreases Hepatic Glucose Production in Isolated Hepatocytes



- These experiments were performed in both male and female mice.

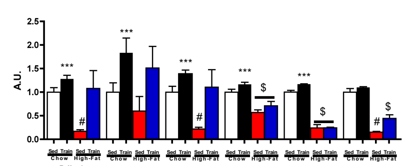
Stanford et al. *Diabetes* 2017

Maternal High-Fat Diet Alters Hepatic Gene Expression; Maternal Exercise Restores



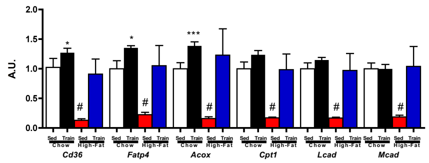
Stanford et al. *Diabetes* 2017

Maternal High-Fat Diet Decreases Expression of Krebs Cycle Enzymes; Maternal Exercise Restores



Stanford et al. *Diabetes* 2017

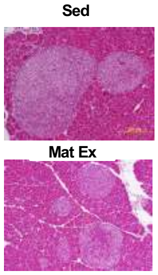
Maternal High-Fat Diet Decreases Expression of Genes Involved in Fatty Acid Oxidation; Maternal Exercise Restores

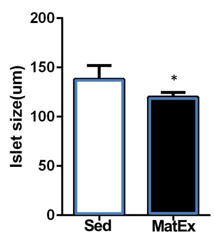


Stanford et al. *Diabetes* 2017

Does Maternal Exercise Affect Insulin Secretion?

Maternal Exercise Decreases Islets Size in Offspring

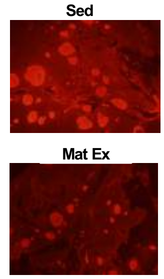


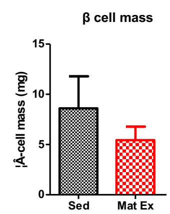


➢ These experiments were performed in male mice from high-fat fed dams.

Zheng et al. *BMJ Open Diabetes Res Care*, 2020

Offspring from Trained Dams Have Decreased Insulin-positive Area and β Cell Mass

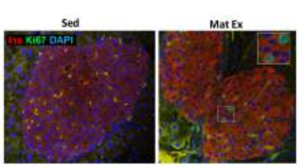


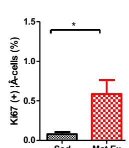


Insulin IF staining
Microscope: ×4

Zheng et al. *BMJ Open Diabetes Res Care*, 2020

Higher β Cell Proliferation in Offspring from Trained Dams



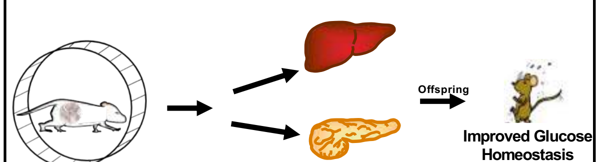


➢ Male offspring from high-fat fed, exercise-trained dams have decreased islet size, decreased insulin positive area, and increased β cell proliferation.

Zheng et al. *BMJ Open Diabetes Res Care*, 2020

Summary II

➢ Maternal exercise improves metabolic health and insulin sensitivity through adaptations to the liver and the pancreas.
➢ The primary mechanism responsible for this improvement is a topic of ongoing investigation.



Outline

- Maternal exercise before and during pregnancy improves the metabolic health of male and female offspring.
- Which tissue is responsible for improvements in metabolic health of offspring after maternal exercise?
- Maternal exercise improves metabolic health of offspring through adaptations to milk.

How Does Maternal Exercise Improve Metabolic Health of Offspring?

- Does maternal exercise alter the metabolome in offspring?
- Are there epigenetic changes (i.e egg, placenta) that could be responsible for the improvements in metabolic health of the offspring?
- Is milk affected by maternal exercise, and could that affect offspring health?

How Does Maternal Exercise Improve Metabolic Health of Offspring?

- Does parental exercise alter the metabolome in offspring?
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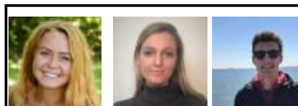
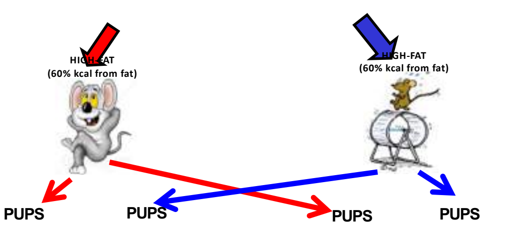


Kelsey Pinckard Katherine Wright Johan Harris

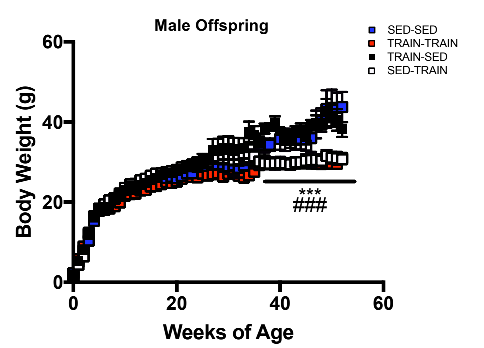
Could exercise-induced changes to milk alter the metabolic health of offspring?

Cross-Foster Offspring



- Pregnancies were timed so litters dropped on same date.
- 24h after birth, cross-fostered sedentary litters were "swapped" with trained litters.
- Offspring nursed with "foster" moms until weaning.

Male Offspring that Nursed with High-Fat Fed Trained Dams had Decreased Body Weight



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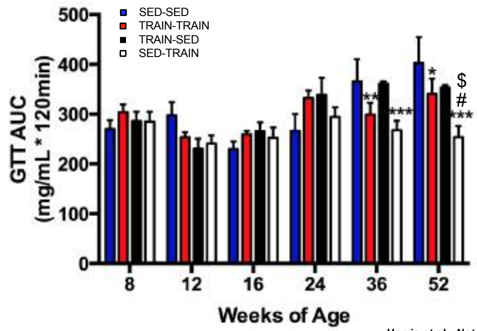
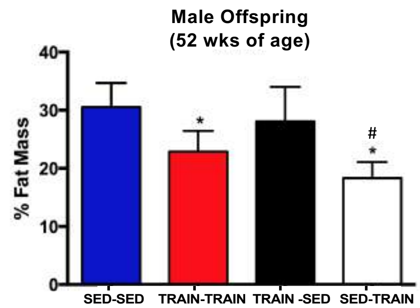
Harris et al., *Nat Metab*, 2020

Milk From Exercise-Trained Dams Improves Glucose Tolerance in Adult Male Offspring



Harris et al., *Nat Metab*, 2020

Male Offspring that Nursed with High-Fat Fed Trained Dams had Decreased % Fat Mass

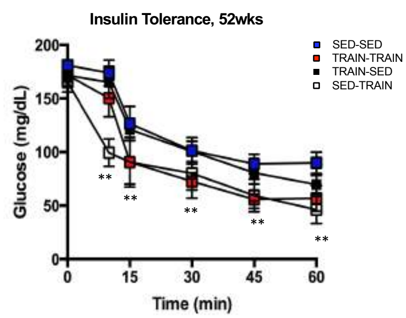


Harris et al., *Nat Metab*, 2020

Male Offspring that Nursed with High-Fat Fed Trained Dams had Decreased Insulin

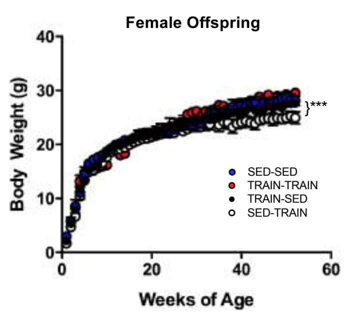
Harris et al., *Nat Metab*, 2020

Male Offspring that Nursed with High-Fat Fed Trained Dams had Improved Insulin Tolerance



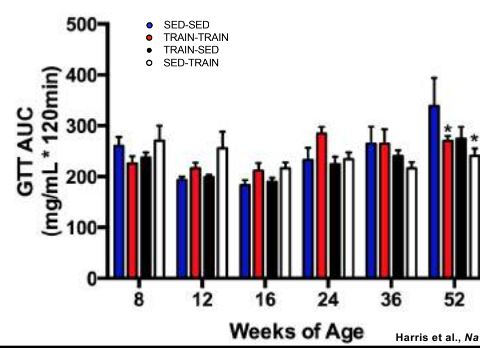
Harris et al., *Nat Metab*, 2020

Female Offspring that Nursed with High-Fat Fed Trained Dams had Decreased Body Weight



Harris et al., *Nat Metab*, 2020

Milk From Exercise-Trained Dams Improves Glucose Tolerance in Adult Female Offspring

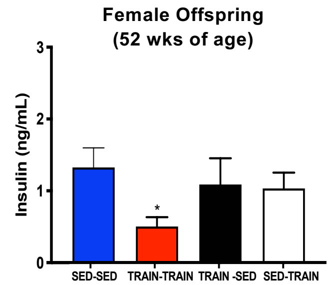


Harris et al., *Nat Metab*, 2020

Female Offspring that Nursed with High-Fat Fed Trained Dams had Decreased % Fat Mass

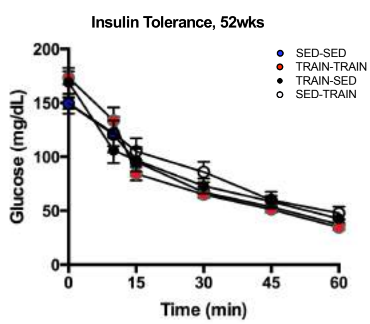
Harris et al., *Nat Metab*, 2020

Female Offspring From High-Fat Fed Trained Dams had Decreased Fasting Insulin



Harris et al., *Nat Metab*, 2020

No Change in Insulin Tolerance in Female Offspring that Nursed with High-Fat Fed Trained Dams



Harris et al., *Nat Metab*, 2020

Summary III

- Consumption of milk from exercise-trained dams improves metabolic health of offspring, regardless of maternal phenotype.

How does maternal exercise alter the composition of milk to improve metabolic health of offspring?

Lars Bode, Ph.D.

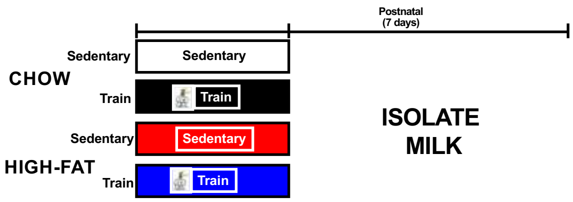
Does Maternal Exercise Alter the Composition of Breast Milk?

Human Milk Oligosaccharides in Breastmilk

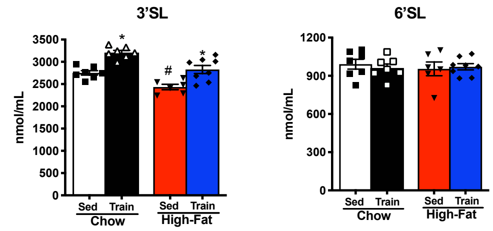
- Studies have indicated that exercise reduces the fat content of milk (in humans and rodents), but the effects of exercise on the composition of the milk has not been investigated.
- Human milk oligosaccharides (HMO) account for 5-15% of human milk, while only comprise 0.5-5% of bovine milk.
- HMO structure varies; milk can contain 23-130 different oligosaccharides. The functional impact of this diversity, as well as how it is regulated (i.e. diet, exercise, age) are unknown.
- A role for milk oligosaccharides in metabolism has not been investigated.

Does Maternal Exercise Alter the HMO Content of Milk?

- Isolated milk, performed HPLC to identify HMOs altered in response to diet and exercise in rodents.



Maternal Exercise Increased 3'Siallylactose (3'SL) Content in Milk; High-Fat Diet Decreased 3'SL Content.

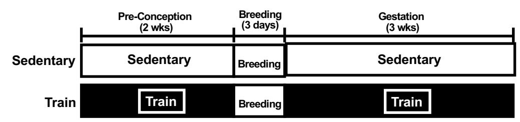


- 3'-SL is the dominant sialylated milk oligosaccharide in human milk, and is the predominant oligosaccharide in mouse milk, accounting for 90–95% of the HMO content.

Harris et al., *Nat Metab*, 2020

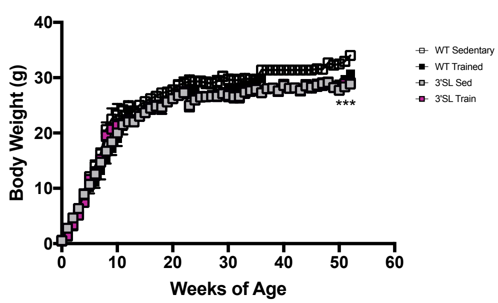
Is 3'SL the Predominant Component Responsible for the Improved Metabolic Health in Offspring from Exercise-Trained Dams?

