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HEADLINE

Harmony in diversity — A new perspective on human milk oligosaccharides

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The diversity of human milk oligosaccharides (HMOs) has been rarely discussed despite the expanding research on this unique category of human milk components. In principle, **HMO diversity is subject to two major determinants:**

Richness

The total HMO level in human milk has been reported at the range of ~22-24 g/L in colostrum which then gradually declines to ~12-13 g/L in mature milk[1]. Majority of HMOs follow the same descending trend with a few exceptions such as 3'-FL, 3'-SL, DSLNT and LNnT which increase overtime instead[2-4]. A recent longitudinal study by Wu J *et al.* (2020) analyzed milk samples from 59 Chinese mothers and revealed a significant decrease of mean total HMO levels from 10.59 ± 0.30 g/L (postpartum day 3) to 4.90 ± 0.18 g/L (postpartum day 168) in secretors and 7.31 ± 0.32 g/L to 3.65 ± 1.15 g/L in non-secretors respectively[2]. **Non-modifiable and modifiable factors both contribute to HMO richness:**

Genetics	*FUT2* gene expressions determine the mother's secretor status, hence, the presence of α1-2-fucosylated HMOs and *FUT3* with that of α1-3/4-fucosylated HMOs[3]
Ethnicity	Asian secretors may have a mean 2'-FL level lower than their Caucasian counterparts but higher than their African counterparts[2]
Maternal age	Negatively correlated with DFLNT levels[4]
Parity	Positively correlated with LNnT and LNT, negatively correlated with 3'-FL levels[4]
Preterm birth	Positively correlated with 3'-SL (postpartum week 2 to 8), negatively correlated with 6'-SL levels (week 2 to 4)[3]
Breastfeeding duration	Positively correlated with LNH (+ 0.96 month increase in breastfeeding duration each +1 *z* score) and FDSLNH levels (+0.64 month each +1 *z* score)[4]
Solid food introduction	Positively correlated with LNnT (generally lower in early lactation), negatively correlated with 3'-FL levels (otherwise increases overtime)[4]

Structural Variety

All HMOs contain a lactose at the reducing end. This starting unit can be affixed to five key monosaccharides (glucose, galactose, fucose, N-acetyl-glucosamine and/or N-acetyl-neuraminic acid) via numerous variations of molecular bonds to create basic trisaccharides or complex structures with more than a dozen repeats, resulting in the extensive derivation of more than hundred types identified to date[5]. **Aside from the well-studied 2'-FL, new research has begun to investigate the potential physiological role of other predominant HMOs such as LNnT with gut metabolite profiling[6] and food responsiveness in infants[7], 3'-SL with third-trimester glucose homeostasis in non-secretor mothers[8] and LDFT (also known as DFL) with *in vitro* inhibition of inflammatory cytokine release in platelets[9].**

These findings altogether depict the dynamic oligosaccharide profile in human milk. Perhaps in the near future, new evidence will contribute to our understanding of the synergy between individual HMOs in supporting fundamental growth and development of the newborn.

More from WNSC HK...
Human Milk Oligosaccharides (HMOs): magic bullets for optimal immune health

FUT2 = *Fucosyltransferase 2;* ***FUT3*** = *Fucosyltransferase 3;* ***2'-FL*** = *2'-Fucosyllactose;* ***3'-FL*** = *3'-Fucosyllactose;* ***3'-SL*** = *3'-Sialyllactose;* ***6'-SL*** = *6'-Sialyllactose;* ***DSLNT*** = *Disialyllacto-N-tetraose;* ***LNT*** = *Lacto-N-tetraose;* ***LNnT*** = *Lacto-N-neotetraose;* ***LNH*** = *Lacto-N-hexaose;* ***LDFT (or DFL)*** = *Lactodifucotetraose (or Difucosyllactose)*

References: ***1.*** *Urashima T et al. Adv Nutr. 2012;3:473-482S.* ***2.*** *Wu J et al. Curr Dev Nutr. 2020;4(8):nzaa113.* ***3.*** *Austin S et al. Nutrients. 2019;11:1282.* ***4.*** *Azad M et al. J Nutr. 2018;148:1-10.* ***5.*** *Bode L et al. Adv Nutr. 2012;3:383-391S.* ***6.*** *Steenhout P et al. JPGN. 2016;63:S55.* ***7.*** *Plows J et al. Pediatr Obes. 2020:e12686.* ***8.*** *Saben L et al. Nutrients. 2020;12:2209.* ***9.*** *Newburg D et al. J Thromb Thrombolysis. 2016;42:46-55.*