Maternal Training Paradigm



- Dams were either wild-type or St3Gal4 knockout (*3'SL*$^{-/-}$)
- Dams were exercise-trained on a treadmill; 40min/day at 0.8mph, 10% incline, 5 days/week
- Dams were chow-fed (20% kcal from fat)
- Offspring were sedentary and chow-fed

Maternal Exercise in *3'SL*$^{-/-}$ Mice Does Not Affect Body Weight in Male Offspring



- *3'SL*$^{-/-}$ mice had lower body weight than WT mice.

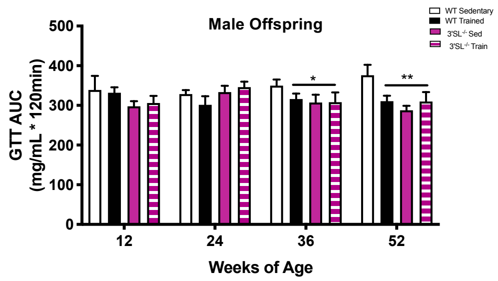
Harris et al., *Nat Metab*, 2020

Maternal Exercise in *3'SL*$^{-/-}$ Mice Does Not Affect % Fat Mass in Male Offspring

- *3'SL*$^{-/-}$ mice had lower % fat mass than WT mice.

Harris et al., *Nat Metab*, 2020

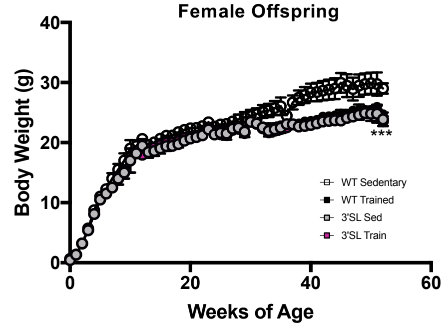
Maternal Exercise in *3'SL^-/-^* Mice Does Not Affect Glucose Tolerance in Male Offspring



- *3'SL-/-* mice are more glucose tolerant than WT mice.

Harris et al., *Nat Metab*, 2020

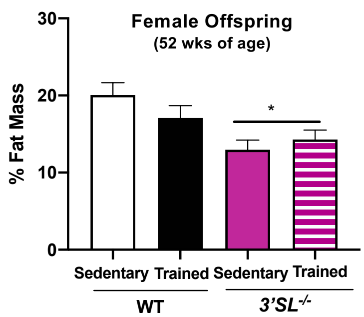
Maternal Exercise in *3'SL-/-* Mice Does Not Affect Body Weight in Female Offspring



- *3'SL-/-* mice had lower body weight than WT mice.

Harris et al., *Nat Metab*, 2020

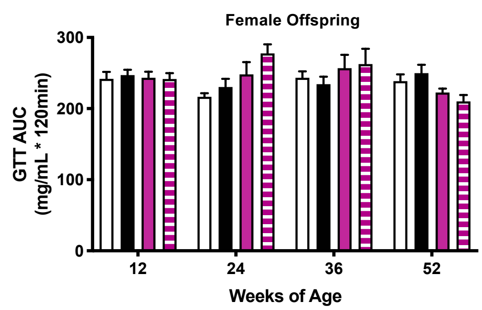
Maternal Exercise in *3'SL-/-* Mice Does Not Affect % Fat Mass in Female Offspring



- *3'SL-/-* mice had lower % fat mass than WT mice.

Harris et al., *Nat Metab*, 2020

Maternal Exercise in *3'SL-/-* Mice Does Not Affect Glucose Tolerance in Female Offspring



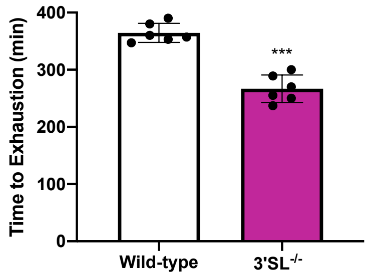
Harris et al., *Nat Metab*, 2020

Summary IV

- Forced maternal exercise improved metabolic health of male offspring from WT dams.
- The beneficial effects of maternal exercise were lost in offspring from *3'SL-/-* dams.
- Importantly, *3'SL-/-* mice were leaner and had improved glucose tolerance compared to WT mice.

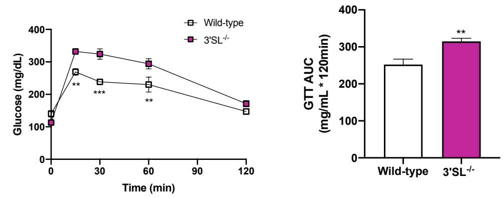
Do *3'SL-/-* mice have an impaired baseline metabolic phenotype?

*3'SL^-/-^* Mice have Impaired Exercise Capacity



Harris et al., *Nat Metab*, 2020

*3'SL^-/-^* Mice have Impaired Glucose Tolerance Per Lean Mass



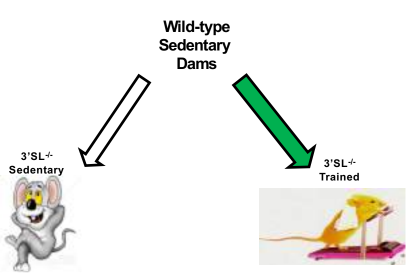
Harris et al., *Nat Metab*, 2020

Summary IV

- Forced maternal exercise improved metabolic health of male offspring from WT dams.
- The beneficial effects of maternal exercise were lost in offspring from *3'SL^-/-^* dams.
- Importantly, *3'SL^-/-^* mice had an altered baseline phenotype.
- *3'SL^-/-^* mice have reduced exercise capacity and impaired glucose tolerance, suggesting undefined metabolic impairments in this mouse model.

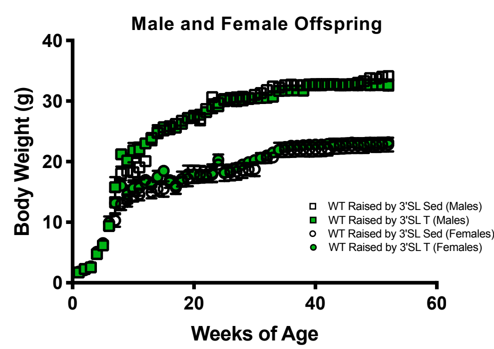
Determine if 3'SL is the Critical Mediator for the Beneficial Effects of Maternal Exercise

Cross-Foster Offspring



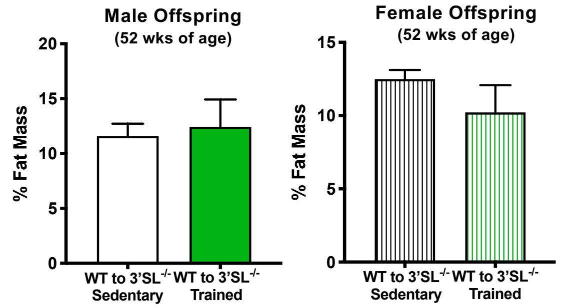
- Pregnancies were timed so litters dropped on same date.
- 24h after birth, cross-fostered sedentary litters were "swapped" with trained litters.
- Offspring nursed with "foster" moms until weaning.

Milk From Exercise-Trained *3'SL^-/-^* Dams Does Not Affect Body Weight in Offspring



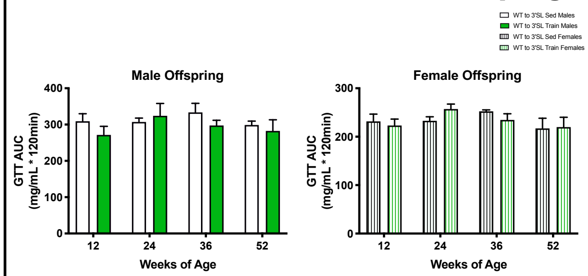
Harris et al., *Nat Metab*, 2020

Milk From Exercise-Trained *$3'SL^{-/-}$* Dams Does Not Affect % Fat Mass in Offspring



Harris et al., *Nat Metab*, 2020

Milk From Exercise-Trained *$3'SL^{-/-}$* Dams Does Not Affect Glucose Tolerance in Offspring



- In contrast to breastmilk from WT exercise-trained mice, breastmilk from exercise-trained, *$3'SL^{-/-}$* dams does not confer any beneficial effects to WT offspring.

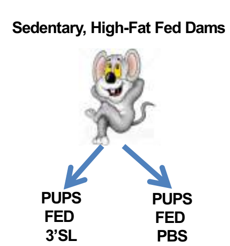
Harris et al., *Nat Metab*, 2020

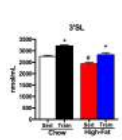
Summary V

- Breastmilk from exercise-trained *$3'SL^{-/-}$* dams does not confer any beneficial effects to WT offspring.
- These data indicate that 3'SL is critical to mediate beneficial effects of maternal exercise on offspring health.

Does supplementing 3'SL improve metabolic health of offspring?

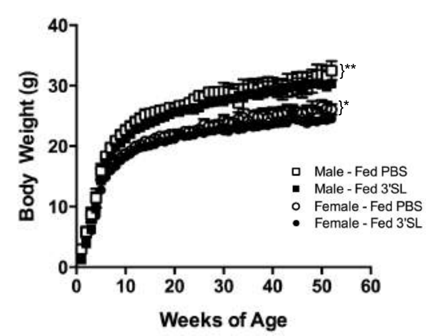
Does Increasing 3'SL in Offspring Improve Metabolic Health?





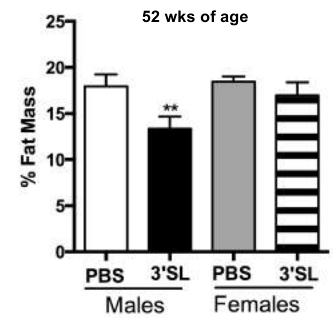
- Pups were fed 150nmol 3'SL/day on days 1-3.
- Pups were fed 300nmol 3'SL/day on days 4-6.
- Pups were fed 600nmol 3'SL/day on days 7-21.
- Control pups were fed with an equal volume of PBS.

Supplementation of 3'SL Decreases Body Weight in Male and Female Offspring



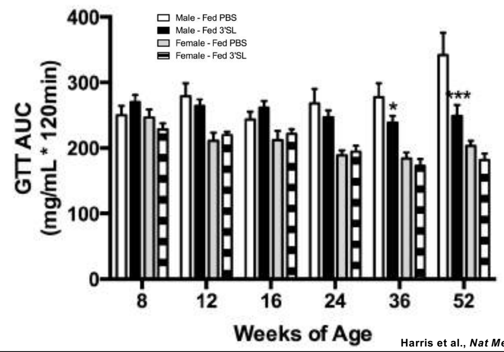
Harris et al., *Nat Metab*, 2020

Supplementation of 3'SL Decreased Fat Mass in Male Offspring



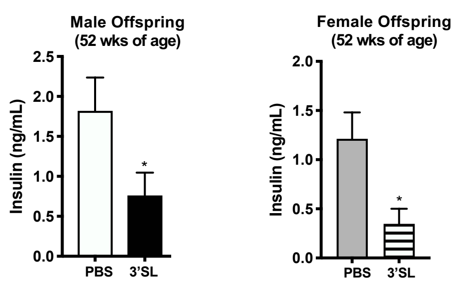
Harris et al., *Nat Metab*, 2020

Supplementation of 3'SL Improves Glucose Tolerance in Adult Male Offspring



Harris et al., *Nat Metab*, 2020

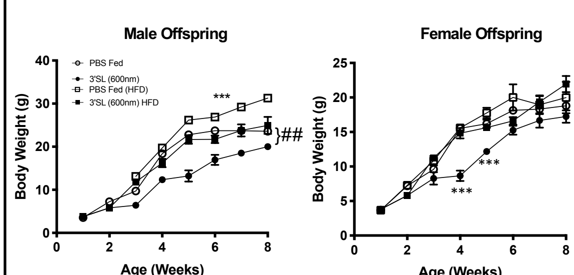
Supplementation of 3'SL Reduces Fasting Insulin in Male and Female Offspring



Harris et al., *Nat Metab*, 2020

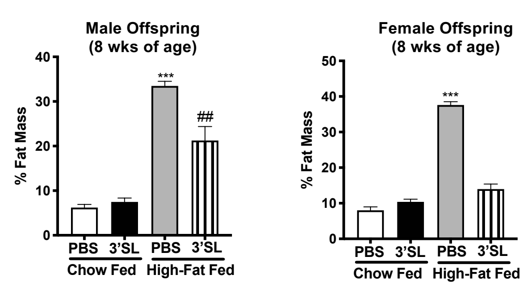
Does supplementation of 3'SL protects against the detrimental effects of a high-fat diet?

Supplementation of 3'SL Protects Against the Detrimental Effects of a High-Fat Diet on Body Weight



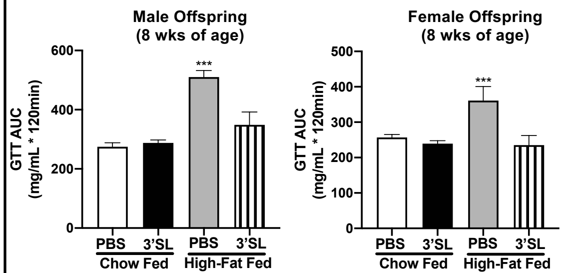
Harris et al., *Nat Metab*, 2020

Supplementation of 3'SL Protects Against the Detrimental Effects of a High-Fat Diet on Fat Mass



Harris et al., *Nat Metab*, 2020

Supplementation of 3'SL Protects Against the Detrimental Effects of a High-Fat Diet on Glucose Tolerance



Harris et al., *Nat Metab*, 2020

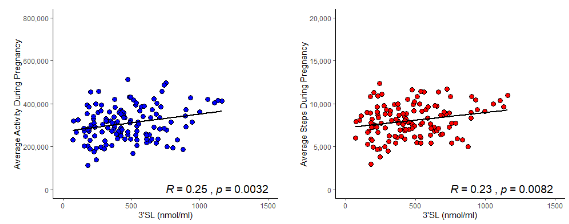
Summary VI

- Supplementation of a physiological dose of 3'SL during the nursing period improves glucose metabolism and decreases body weight in adult male offspring.
- Supplementation of a physiological dose of 3'SL during the nursing period decreases fasting insulin in adult male and female offspring.
- Supplementation of a physiological dose of 3'SL protects against the detrimental effects of a high-fat diet on body weight, fat mass, and glucose tolerance.

Aline Andres, Ph.D.

Does Maternal Exercise Affect 3'SL in Humans?

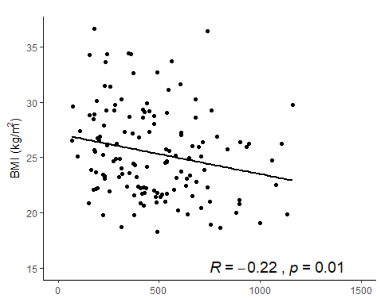
Maternal Physical Activity throughout Pregnancy is Correlated to Increased 3'SL



- 3'SL was the only HMO that was increased with maternal physical activity.

Harris et al., *Nat Metab*, 2020

Maternal BMI is Negatively Correlated to 3'SL



Harris et al., *Nat Metab*, 2020

Summary VII

- Maternal physical activity is positively correlated with 3'SL in humans, and BMI is negatively correlated with 3'SL.
- Future studies will look at a true exercise effect on HMOs in humans.

Conclusions

- Maternal exercise improves metabolic health of offspring.
- Exercise alters the HMO composition of milk; this may provide a mechanism for metabolic improvements in a maternal exercise model.
- These findings, if translated to humans, will have enormous implications for the prevention of obesity and type 2 diabetes.

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@kistanford6

Impact of early weight gain on odds for overweight at one year differs between breastfed and formula-fed infants

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Mia A. Papas PhD, Virginia Stallings MD, Julie A. Mennella PhD
Pediatric Obesity. 2020;1–10.

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Dare to be first. University of Delaware | Monell Center | The Children's Hospital of Philadelphia | Christiana Care Health System

2

Sensitive periods

- **Concept of 'sensitive periods' and 'programming' proposed 1980s/90s**
  - Significant association between premature birth/low birth weight and the occurrence of hypertension and coronary heart disease in adulthood (Barker 1986)
  - Preterm infants fed unfortified donor breast milk as a supplement to their mother's milk, had lower IQ later in life compared to infants who received preterm infant formula as a supplement to their mother's milk (Lucas 1990)

'Programming' or 'sensitive periods'—"a process whereby a stimulus or insult at a critical period of development, has lasting or lifelong significance"

(Lucas 1990, Lucas 1991, Barker 1986)

3

Sensitive periods

- **Infancy is recognized as a sensitive period when weight gain and diet program risk for later diseases** (Barker 1989 ,Lucas 1990 & 1991, Newhamn 2002, Koletzko 2009, Mihrshahi 2011)

4

Sensitive periods

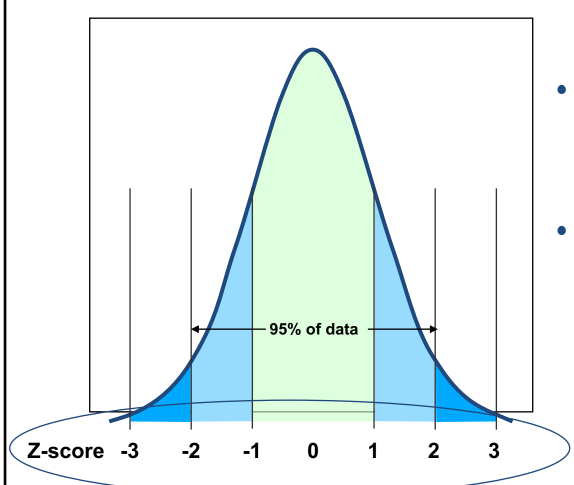
- **Infancy is recognized as a sensitive period when weight gain and diet program risk for later diseases** (Barker 1989 ,Lucas 1990 & 1991, Newhamn 2002, Koletzko 2009, Mihrshahi 2011)

- **Evidence indicates that rapid weight gain (RWG) in infancy increases odds for obesity in child- and adulthood**
  - prospective and retrospective studies (Taveras 2009, Ong 2009, Ekelund 2008, Karaolis Danckert 2006, Stettler 2005, Toschke 2004, Melbin1976)
  - systematic reviews (Monteiro 2005, Ong 2006)
  - meta-analyses (Druet 2012, Weng 2012)

5

RWG can be defined in terms of Z-scores

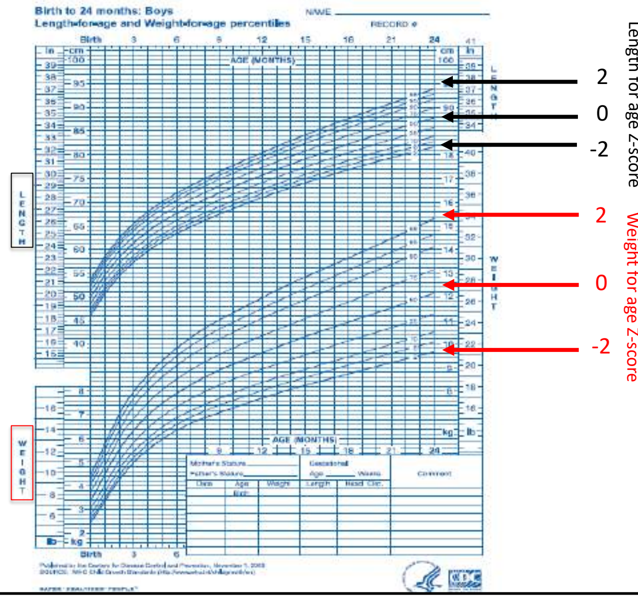
Z-scores are used to assess growth in infants and children



- Z-score represents the deviation of a measurement from the reference group mean
- Nearly all infants (95%) of infants in a population should fall somewhere between -2.0 and +2.0 Z-score

6

Weight for age and Length for age



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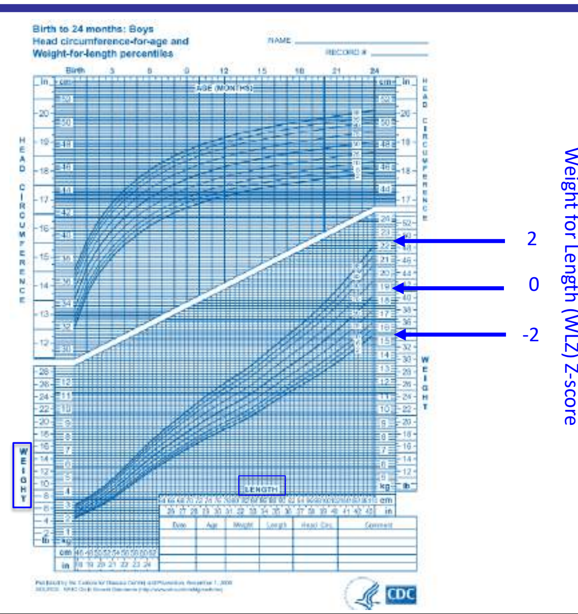
Weight for length (similar to BMI)



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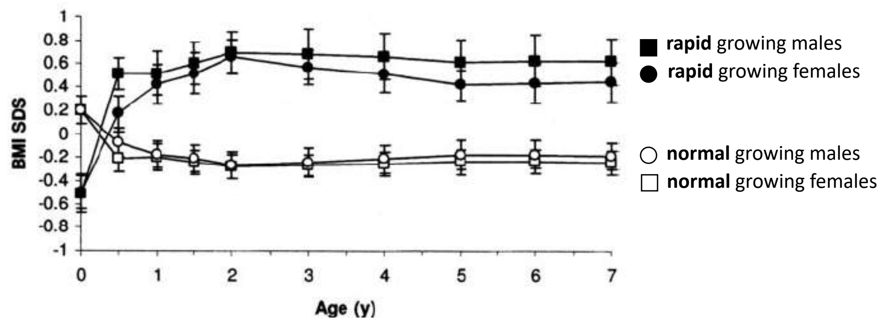
Infants with RWG often achieve a higher BMI - which can track from infancy into childhood

rapid = weight z-score increase > 0.67 (from 0 to 6 months)
normal = weight z-score increase $\leq$ 0.67 (from 0 to 6 months)



Karaolis-Danckert et al, AJCN 2006

9

What an infant is fed, affects health outcomes

One of the largest differentiators of diet in infancy is:

- **Human milk (HM) fed versus infant formula (IF) fed**

- **HM is the preferred source of nutrition during the first year of life**
  (American Academy of Pediatrics, World Health Organization, European Society for Gastroenterology, Hepatology, and Nutrition)

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Human milk (HM) confers health benefits to the infant

- **Nutritional composition**
  - HM is rich in high quality proteins; high nutrient bioavailability
  - HM contains whey proteins lactoferrin, lysozymes, and immunoglobulin are involved in host defense; they resist proteolytic digestion, and serve as first line of defense by lining the gastrointestinal tract
- **Gastrointestinal function**
  - HM contains growth factors that are thought to stimulate gastrointestinal growth and enhance maturity of the gastrointestinal tract

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Human milk (HM) confers health benefits to the infant

- **Host defense (immunology)**
  - HM contains IgA which provides passive immunity from mother to infant
    - reduction in gastrointestinal and respiratory diseases (such as influenza, wheezing) and otitis media has been observed in breastfed infants
- **Psychosocial**
  - Facilitates mother-infant bonding

When an infant is not/cannot be breastfed,
IF is considered the next best feeding alternative
(American Academy of Pediatrics, Academy of Nutrition and Dietetics, WHO)

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Millions of US infants receive infant formula (IF)

In combination with human milk or as a sole source of nutrition

CDC Breastfeeding Reportcard 2020

Breastfeeding in the US	Rate
Ever Breastfed	84.1%
Breastfeeding at 6 months	58.3%
Breastfeeding at 12 months	35.3%
*Exclusive breastfeeding at 3 months	46.9%
*Exclusive breastfeeding at 6 months	25.6%

[1]https://www.cdc.gov/breastfeeding/pdf/2020breastfeedingreportcard.pdf

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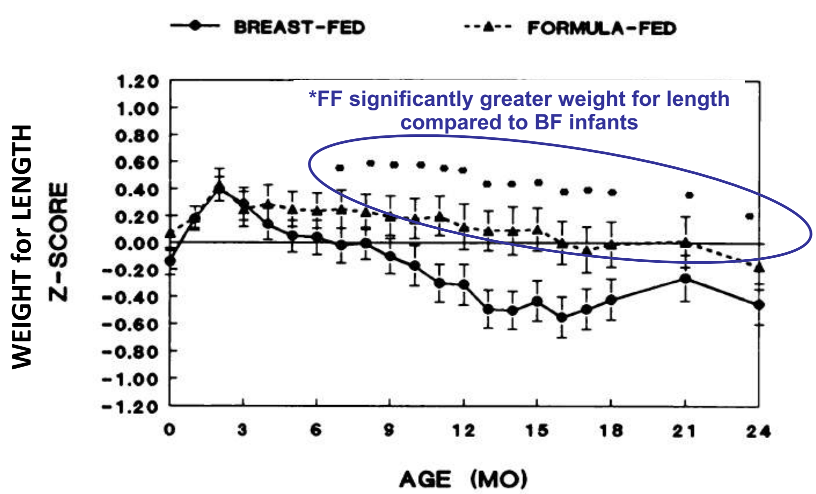
Differences in health outcomes in breastfed (BF) versus (FF) infants



Dewey KG, et al. The DARLING study. *Am J Clin Nutr*. 1993;57:140-5.