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Choline in the first 1000 days of life

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Choline is an essential nutrient for health, where it has important roles including in lipid transport, neurotransmission, and cell membrane structural support as part of phosphatidylcholine and sphingomyelin[1,2]. Choline is critical during pregnancy for maternal health, as well as supporting membrane biosynthesis for placental development and fetal organ growth[2]. **Beyond prenatal development, choline continues to influence infant health with the growth of the brain and in cognitive measures**[2].

A recent systematic review including evidence from 38 animal and 16 human studies was conducted to look into the inter-relationships between choline and brain development during the first 1000 days of life[1]. Findings from both animal and human studies showed that **choline is a 'neurocognitive' nutrient that has a pivotal role in proper neurodevelopment, where most offspring would benefit from increased dietary intake during this critical period**[1].

In context of the current global COVID-19 pandemic, a study by Freedman *et al.* (2020) suggested choline supplements along with other prenatal vitamins may be important in protecting the fetal brain. It was found that **higher prenatal choline serum levels may help to decrease adverse effects and protect the fetus' developing brain if the mother contracts a moderately severe respiratory virus infection** in early pregnancy at 16 weeks gestation[3]. Infants of infected mothers with higher prenatal serum choline levels (≥ 7.5 mM) had significantly increased ability to maintain attention and to interact with their parents at three months of age based on parent reports, compared to infants of those who had lower prenatal choline levels (< 7.5 mM) (p = 0.006)[3].

Different evidence point to the importance of adequate choline intake during the first 1000 days to support the foundations of neurodevelopment, however **there seems to be a general lack of awareness where many are not meeting dietary intake recommendations**[1,2]. For example, a study found that mean total

choline intake was 173 mg/day in women living in Guangdong (25 to 70 years old, patients admitted to hospital, n = 807)[4], which is well below the 2013 Chinese Recommended Nutrient Intake (Adequate Intake) of 400 mg/day for female adults[5]. In fact, the recently published Scientific Report of the 2020 U.S Dietary Guidelines Advisory Committee highlighted choline as a nutrient that may pose special public health challenges, as it **is widely under consumed including in infants, children, pregnant and lactating women**[6].

The importance of choline across the crucial first 1000 days of life should be reinforced, including in women of childbearing age who could fall pregnant, where **dietary intakes need to be improved through consumption of choline-rich foods and/or dietary supplementation to especially support neurological development and brain function in children**[1,2]. In the previously mentioned Chinese study, it was found that **eggs, chicken and whole milk were the main food sources of choline** in the studied population[4]. It is also important to note that choline does not work in isolation and **evidence shows synergistic effects with other nutrients such as DHA and lutein in human milk on infant neurocognitive development**[2,7].

References: ***1.*** *Derbyshire E and Obeid R. Nutrients. 2020;2:1731.* ***2.*** *Mun JG et al. Nutrients. 2019;11:1125.* ***3.*** *Freeman R et al. J Psychiatr Res. 2020;128:104.* ***4.*** *Zhang CX et al. Cancer Sci. 2013;104:250-258.* ***4.*** *Chinese Nutrition Society. Chinese DRIs Handbook. 2013.* ***6.*** *USDA. Scientific Report of the 2020 Dietary Guidelines Advisory Committee. 2020.* ***7.*** *Cheatham CL and Sheppard KW. Nutrients. 2015;7:9079-9095.*

How to support dietary intake of choline?
Learn more from the WSNC HK info card here!

https://hongkong.wyethnutritionsc.org/brain-science/wsnc-hong-kong-info-card-2017-issue-3-choline-fact-sheet