14

Numerous studies have found FF weigh more than BF infants by one year of age

- Koletzko et al (2009)
  - Europe:
  - 1138 infants
- Kramer et al (2004)
  - Republic of Belarus
  - 16,755 infants
- Agostoni et al (1990)
  - Italy
  - 119 infants
- Dewey et al (1993)
  - United States
  - 80 infants

FF infants as a group are 'bigger' than BF infants as a group [greater weight for age z-score (WAZ) or weight for length z-score (WLZ)]

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Being 'big' in infancy is a risk factor for obesity

High weight for length Z-score (WLZ) **or** **high body mass index Z-score (BMIZ) in infancy** is associated with **increased obesity risk** at many ages across the life span

- **1-4** years of age (Mei 2004)
- **2** years old (Roy 2013)
- **5** years old (Asher 1966)
- **7** years old (Reilly 2005)
- **14** years old (Stettler 2002)
- **14-16** years of age (Monteiro 2003)
- **20-30** years of age (Charney 1976, Rolland-Cachera 1987)
- **60-70** years of age (Eriksson 2003)

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Gaining weight rapidly in infancy is a risk factor for obesity

High weight gain velocity (g/d) or 'rapid weight gain'
in infancy is associated with greater risk for obesity at many ages across the life span:

- **3** years of age (Taveras 2009)
- **5** years of age (Toscheke 2004)
- **7** years of age (Karaolis-Danckert 2006)
- **10** years of age (Ong 2009, Melbin 1976)
- **17** years of age (Ekelund 2007)
- **20-32** years of age (Stettler 2005)

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Breastfeeding (BF) is beneficial

- **Longer duration of breastfeeding has been associated with lower odds of early RWG** (Taveras 2009, Mihrshahi 2011)
- **Longer duration of breastfeeding associated with lower odds of later overweight/obesity** (von Kries 2000, Harder 2005, Rzehak 2017, Eny 2018, Bell 2018)

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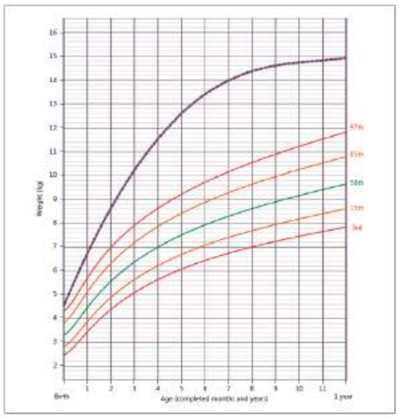
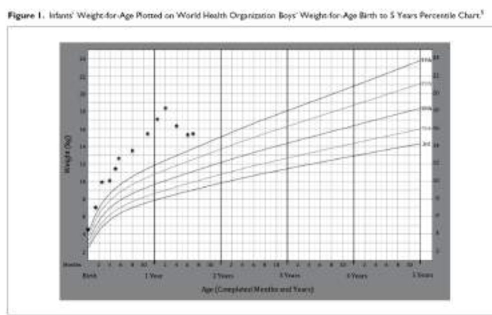
Focusing on the individual infant

Case reports of BF infants with rapid or high weight gain



(Grunewald 2014)



(Perrella 2016)

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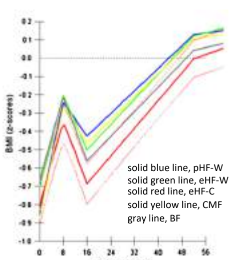
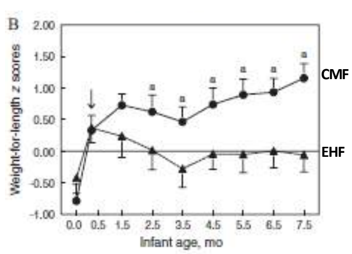
Categorizing FF growth pattern

Not all FF infants exhibit the same growth patterns

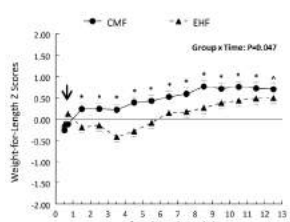
- **Three** RCTs of healthy infants found infants fed cow milk formula (CMF), as a group, had accelerated weight gain compared to infants fed extensive protein hydrolysate formula (EHF), whose patterns of weight gain was more normative (Rzehak 2009, Mennella 2011, Mennella, Trabulsi 2018)



(Rzehak 2009)



(Mennella 2011)



(Mennella, Trabulsi 2018)

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Take home messages

1. ‘Sensitive periods’ refers to ”a process whereby a stimulus or insult (such as diet or weight gain) at a critical period of development, has lasting or lifelong significance”
2. Early rapid weight gain (RWG) increases odds for later overweight or obesity
3. Breastfeeding decreases odds for later overweight or obesity
4. However, not all infants within a diet group (breastfed or formula fed) exhibit the same growth pattern

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Purpose

- Determine whether weight status (WLZ) in the first year of life and risk for overweight at 1 year, differed based on the **interaction** between **early rapid weight gain (RWG)** and **diet** [breast feeding (BF) or formula feeding (FF)] in the first year of life.
- **Hypotheses:**
  - that increases in WLZ would be lower in BF infants with early RWG, when compared to FF infants with RWG.
  - FF infants with RWG would have greater odds for overweight at 1 year, whereas BF infants with RWG would not

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Subjects

Data from two longitudinal RCTs of healthy, term infants that collected repeated measures of infant anthropometry from birth through 12.5 months

Study 1

RCT HD072307 (Formula fed infants)
2012-2015
randomized at 0.5 months
N=113

↓

FF infants
completed 12.5 mo. visit
N=83 (74%)

Study 2

RCT HD037119 (Breastfed infants)
2012-2015
randomized at 0.5 months
N=97

↓

BF infants
completed 12.5 mo. visit
N=77 (79%)

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Study Design

- Early weight gain groups were determined based on changes in WLZ from 0.5 month to 4.5 months (Wang 2016, Salgin 2015)
  - **<u>Slow weight gain</u> (SWG):** WLZ change <−0.67 SD
  - **<u>Normal weight gain</u> (NWG):** WLZ change −0.67 and 0.67 SD
  - **<u>Rapid weight gain</u> (RWG):** WLZ change >0.67 SD

- Overweight status at 1 year was defined as WLZ > 1.0364 (> 85th percentile)

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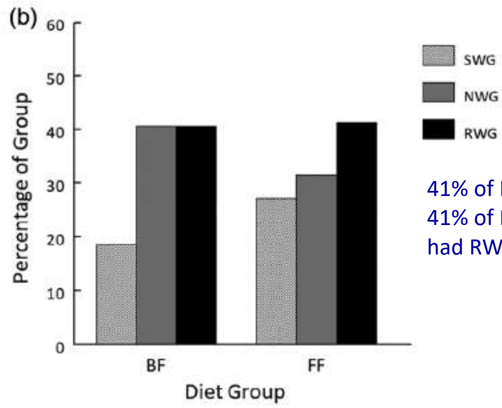
Results: Weight gain categories

No difference in the percentage of breastfed (BF) and formula-fed (FF) infants in each early weight gain category (SWG, NWG, RWG)

(Chi-squared test, P = 0.298)



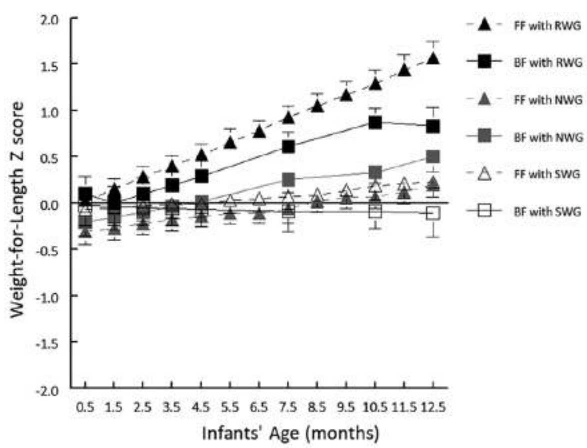
41% of BF infants
41% of FF infants
had RWG

25

Results: WLZ over time

Linear-mixed effects model found a significant interaction between diet and early weight gain category on changes in WLZ in first year

(P < 0.001)



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Results: odds for overweight

Reference group = BF infants with NWG
FF infants with RWG had 25 times greater odds for overweight at 1 year whereas BF infants with RWG did not have increased odds
($P < 0.001$)

	Odds ratio[a]	95% Confidence interval
Breastfed infants		
NWG	1.00	-
SWG	1.11	(0.23, 5.47)
RWG	0.56	(0.12, 2.55)
Formula-fed Infants		
NWG	0.43	(0.19, 1.97)
SWG	1.92	(0.21, 17.81)
RWG	25.3	(3.21, 199.70)

Abbreviations: NWG, normal weight gain; SWG, slow weight gain; RWG, rapid weight gain.
[a]Crude model coefficients from logistic regression using breastfed infants with NWG as reference group.

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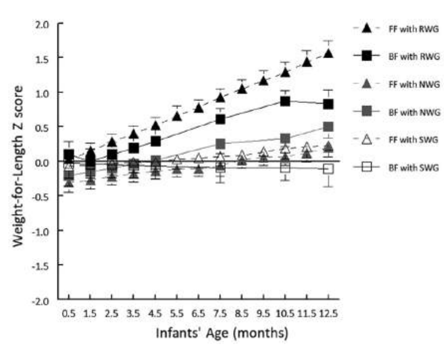
Take home messages

- Just under half of the BF (41%) and FF (41%) infants experienced early RWG in the first 4 months of life
- Both BF and FF infants with RWG had greater increases in WLZ over time, however the mean WLZ of BF infants with RWG at 1 year was 0.74 SD lower than FF with RWG infants.
- Additionally, FF infants with RWG had higher odds of overweight at 1 year, BF infants with RWG did not.



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Potential Mechanisms

- Several explanations, not mutually exclusive, may contribute to the protective effects of breastfeeding among infants with RWG

  1. Differences in composition between breastmilk and infant formula – infant formula has higher protein concentration than mature breastmilk leading to greater protein intake in FF infants (Feng 2016, Heinig 1993, Picone 1989, Trabulsi 2011, Fledderman 2017)

  2. Differences in complementary diet in latter 6 months of infancy - energy intake from complementary foods is higher in FF compared to BF infants (Heinig 1992)

  3. Differences in feeding beliefs and practices of mothers –we found lactating mothers were less indulgent or pressuring and more responsive in their feeding beliefs than mothers of FF infants

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Future Directions

CDC Breastfeeding Scorecard 2020

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Ever Breastfed	84.1%
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Breastfeeding at 12 months	35.3%
*Exclusive breastfeeding at 3 months	46.9%
*Exclusive breastfeeding at 6 months	25.6%

[1]https://www.cdc.gov/breastfeeding/pdf/2018breastfeedingreportcard.pdf

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Future Directions

1. Continued efforts to support BF initiation and duration are essential, since BF exclusivity and duration is protective against later obesity
2. Healthcare providers should pay particular attention to the FF infant with early RWG, since these infants are at greater odds for later overweight
3. Additional research on early diet composition (breast milk and infant formula), the complementary diet, maternal feeding beliefs

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Overarching goal

To prevent excess weight gain in infants who receive infant formula via improved understanding of the effect of formula composition on energy balance and weight gain, thus reducing the risk of obesity for millions of infants who are fed infant formula.