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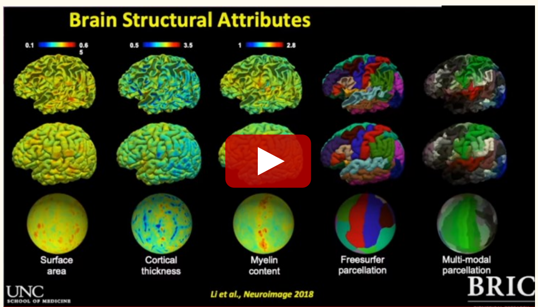
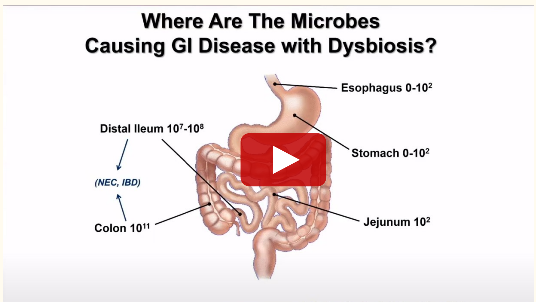


Brain development and nutrition in toddlers
Update from the Baby Connectome Project



Importance of faecal biomarkers and the microbiome's role in child health and disease… Is it really all about the poop?

SCAN HERE TO WATCH

Fermented food and health — Far beyond gut health?

Emily Tai PhD, Mphil, MSc, BSc (Hons)

Fermented food has been an integral part of the daily diet in various cultures over the world[1]. Microorganisms contributing to the fermentation process and their bioactive metabolites have been associated with diverse health benefits including risk reduction of diarrhea, obesity, hypertension and high cholesterol[1,2].

A breakthrough finding in recent years could be the potential benefits on perinatal outcome. In a Japanese cohort study including 77,667 pregnancy cases at low risk of preterm birth, **the risk of early preterm birth (< 34 weeks) was significantly lowered in women with high consumption of miso soup, yogurt and fermented soybeans before pregnancy**[3]. The adjusted odds ratio (OR) of women having miso soup one to two, three to four and ≥ five days per week were 0.58, 0.69 and 0.62 respectively (95% CI: 0.40-0.85, 0.49-0.98, 0.44-0.87), versus those having miso soup < one day per week; the adjusted OR of women eating yogurt ≥ three times weekly was 0.62 (95% CI: 0.44-0.87) compared with those eating yogurt < one time weekly; the adjusted OR of women consuming fermented soybeans ≥ three times weekly was 0.60 (95% CI: 0.43-0.84) when compared with those consuming < one time weekly[3].

Another cross-sectional study including over 600 lactating mothers in Turkey additionally demonstrated a declined incidence of mastitis with increasing consumption of fermented food. Daily consumption of *kefir* (OR = 0.69, 95% CI: 1.18-2.22), home-made yogurt (OR = 0.78, 95% CI: 1.14-1.87), conventional yogurt (OR = 0.81, 95% CI: 1.24-2.46), boza (OR = 0.79, 95% CI 2.19-2.99), tarhana (OR = 0.52, 95% CI 2.47-2.81) and pickle (OR = 0.22, 95% CI: 1.22-2.34) during pregnancy and lactation significantly reduced the risk of mastitis[4]. Diversity of consumed fermented food could protect mothers from mastitis (OR = 0.34, 95% CI: 1.34-2.35)[4]. The study also identified **a few protective variables against mastitis such as starting breastfeeding within the first hour of delivery, longer breastfeeding duration, breastfeeding on both breasts, use of cream on nipple, oral probiotic use and receiving breastfeeding education from an expert**[4].

The protective effect of fermented food may be explained by its beneficial microbial content since microbial dysbiosis has been proposed to associate with the development of mastitis. Women with mastitis had declined microbial diversity, enriched opportunistic pathogens and depleted commensal obligate anaerobes[5]. Hurtado *et al.* (2017) revealed that **oral administration of a probiotic strain *Lactobacillus fermentum* CECT5716 during lactation could significantly reduce the incidence rate (IR) of mastitis among women receiving preventive dose of antibiotic in the context of delivery** (Probiotic group IR = 0.130; Control group IR = 0.263; p = 0.021)[6]. Furthermore, this probiotic intervention in lactating women significantly decreased the incidence of conjunctivitis in their infants (Probiotic group IR = 0.014; Control group IR = 0.070; p = 0.023) whereas the protection against respiratory infections among infants depends on *Staphylococcus* load in human milk and infant faeces[7].