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Not all infant formulas are alike, they differ by protein type and protein form

Increasing protein hydrolysis

Standard formula (CMF)	Partially Hydrolyzed Protein (PHF)	Extensively Hydrolyzed Protein (EHF)
Intact protein	Small peptides/ some free amino acids (FAA)	Free amino acids (FAA)/ small peptides

33

Not all infant formulas are alike, they differ by protein type and protein form

Increasing protein hydrolysis

Standard formula (CMF)	Partially Hydrolyzed Protein (PHF)	Extensively Hydrolyzed Protein (EHF)
Intact protein	Small peptides/ some free amino acids (FAA	Free amino acids (FAA)/ small peptides

80% of infants on CMF

34

Not all infant formulas are alike, they differ by protein type and protein form

Increasing protein hydrolysis

Standard formula (CMF)
Intact protein

Partially Hydrolyzed Protein (PHF)
Small peptides/
some free amino acids (FAA)

Extensively Hydrolyzed Protein (EHF)
Free amino acids (FAA)/
small peptides

80% of infants on CMF

<5% of infants on EHF

35

Extensive protein hydrolysate formula (EHF)

- **Extensive protein hydrolysate formula (EHF)** developed for infants who have cow milk protein allergy or intolerance to intact proteins
- **EHF** milk proteins are treated with enzymes to break down peptide bonds (reducing allergenicity to proteins), resulting in **high levels of free amino acids (FAA) and low-molecular-weight peptides**

Table 1. Caloric, Macronutrient and Free Amino Acid (FAA) Content of Formulas and Breast Milk

	CMF[a]	EHF[a]	Breast Milk[2]
Calories (kcal/100ml)	67	67	62.0-70.0
Macronutrients (g/100kcal)			
Carbohydrates	7.4	7.0	6.5-7.8
Fat	3.6	3.6	3.0-3.6
Protein or protein equivalent	1.4	1.9	1.0-1.3
Sources of protein	Cow Milk whey, casein	Hydrolyzed casein	Whey, casein,
FAA(μmol/L)			
Total FAA	864	80,375	3020
Essential FAA	57	47,523	203
Semi/NonEss FAA	807	32,852	2,825
-Free Glutamate	109	7,472	1,203

[a]CMF(Enfamil); EHF(Nutramigen). Macronutrient estimates for formulas from Mead Johnson Nutrition websites[39,40] and for mature breast milk[33,41]. FAA values from refs[34-5]

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Extensive protein hydrolysate formula (EHF)

- **EHF has a distinctive flavor** because the hydrolysis of protein results in high concentrations of FAAs and small peptides, which taste sour, bitter, and savory and produce odors that affect flavor (Cook 1982, Schiffman1975, Pedrosa 2006)
- Some may hypothesize that infants dislike the taste of EHF….
  - However there is a sensitive period for flavor programming such that feeding EHF renders this formula highly palatable and accepted throughout infancy (Mennella 2004, Mennella 2011)

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Extensive protein hydrolysate formula (EHF)

- **If infants are exposed to EHF for at least one month during the first 3.5 months of life (sensitive period), they do not reject EHF taste when older**: they feed EHF to satiation; prefer EHF to CMF and do not display facial expressions of distaste during its feeding (Ventura 2015, Mennella 2011)

From the *American Journal of Clinical Nutrition*, 2011, 93, 1019–1024, American Society for Nutrition.

Infant A received CMF for past 7 months and was given an EHF feeding

Infant B received EHF for past 7 months and was given an EHF feeding

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Extensive protein hydrolysate formula (EHF)

- **Children fed EHF during infancy** are not only programmed to like the taste of EHF, but **also like the taste of foods that are more savory (e.g. chicken), sour (e.g., lemon) and bitter (e.g., broccoli)**
  (Liem 2002, Mennella 2002, 2006, 2009, Owada 2000, Schuet 1980)

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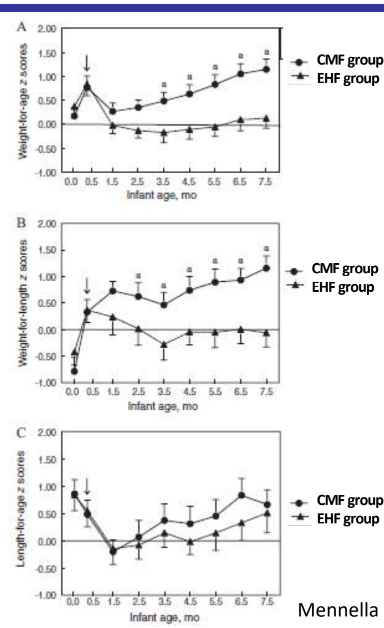
Differential Growth Patterns Among Healthy Infants Fed Protein Hydrolysate or Cow-Milk Formulas
Julie A. Mennella, Alison K. Ventura and Gary K. Beauchamp

While studying influence of feeding EHF on flavor learning,found that **<u>EHF-fed infants also had more normative weight gain</u>** compared to CMF-fed infants



Mennella et al, Pediatrics 2011

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Other studies of Extensive protein Hydrolysate Formulas (EHF)

Study Population	Age infants first fed study formula	Exclusive formula feeding?	Intake and growth outcomes	Reference
FHA *	Birth	Yes, exclusively FF until 4 months, when solids were introduced	• Intake data not provided • **CMF- and PHF-fed infants tended to be heavier than BF infants**; weight-for-length not presented	Roche et al., 1993
FHA *	5 - 6 weeks old	No, BF for first 5-6 weeks, then received mixed feedings (breast milk and formula) or exclusively FF	• Intake not assessed • **CMF-fed infants exhibited greater BMI change than did EHF-fed infants between 2 and 12 months; no group differences after 12 months**	Rzehak et al., 2009
FHA *	4 weeks old	No, BF for first 4 weeks of life, then received mixed feedings or exclusively FF	• No difference in intake among groups • **BMI of infants fed EHF was significantly lower at 3 months compared to BF and SF-fed infants**	Giovannini et al., 1994
Healthy	Birth	Yes	• EHF-fed infants consumed less formula than did CMF-fed infants • No significant differences in weight, length, or HC gain during the 13-week study period	Hauser et al., 1993 Vandenplas et al., 1993
Healthy	4 weeks old	Yes	• EHF-fed infants consumed less formula than did CMF-fed infants • No differences in weight gain during 2-wk study	Hyams et al., 1995
Healthy	6 weeks old	No, predominantly BF prior to study	• Intake data not provided • No significant differences in weight, length, or weight or height gain were found btwn groups, but study not powered to detect such differences	Hernell & Lonnerdal, 2003
Healthy *	2 weeks old	Yes	• **EHF-fed infants consumed less formula to satiation than did CMF-fed infants** • **EHF-fed infants had significantly lower weight-for-length z-scores across ages 2.5-7.5 months and slower weight gain velocity than did CMF-fed infants**	Mennella et al., 2011)

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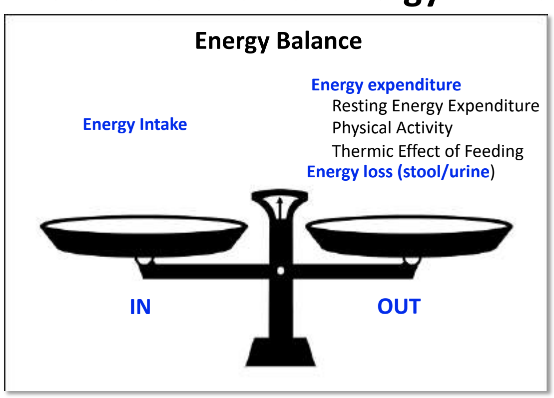
What components of energy balance led to the differential weight gain?

Energy balance is a function of Energy In and Energy out:



Energy balance

- Positive energy balance (weight gain) when Energy IN > Energy OUT
- Negative energy balance (weight loss) when Energy OUT > Energy IN

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Differential Growth Patterns Among Healthy Infants Fed Protein Hydrolysate or Cow-Milk Formulas

Julie A. Mennella, Alison K. Ventura and Gary K. Beauchamp

TABLE 2 Number of Daily Formula Feedings and Age of Solid-Food Introduction as Determined by Maternal Reports and Intake of Assigned Formula as Determined by Laboratory-Based Monthly Assessments

	CMF Group (N = 32)	PHF Group (N = 24)	F	P
No. of daily formula feedings, mean ± SE				
0.5 mo	7.7 ± 0.3	7.4 ± 0.5	—	—
1.5 mo	7.3 ± 0.4	6.4 ± 0.3	—	—
2.5 mo	6.9 ± 0.4	5.8 ± 0.4	—	—
3.5 mo	6.2 ± 0.3	5.7 ± 0.4	—	—
4.5 mo	5.9 ± 0.3	5.6 ± 0.3	—	—
5.5 mo	5.2 ± 0.4	5.8 ± 0.3	—	—
6.5 mo	5.0 ± 0.4	5.1 ± 0.4	—	—
7.5 mo	4.8 ± 0.3	5.0 ± 0.4	—	—
Average	6.2 ± 0.1	5.9 ± 0.1	2.6[a]	.12
Intake of assigned formula at laboratory-based assessment, least-squares mean ± SE, mL[b]				
1.5 mo	130.1 ± 8.8	94.7 ± 10.1	—	—
2.5 mo	157.2 ± 12.1	124.3 ± 14.0	—	—
3.5 mo	160.8 ± 12.7	152.1 ± 13.5	—	—
4.5 mo	190.8 ± 14.6	128.4 ± 17.0	—	—
5.5 mo	180.2 ± 15.2	152.8 ± 16.9	—	—
6.5 mo	160.7 ± 17.1	154.1 ± 18.7	—	—
7.5 mo	190.1 ± 22.4	188.8 ± 24.0	—	—
Average	164.9 ± 5.6	143.4 ± 6.7	3.96[a]	.05
Age at solid-food introduction, mean ± SE, mo				
Cereal	3.6 ± 0.3	3.5 ± 0.3	0.03	.86
Fruit	4.9 ± 0.3	4.5 ± 0.3	0.87	.36
Vegetables	5.3 ± 0.3	5.0 ± 0.3	0.43	.51
Meat	6.3 ± 0.2	6.0 ± 0.3	0.47	.50

[a] Main effect of group; group-×-time interaction was not significant.
[b] Analysis adjusted for time since last formula or solid-food feeding.

No difference in number of feedings/d

EHF-fed consumed lower volume per feed during in-lab feeding session

Mennella et al, Pediatrics 2011

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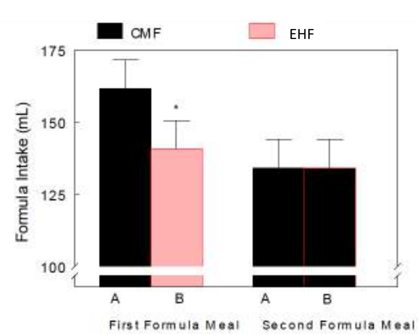
What could lead to differential weight gain?

- **Differences in Energy Intake?**
  - EHF fed infants had lower energy intake per feeding
    - **However, intake volume** (Mennella 2011) **was based on only one observed laboratory feeding session each month**



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Other studies of Extensive protein Hydrolysate Formulas (EHF)

Study Population	Age infants first fed study formula	Exclusive formula feeding?	Intake and growth outcomes	Reference
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FHA	5 - 6 weeks old	No, BF for first 5-6 weeks, then received mixed feedings (breast milk and formula) or exclusively FF	• Intake not assessed • CMF-fed infants exhibited greater BMI change than did EHF-fed infants between 2 and 12 months; no group differences after 12 months	Rzehak et al., 2009
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Healthy *	2 weeks old	Yes	• **EHF-fed infants consumed less formula to satiation than did CMF-fed infants** • EHF-fed infants had significantly lower weight-for-length z-scores across ages 2.5-7.5 months and slower weight gain velocity than did CMF-fed infants	Mennella et al., 2011)

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What could lead to differential weight gain?

- **Differences in Energy Expenditure?**
- EHF is higher in total protein concentration compared to CMF
  - Nutramigen ~18.6 g pro/L
  - Enfamil ~14 g pro/L
- In adults, diets higher in protein have been shown to result in increased thermogenesis and sleeping metabolic rate, which may lead to increased total energy expenditure in adults (Lejeune et al, AJCN 2006)

No research to date had focused on the effects of hydrolysate protein IF infant on energy expenditure in infancy

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What could lead to differential weight gain?

- **Differences in Energy Loss from gastrointestinal tract?**
- EHF transits the gastrointestinal tract at faster rate than CMF (Mihatsch 2011)
- When infants are switched from CMF to EHF, the consistency of the stool changes, resembling the watery stools characteristic of breastfed infants for 3-7 days (Hyams 1995)

No research to date had focused on the effects of hydrolysate protein IF infant on energy absorption in infancy

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Take home messages

- In healthy term infants fed EHF, 3 of 4 studies that measured energy intake found EHF infants consumed lower energy intake.
  - However, in one study it was an in laboratory feeding session
- No research to date had focused on the effects of hydrolysate protein in infant formula on:
  - Energy expenditure
  - Energy loss

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Investigators and Collaborators

Principal Investigators

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Loma Inamdar, BS
Ashley Reiter, MS
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University of Wisconsin – Madison
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This work was supported by NIH grant R01HD072309 (Mennella/Trabulsi; Multiple PI) and NIH grant HD072309S (Mennella/Trabulsi; Multiple PI)

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(NIH R01HD072307 & NIH R01HD072309S) Effect of infant formula composition on weight gain

Formula Fed infants
n = 113

Randomized at 1-2 weeks of age

Commercially available
EHF infant formula
(n=54)

Commercially available
CMF infant formula
(n=59)

Subjects: Healthy term infants, 5 to 14 days old
Enrollment duration: 12 months
Primary objectives: Energy balance and growth
Secondary objective: Gut microbiome and metabolome

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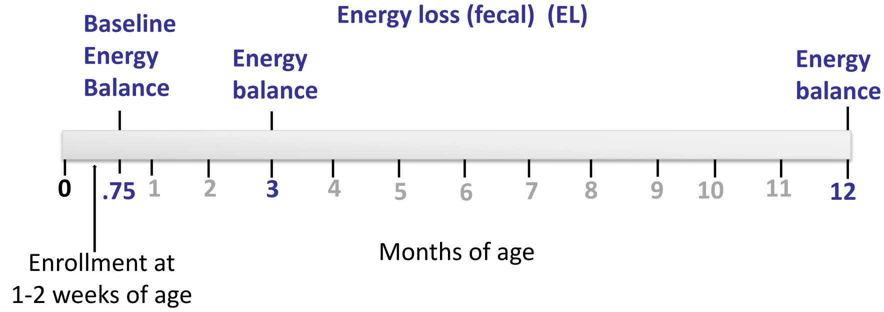
Study Design

Comprehensive Energy Balance measures:
Total energy expenditure (TEE)
Sleeping energy expenditure (SEE)
Energy intake (EI)
Energy loss (fecal) (EL)



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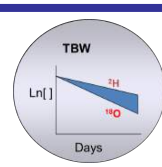
Comprehensive Energy Balance Methods

- **Total Energy Expenditure (TEE) (kcal/day)** Measured over 7 days by stable isotope (doubly-labeled water; DLW) method



- **Sleeping Energy Expenditure (SEE) (kcal/day)** Measured by indirect calorimetry

- **Energy intake (kcal/d)** determined by 3-day weighed bottle method with diet record

- **Fecal energy loss (kcal/day)** measured over 3 days by bomb calorimetry

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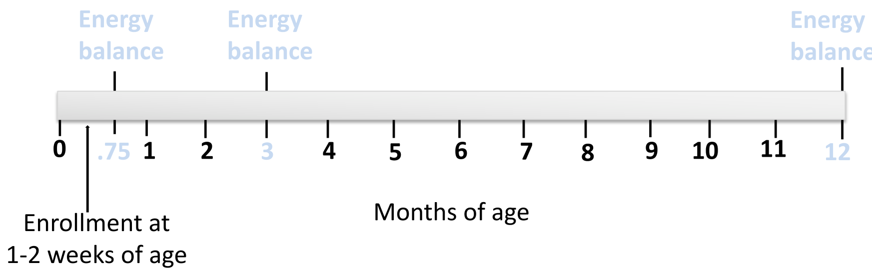
Study Design

Comprehensive Energy Balance measures:
Total energy expenditure
Sleeping energy expenditure
Energy intake
Energy loss (fecal)



Monthly measures:
Energy intake (diet records)
Anthropometric measures
In-laboratory feeding session

Weight gain differed by formula group

CMF fed infants had significantly greater
WLZ, greater early weight gain velocity, and
higher proportion of infants with rapid weight gain (CMF:56%, EHF: 25%)

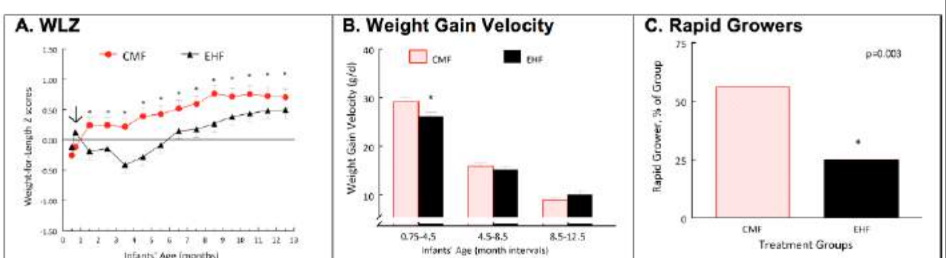


Figure 1. Panel A: CMF fed infants had greater weight for length (WLZ) compared to EHF fed infants (arrow indicates when infants began randomized formula, *indicates significant difference between CMF and EHF). **Panel B:** CMF infants had greater weight gain velocity (g/d) (p=0.003). **Panel C**: Significantly greater percentage of CMF fed infants were rapid growers (p<0.003).

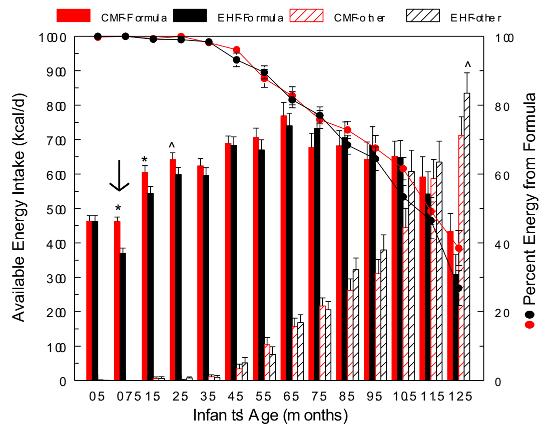
What were the energy balance mechanisms that led to differential weight gain?

Energy intake differed by formula group

From 0.75 to 2.5 months
CMF fed infants ingested significantly:

- **More** kcal/d
- **More** kcal/kg/d
- **More** formula per feed (ml/feed)

than EHF fed infants



*p<0.05 ^p<0.08

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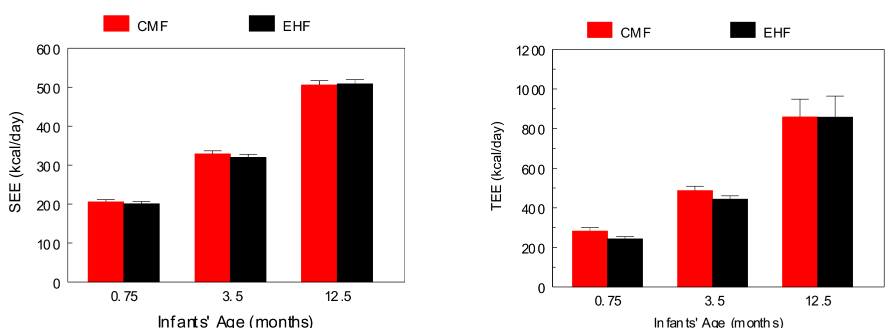
Sleeping and Total Energy Expenditure did NOT differ by formula group



SEE and TEE did not differ at any time point

(both with and without adjustment for fat free mass (FFM)[1]; repeated measures ANOVA p=0.72)

[1] FFM = total body water (derived from deuterium and oxygen-18 dilution) by age-specific hydration constants

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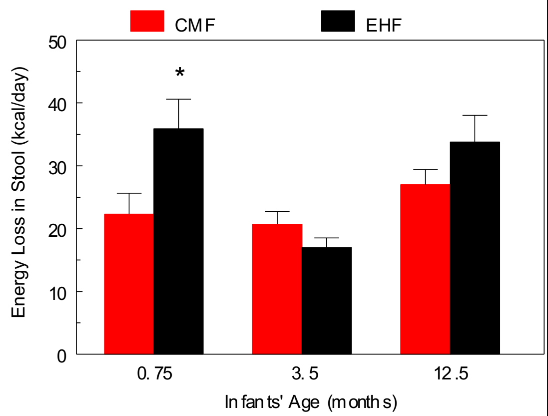
Fecal Energy Loss (EL) differed by formula group initially

At 0.75 months:

CMF fed infants had:

- **Lower fecal EL** compared to EHF

No differences at 3.5 or 12.5 months



*p=0.02

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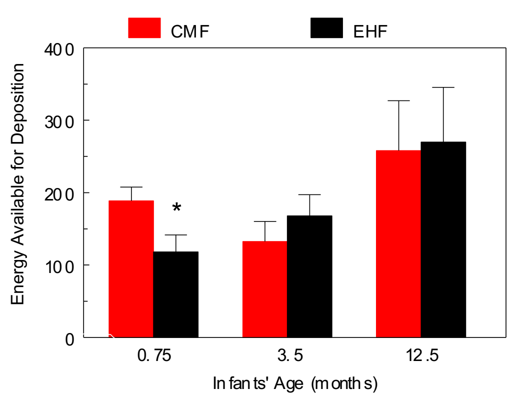
Energy Available for Deposition differed by formula group

At 0.75 months:

CMF fed infants had:

- **More energy available for deposition** compared to EHF

No differences at 3.5 or 12.5 months



*p=0.02

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Take home messages

- Composition of commercial infant formulas can impact energy balance
  - Differences in weight gain with led to differences in infant weight status
- CMF and EHF are isocaloric, but differ form of protein
  - intact versus extensively hydrolyzed protein
- Infants randomized to CMF had higher early weight gain compared to EHF fed infants, due to:
  - Early greater Energy Intake and an initial lower fecal Energy Loss
  - Not due to differences in energy expenditure

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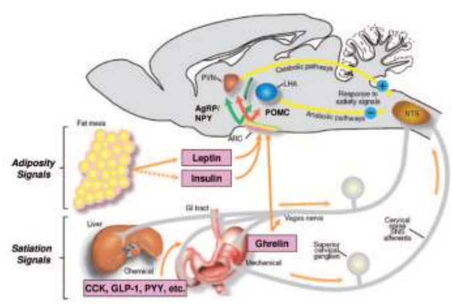
Why do infants satiate at lower volume (energy) when fed EHF?

- **FAA in EHF** are more rapidly digested and absorbed (Koopman 2009,Keohane 1985) which may lead to earlier peaks in amino acid concentrations in the blood and hypothalamus
- **FAA in EHF** may, via vagal afferents, transmit signals to the nucleus tractus solitarius (NTS) and hypothalamus, which regulates food intake



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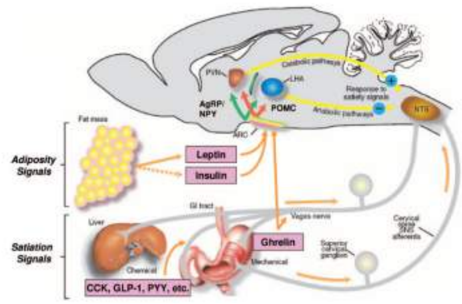
Why do infants satiate at lower volume (energy) when fed EHF?

- **EHF** has faster gastric emptying rate (Staelens 2016) and faster GI transit time compared to standard intact CMF (Mihatsch 2001)



- **FAA in EHF** bind to receptors in the gut earlier than intact protein formulas (CMF), stimulating gastrointestinal orexigenic peptides (CCK, GLP-1, PYY) that signal satiation

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How can we prevent rapid weight gain in infants who receive infant formula

- One strategy would be to feed all infants EHF instead of CMF
  - EHF costs 40% more than standard CMF, diminishing the feasibility from a public health perspective
- Alternatively, partial hydrolysate infant formulas (PHF), are closer in cost to CMF, and contain smaller peptides/more FAA than CMF, but not as much as EHF, may impact satiation.

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Very little is known about the FAA content of PHF formulas

Increasing protein hydrolysis

Standard formula (CMF)
Intact protein

Partially Hydrolyzed Protein (PHF)
Small peptides/
some free amino acids (FAA)

Extensively Hydrolyzed Protein (EHF)
Free amino acids (FAA)/
small peptides

Effect of PHF on satiation (volume consumed per feeding) is not known.