Research is still ongoing to further elucidate the health impact of fermented food and probiotics. Adding fermented food may be a nice idea to enrich flavor and nutritional values of our diet. Let's prepare some tasty fermented choices at home!

Home-made yogurt[9]

Ingredients:
- Milk
- Pre-existing yogurt

Directions:
(1) Create a double boiler with two pots.
(2) Heat the milk to 85°C and then cool down to ~43°C.
(3) Add the starter yogurt to the milk and stir.
(4) Leave it to sit in a warm environment for ~7 hours. Use a crockpot or heating pad to keep the milk warm.
(5) Chill the whole mixture and it is ready to eat!

Home-made *kefir*[8,9]

Ingredients:
- Milk
- *Kefir* grains (comprise a specific and complex mixture of bacteria and yeasts)

Directions:
(1) Add milk to kefir grains in a jar
(2) Stir and cover with a cloth and rubber band
(3) Let the jar sit at room temperature to ferment for 10 to 24 hours
  - Sitting for 12 hours will create a thinner liquid with mild taste
  - Sitting for a longer duration will create a sour taste
(4) Filter and separate *kefir* grains
(5) Keep the *kefir* grains for starting a new fermentation
(6) The *kefir* is ready to drink and can be refrigerated for later enjoyment!

References: 1. Şanlier N et al. Crit Rev Food Sci Nutr. 2019;59(3):506-527. **2.** Marco ML et al. Curr Opin Biotechnol. 2017;44:94-102. **3.** Ito M et al. Environ Health Prev Med. 2019;24(1):25. **4.** Basım P et al. Breastfeed Med. 2020;15(3):163-169. **5.** Patel SH et al. Sci Rep. 2017;7(1):7804. **6.** Hurtado JA et al. Breastfeed Med. 2017;12(4):202-209. **7.** Pastor-Villaescusa B et al. Benef Microbes. 2020;11(3):235-244. **8.** Rosa DD et al. Nutr Res Rev. 2017;30(1):82-96. **9.** Bastyer University. Available at: https://bastyr.edu/news/health-tips-spotlight-1/2013/01/how-make-homemade-yogurt-and-kefir. Accessed on 04Aug2020.

Nutrition News Columns

Bringing to your attention the latest updates from ACIP, SOMANZ and USDA…

National recommendations on the prevention of hepatitis A virus infection in the United States

The Advisory Committee on Immunization Practices (ACIP) has released updates on hepatitis A (HepA) vaccination recommendations. In 2006, ACIP recommended routine HepA vaccination of all children aged 12-23 months. Current new recommendations include a catch-up vaccination for anyone aged 2-18 years who have not previously received HepA vaccine. All persons aged 1 year or older with human immunodeficiency virus (HIV) should also be vaccinated.

Read more from:

U.S. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. 2020;69(5);1-38.

https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6905a1-H.pdf

SOMANZ position paper on nausea and vomiting during pregnancy (NVP) and hyperemesis gravidarum (HG)

The Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) summarized evidence-based practical advice on investigation and management of NVP, HG and associated conditions such as thyroid dysfunction. An algorithm for assessment and management, individual patient management plan and self-assessment tools were also included.

Read more from:

Lowe SA et al. Aust N Z J Obstet Gynaecol. 2020;60(1):34-43.

https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1111/ajo.13084

Scientific Report of 2020 U.S. Dietary Guidelines

In the 2020-2025 Dietary Guidelines for Americans to be published this year, the U.S. Department of Agriculture (USDA) has added recommendations specific to infants, toddlers and women who are pregnant or lactating. This major update enables the new edition to cover dietary recommendations across the entire lifespan.

Read more from:

Dietary Guidelines Advisory Committee. 2020.

Scientific Report of the 2020 Dietary Guidelines Advisory Committee.

https://www.dietaryguidelines.gov/sites/default/files/2020-07/ScientificReport_of_the_2020DietaryGuidelinesAdvisoryCommittee_first-print.pdf

3-Monochloropropane-1,2-diol (3-MCPD) & Glycidol Fatty Acid Esters (GEs)

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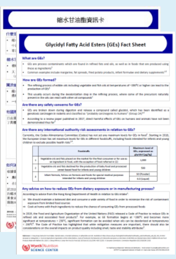

Infographic and expert interview with Mr Gordon Cheung