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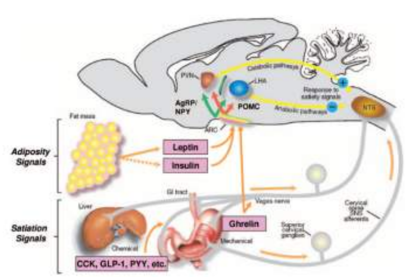
Current study

The primary **objectives** of the study are to determine FAA concentrations of common PHFs, and to evaluate the effect of PHF on intake volume and feeding behaviors



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Thank you

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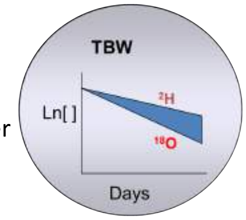
66

Methods

TEE (kcal/day) measured over 7 days by doubly-labeled water (DLW)



- Baseline urine sample obtained
- Infants dosed with DLW
  - 0.3 g $H_2{}^{18}O$ and 0.15 g ^2H_2O/kg estimated total body water
- Morning urine sample collected x 7 days
- Deuterium (^2H) and oxygen-18 (^{18}O) abundance in dose water/urine samples determined
  - isotope ratio mass spectrometry (University of Wisconsin, Madison, WI)
- Difference in elimination rate ($k_O - k_H$) = rCO_2 production
  - $rCO_2=1/2*TBW(k_O-k_H)$
  - Weir equation to calculate expenditure (TEE = 9.9 x L O_2 used + 1.1 L CO_2 produced)

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Methods

SEE (kcal/day) measured by indirect calorimetry

- Computerized metabolic cart (model 2900 Z; Sensor Medics) (The Children's Hospital of Philadelphia)

- Measured post-prandially for 60 minutes in a quiet, thermo-neutral room
  - Infants slept in supine position under a large, clear, ventilated hood
  - Gases were sampled and analyzed every second, and 1-minute averages recorded
- First 10 minutes were devoted to environmental acclimation of infant and were not used in calculations
- Weir equation to calculate energy expenditure

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Methods

Energy intake (kcal/d) determined by 3-day weighed bottle method and diet record

- Mothers provided a 3-day supply of pre-weighed bottles with powder formula, and filled water to a line designated on bottle
- Instructed to feed infant as usual and return all bottles (empty or partial consumed)
- Bottles weighed upon return; grams consumed converted to milliters by formula density
- Mothers also given 3-day diet record to record time of each feeding, anything added to the bottles, food

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Methods

Energy intake (kcal/d) determined by diet records

- 1-day diet record completed all other months (0.5, 1.5, 2.5, 4.5, 5.5, 6.5, 7.5, 8.5, 9.5, 10.5, 11.5 months)
- Formula intake and diet record data were analyzed using Nutrient Data System for Research (NDS-R, Minneapolis, MN) to determine *available* Energy Intake (EI) (University of Delaware)
- Records were reviewed by a registered dietitian; records with physiologically implausible EI, because incomplete or based on energy needs, were eliminated.

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Methods

Fecal energy loss (kcal/day) measured over 3 days by bomb calorimetry

- Mothers collected all stools for a 3 day period in plastic containers stored in the freezer between use.
- An aliquot from each day (day 1, day 2, day 3) was homogenized and the composite sample analyzed for total energy via bomb calorimetry (Covance Laboratories, Madison, Wisconsin)

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Bedsharing and Breastfeeding: Evidence and Recommendations

Melissa Bartick, MD, MS, FABM
IABLE

January 23, 2021

Harvard Medical School

1

Disclosures

I have no actual or potential conflict of interests for this activity.

2

Objectives

1) Describe the normal sleep patterns of breastfeeding dyads.
2) Describe the circumstances in which bedsharing might be hazardous.
3) Explain strategies for counseling parents on safe sleep.

This content will be available on the GOLD Learning Lecture Library until June 17, 2023.

3

Bedsharing and Breastfeeding: The Issue

- Most countries' recommendations state "the safest place for infant to sleep is on a separate surface" from mother. (SIDS prevention)
- Yet, separate sleep has been shown to hinder breastfeeding success.

4

Mainstay of recent SIDS prevention emphasized on "no bedsharing"

Milwaukee, 2010-2011

5

Definitions

- SIDS: unexplained infant death after full investigation (including autopsy)
- Sudden Unexpected Infant Death (SUID; SUDI)
  - Includes SIDS (R95)
  - Includes "Ill-defined unknown cause" (R99)
  - Includes Accidental Suffocation and Strangulation in Bed (ASSB) (W75) (asphyxia, overlying)
    - Can include death on a sofa or chair

6

SUID/SUDI: Umbrella Term

- "SUID/SUDI" accounts for the wide variability in coroners' diagnoses for potential SIDS
- R99 is often used if there was not a full investigation– most common diagnosis
- SIDS (R95) stats are readily reported & obtained
  -SUID stats are not

Recommendations

- Germany (2018): Separate sleep
- US (AAP, 2016): Separate sleep
- Canada (2018): Separate sleep
- Europe(EFCNI) (2018): Separate sleep

Recommendations

- Australia (2018): Risk minimization: "safer co-sleeping": separate sleep but instruct on bedsharing
- UK (2019): Risk minimization: separate sleep but instruct on bedsharing
- NZ (2019): Separate sleep in bassinet, wahakura, Pēpi-pod

New Zealand

Wahakura

Pēpi-Pod

What Is Normal Infant Sleep Physiology?

versus

Traditional Societies

Ethnographic data from societies around the world confirm that mothers in traditional human cultures are in contact with their infants 24 hours a day, carrying them strapped to their bodies by day and sleeping with them by night and feeding at will.

-Helen Ball

Ball H. Bed-sharing and co-sleeping: Research overview. NCT New Digest. 2009;48:22-7. *(from Barry and Paxton, 1971)*

Why Do Moms Sleep With Babies?

Because we are not echidnas!

Echidna milk: High fat and/or high protein ->
Echnida baby can sleep alone
Deep sleep does not attract predators!

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We Are Primates!

- Milk w/low fat or low protein ->
  - baby needs frequent feeds and cannot be left alone
- Oxytocin causes sleepiness in mom and baby

Chimpanzee

Humans feed every 2-3 hours

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"Breastsleeping"

- Coined by McKenna and Gettler in 2015
- Denotes that breastfeeding and bedsharing are an inextricably bound together as an evolutionary imperative
- Mother and infant sleep cycles and cortisol levels are in sync

Sources: McKenna J and Gettler L 2015 Acta Paediatrica 105(1); Middelmiss 2012 *Early Hum Dev* 88(4); Mosko 1997 *Sleep* 20(2); Mosko 1997 *Pediatrics* 100(5).

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Bedsharing Promotes Breastfeeding

- Dyads who "bedshared routinely at home breastfed 3 times longer during the night than infants who routinely slept separately, when tested in their routine conditions."

Mosko S, Richard C, McKenna J. Infant arousals during mother-infant bed sharing: implications for infant sleep and sudden infant death syndrome research. Pediatrics. 1997;100(5):841-849. 16

Bedsharing Promotes Breastfeeding

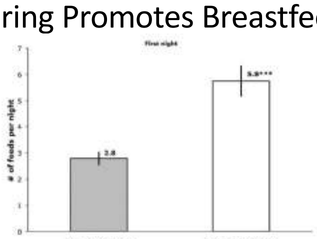
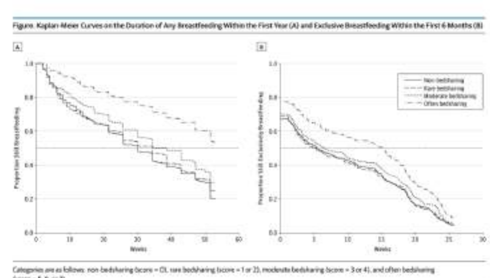


Fig. 2.
Mean number of breastfeeds per night (with SE) for routine solitary sleepers (while sleeping separately, $n = 14$) and routine bedsharers (while bedsharing, $n = 12$) on the first laboratory night. Significant between group difference, *** $P < 0.001$.

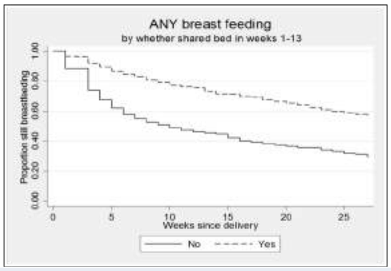
Gettler LT, McKenna JJ. Evolutionary perspectives on mother-infant sleep proximity and breastfeeding in a laboratory setting. Am J Phys Anthropol. 2011;144(3):454-462. 17

Bedsharing Promotes Breastfeeding



Huang Y, Hauck FR, Signore C, et al. Influence of bedsharing activity on breastfeeding duration among US mothers. JAMA Pediatrics. 2013;167(11):1038-1044. 18

Bedsharing Promotes Breastfeeding



Ball HL, Howel D, Bryant A, Best E, Russell C, Ward-Platt M. Bed-sharing by breastfeeding mothers: who bed-shares and what is the relationship with breastfeeding duration? Acta Paediatr. 2016;105(6):628-634.

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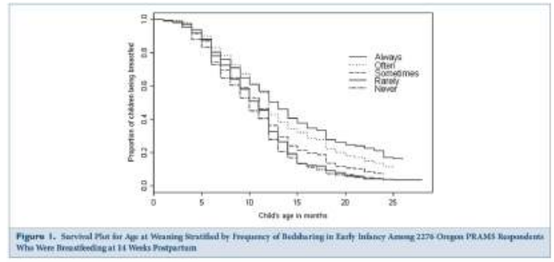
25 Months Of Breastfeeding Duration



Bovbjerg, M. L., et al. (2018). "Women Who Bedshare More Frequently at 14 Weeks Postpartum Subsequently Report Longer Durations of Breastfeeding." J Midwifery Womens Health 63(4): 418-424.

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Bedsharing Is A Biological Imperative

Even babies sleep with their babies.

Note: Sleeping with stuffed animals is not recommended

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History

How did we get to "never bedshare"?

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History (Western countries)

- Infant sleep was not a "problem" until early 20th century
- Solitary sleep arose around 1910s with:
  - Births now occurring in hospitals
  - Rise in artificial feeding

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The Rise of Pediatrics and Obstetrics

mid 1800's to early 1900s++

- Male obstetricians took over from midwives
- Pediatricians (mostly men) prescribed artificial milk "formulas" as a growing part of practice

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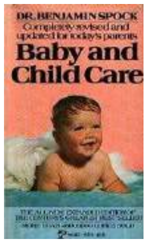
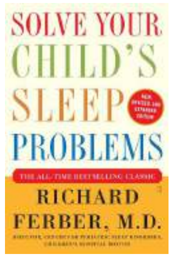
1917 1942-1976+ 1985





Men wrote books on raising children (!!!), which had always been done by women

The Rise Of Artificial Feeding:

Parallels Separate Sleep

Artificial Feeding . . .

How are cows different from humans?

Hoofed animals walk independently *from birth*; they cannot be carried

Their mothers go off to graze; newborn cows sleep alone

Calf

Baby giraffe

[Newborn calves sleep alone days after birth when they are too weak to follow mom; soon they follow her].

Cows' Milk: Designed So Calves Can Sleep Alone

- Higher protein = long feeding interval
- Can eat as little as 2-3 times a day (on a farm)
- Sleep deeply

Formula Goes With Separate Sleep

- Infants sleep longer and more deeply when fed formula (based on cow's milk)

Centers for Disease Control and Prevention (2008). Infant Feeding Practices Study II, Chapter 3, Infant Feeding. Atlanta

Horne, R. S., et al. (2004). "Comparison of evoked arousability in breast and formula fed infants." Arch Dis Child 89(1): 22-25.

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When a human infant is fed the milk of a cow . . .

. . . the infant may behave as if the mother is absent.

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Separate sleep policy was developed when formula feeding was the norm

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Bedsharing And Feeding Method

- Bedsharing with formula feeding is *not* safe
- Bedsharing with breastfeeding does NOT confer the same risk

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Bedsharing With Formula Feeding

- Mothers more frequently noted to put infant on a pillow
- Infant more frequently may be put prone
- Sleep cycles may not be in sync
- Both are less arousable

- ->These together may increase risk of death

Sources: McKenna, McDade 2005 Ped Resp Rev; Ball 2006 Hum Nat

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Bedsharing With Breastfeeding

- Infant is very unlikely to be prone
- They tend to face each other
- Higher infant and maternal arousals
- Infant's head is below the pillow, across from breast
- Sleep cycles and cortisol levels are in sync

Sources: McKenna, McDade 2005 *Ped Resp Rev*; Ball 2006 *Hum Nat* 17(3), Baddock *Sleep Med Rev* 43: 2019

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Formula feeding increases risk of death with bedsharing.

How a formula feeding dyad *might* bedshare

A breastfeeding dyad

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Positions Not Seen With Breastfeeding

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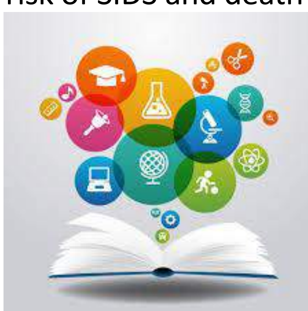
What does the literature say about risk of SIDS and death?



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Breastfeeding Protects Against SIDS: 2017 Meta-analysis

- Breastfeeding 2-4 mos protective: aOR 0.60
- Breastfeeding 4-6 mos even more: aOR 0.40
- Breastfeeding>6 months even more: aOR 0.36
  - Exclusive breastfeeding (0.61 for 2-4 mos, 0.46 for 4-6 mos).

Thompson JMD, Tanabe K, Moon RY, et al. Duration of Breastfeeding and Risk of SIDS: An Individual Participant Data Meta-analysis. Pediatrics. 2017;140(5).

40

The Evidence On Bedsharing And Infant Death

- Bedsharing has increased risk of death when combined with certain "hazardous risks"
- Is bedsharing risky if such risks are absent?

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Bedsharing and Hazardous Risks

- Hazardous Risks include:
  - Sleeping on sofa with an adult ("sofa-sharing")
  - Sleeping with adult impaired by alcohol/drugs
  - Infant placed prone (or non-supine)
  - Infant exposed to antenatal/postnatal tobacco
  - Infant was preterm
  - Infant is not breastfed (formula fed)

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Bedsharing Without Hazardous Risks

Blair PS, Sidebotham P, Pease A, Fleming PJ. Bed-sharing in the absence of hazardous circumstances: Is there a risk of sudden infant death syndrome? An analysis from two case-control studies conducted in the UK. ***PLoS One.*** **2014**;9(9):e107799

Carpenter R, McGarvey C, Mitchell EA, et al. Bed sharing when parents do not smoke: Is there a risk of SIDS? An individual level analysis of five major case-control studies. ***BMJ Open.*** **2013**;3(5).

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POLL: What are the biggest hazardous risks with bedsharing?

- Sleeping with an adult on a couch
- Sleeping next to an adult who's consumed alcohol
- Sleeping next to a smoker
- Bedsharing if infant was never breastfed
- Sleeping prone

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Blair et al. (2014)

- 2 Case-controls studies, UK, 1993-6
- 400 SIDS infants, 1386 controls

THE ONLY STUDY TO TRACK ALL MAJOR RISKS
  – Sofa-sharing, **OR 18.3**
  – Next to parent ≥2 drinks: **OR 18.3**
  – Next to someone who smoked **if <3 mos: OR 8.9**

Blair PS, Sidebotham P, Pease A, Fleming PJ.. PloS one. 2014;9(9):e107799.

45

Blair et al (2014)

- Not significant risk if NO risk factors (OR 1.1; CI 0.6-2.0)
- Breastfeeding was highly protective
- Note: Comparison group includes both infants who slept in same room and separate room

Blair PS, Sidebotham P, Pease A, Fleming PJ.. PloS one. 2014;9(9):e107799.

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Carpenter et al (2013)

  – Meta-analysis of 5 case control studies
  – Bedsharing associated with 5-fold risk of death in younger infants in non-hazardous circumstances.

Carpenter R, McGarvey C, Mitchell EA, et al. Bed sharing when parents do not smoke: is there a risk of SIDS? An individual level analysis of five major case-control studies. BMJ open. 2013;3(5).

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Carpenter (2013)-Drawbacks

- Comparison group was breastfed girls, supine, next to parents' bed
- Normally recognized group is non-bedsharers
- Data is uninterpretable as some of it magnifies risk, some of it minimizes risk
- 3 of the studies he used did not look at alcohol (a MAJOR risk, per Blair, 18 fold)
- Also used imputed data

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Vennemann (2012)

- Meta-analysis of SIDS and bedsharing
- Routine bedsharing did not increase the risk for SIDS
  - When bedsharing was NOT routine (e.g. unintentional), SIDS risk was increased (OR 2.18).
- Bedsharing with smoking <12 weeks: OR 10.4
- Did not look at breastfeeding

Vennemann MM, Hense HW, Bajanowski T, et al. Bed sharing and the risk of sudden infant death syndrome: can we resolve the debate? J Pediatr. 2012;160(1):44-48 e42.

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Epidemiology of Sudden Infant Death and Bedsharing

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Poll

Is sudden infant death distributed equally among racial, ethnic, and socioeconomic groups?

- Yes
- No
- Not sure

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Most Sudden Infant Deaths occur in marginalized and poor communities

- American Indians/Alaskan Natives
- Non-Hispanic Black Americans
- Indigenous Canadians/Inuit
- New Zealand Māori
- Australian Aborigines
- Low income British

Bartick M, Tomori C. Sudden Infant Death and Social Justice: A syndemics Approach. Matern Child Nutr. Aug 23:e12652. doi: 10.1111/mcn.12652

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ORIGINAL ARTICLE — WILEY | Maternal & Child Nutrition

Sudden infant death and social justice: A syndemics approach

Melissa Bartick[1] | Cecilia Tomori[2]

- Examined high- and low-SIDS prevalence populations globally
- Examined SIDS risk factors for each population, including bedsharing

Bartick M, Tomori C. Sudden Infant Death and Social Justice: A syndemics Approach. Matern Child Nutr. 2018 Aug 23:e12652. doi: 10.1111/mcn.12652

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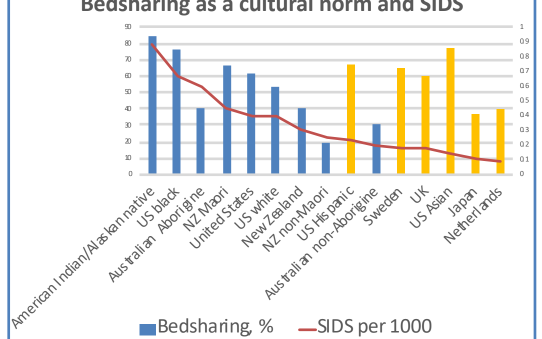

Populations with low SIDS and high to moderate bedsharing

Why? Risk Factor Combinations

- Pregnancy smoking rate*
- Female alcohol use*
- Preterm birth*
- Lack of prenatal care*
- Non-supine sleep
- Formula feeding (lack of breastfeeding)*

*Note overlap with poverty, oppression.

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Asphyxia And Bedsharing

- Much common in marginalized populations
- Associated with hazardous risk factors

Erck Lambert, A. B., et al. (2019). "Sleep-related infant suffocation deaths attributable to soft bedding, overlay, and wedging." Pediatrics 143(5): e20183408.

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Asphyxia And Bedsharing

"Accidental suffocation death is extremely rare among bedsharing breastfeeding infants in the absence of hazardous circumstances."

--**Academy of Breastfeeding Medicine, 2020**

Blair, P. S., Ball H.L, McKenna J.J, Feldman-Winter L, Marinell K.A., Bartick M.C, and ABM. (2020). "Bedsharing and breastfeeding: The Academy of Breastfeeding Medicine protocol #6, Revision 2019." Breastfeed Med 15(1): 5-16.

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Summary

Academy of Breastfeeding Medicine, 2020:

"Existing evidence does not support the conclusion that bedsharing among breastfeeding infants (i.e., breastsleeping) causes sudden infant death syndrome (SIDS) in the absence of known hazards."

Blair, P. S., Ball H.L, McKenna J.J, Feldman-Winter L, Marinell K.A., Bartick M.C, and ABM. (2020). "Bedsharing and breastfeeding: The Academy of Breastfeeding Medicine protocol #6, Revision 2019." Breastfeed Med 15(1): 5-16

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Evidence-based Recommendations For Breastfeeding Dyads

Academy of Breastfeeding Medicine,

Bedsharing and Breastfeeding Protocol, 2020

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Hazardous Circumstances (In Order)

- **Sharing a sofa** with a sleeping adult ("sofa-sharing")
- Infant sleeping next to an adult who is impaired by **alcohol** or drugs
- **Tobacco** exposure
- Sleeping in the prone position
- Never initiating breastfeeding
- Sharing a chair with a sleeping adult
- Sleeping on soft bedding
- Being born preterm or of low birth weight

-Academy of Breastfeeding Medicine, 2020

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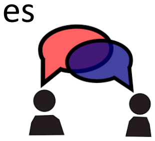
Conversations And Dialogue

- Build trust: Listen, ask questions, don't lecture
- Avoid judgement
- Stigma: prevents people from disclosing long held beliefs

Counseling Strategies



Open-ended questions:

- ''What are your plans for where your baby will sleep?''
- ''What does the sleep area look like?''
- ''Does your baby ever end up in bed with you?'

Emphasis:

- Reduce SOFA-SHARING
- Reduce sharing next to adult with ALCOHOL
  - 18 fold risk for each (Blair 2014)
- Reduce TOBACCO
- Sleep position in bed



Promote Breastfeeding

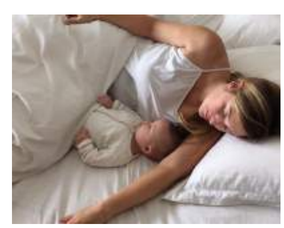
Will reduce prone sleeping
Will reduce sleeping on pillows

Education On Safe Bedsharing To ALL

- Bedsharing is very common
- Is unsafe if unintentional (Vennemann 2012)
- Discussing it will reduce stigma

Safe Bedsharing Also Includes:

- Feed in bed at night
- Bed should be away from a wall, no cords dangling
- No thick covers, etc
- Not on a pillow
  - (firm bed surface)
- Never alone on adult bed
- C-position
  - ("cuddle curl")



Screen Families For High Risk

- Antenatal smoke exposure
- Smokers in the home
- Adults in the house with use of alcohol/drugs
- Preterm infants



What If They Are High Risk?

- Ask questions to encourage dialogue
- Counsel about risks of bedsharing but
- *Educate on safe bedsharing*
- Promote breastfeeding

MANY MAY HAVE LIMITED INTERACTION WITH HEALTHCARE SYSTEM

High Risk Families

- Alternatives include sidecars
- Referral for tobacco, alcohol/substance use disorders
- Consider teaching the “cuddle curl”

Social Determinants of Health

Why are most deaths in marginalized or impoverished communities?

- Mothers alone cannot bear the burden of infant death
- Many moms have min. contact with health care system
- We must look at structural and political factors

Structural Change

Structural Change: Bicycle Fatalities

- “Scan the street for wheels and feet”

Behavioral change

Structural change

Behavioral Change: "Don't Smoke And Bedshare"

BUT moms are hardwired to bedshare, & smoking is addictive & advertised on every corner.

Lahr MB, Rosenberg KD, Lapidus JA. Bedsharing and maternal smoking in a population-based survey of new mothers. Pediatrics. 2005;116(4):e530-542.

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Structural Change: Raise Tobacco Prices, Curb Advertising

Raising tobacco prices associated with markedly and immediate lower infant mortality rates
Filippidis FT, et al. *JAMA Pediatr.* 2017;171(11):1100-1106

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Structural Change: Curbing Tobacco Use Makes Bedsharing Safer

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Structural Change: Increase Baby-friendly Hospitals*

Focus on targeted communities worldwide.

*not in ABM protocol

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Political Changes

- Curbing formula marketing
- Curbing tobacco and alcohol marketing
- Raising tobacco taxes* and alcohol taxes
- Paid sick leave and parental leave

*only tobacco taxes are in ABM protocol

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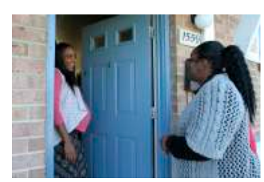
Other Structural Changes*

- ↑Community health workers to at-risk families (increase prenatal care)
- ?Giveaways of sidecars or Pēpi-pods to high risk populations (pilot)
- Ending racial bias in health care* & structural racism



*Only ending racial bias is in ABM Protocol

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Advice Against Bedsharing- Does It Hurt Society?

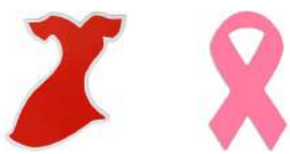
- Undermines breastfeeding
- Moms lose trust in medical system
- Is it effective?
  - Bedsharing rates have gone up in the US
- Takes resources away from where they are needed (eg, advice against couch-sharing)

Summary: Make Bedsharing Safer

- Educate ALL parents on safe bedsharing
- Focus on the most important hazards:
  - Sofas, Alcohol, Tobacco
- Breastfeeding support, Baby-friendly

Why Do I Care As An Internist?

- We will not get women to get the months of lifetime breastfeeding needed to prevent cardiovascular disease, diabetes, and breast cancer if women give up breastfeeding in a few weeks because they can't bedshare.



Thank You!

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