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Significance of breastfeeding in COVID-19: The first dose of defense?

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Key messages

- Vertical transmission of SARS-CoV-2 was shown possible during the third trimester of pregnancy, however, more evidence is needed to confirm whether breastfeeding plays a significant part
- International authorities, including WHO, advise to support breastfeeding for mothers with suspected or confirmed COVID-19 status while standard precautions should be implemented
- Human milk contains various components that may contribute to the maintenance of neonatal immunity and offer an early dose of defense

As of February 2021, the total vaccinations administered for coronavirus disease 2019 (COVID-19) had come on par with the total confirmed cases worldwide, both at a shocking number of ~103 million[1,2]. While humanity continues to march through the mud and cold of the pandemic, it is undoubtedly our principal mission to continue investigating the pathophysiology of this not-so-novel virus. In particular, findings from pregnancy cases may bring more insights to frontline healthcare professionals in the field of paediatrics and obstetrics.

CAN NEWBORNS BE INFECTED VIA VERTICAL TRANSMISSION?

A meta-analysis by Alexander M *et al.* (2020) summarized 38 cohort and case studies and concluded the occurrence of third-trimester vertical transmission based on 27 positive results of SARS-CoV-2 viral RNA nasopharyngeal swab testing among 936 neonates of infected mothers[3]. Test results from other sites were also examined: 0% (0/51) in amniotic fluid, 0% (0/17) in urine, 3.6% (1/28) in cord blood, 7.7% (2/26) in placenta, 9.7% (3/31) via rectal or anal swab, 3.7% (3/81) by serology, and 4.2% (2/47) from human milk specimens[4-6]. Meanwhile, other studies have alluded the need of additional data before confirming the role of human milk in viral transmission considering the randomness and lack of complete/active viral RNA in positive samples as well as the chances of milk contamination via respiratory droplets[7].

AUTHORITY RECOMMENDATIONS?

"[Mothers with suspected/confirmed COVID-19] should be enabled and supported to breastfeed, if this is what they choose."
– Royal College of Obstetricians & Gynaecologist (RCOG), 2020[8]

"Mother and infant should be enabled to remain together… and to practice skin-to-skin contact, including kangaroo mother care… during establishment of breastfeeding, whether they or their infants have suspected or confirmed COVID-19."
– World Health Organization (WHO), 2020[9]

"Wash hands and wear a mask using soap and water before expressing breastmilk either by hand expression or with a breast pump."
– Centers for Disease Control and Prevention (CDC), 2020[10]

POTENTIAL PROTECTION FROM IMMUNE-MODULATORY HUMAN MILK COMPONENTS?

Immunoglobulin A (IgA) was found to dominate early SAR-CoV-2 viral neutralization among antibodies and sustained a long-lasting concentration detectable in saliva up to 73 days post-symptoms[11]. 12 out of 15 human milk samples from previously infected donors exhibited significant and highly correlated IgA and secretory antibody binding to virus spikes, indicating the potential therapeutic use of secretory IgA[12]. Adequate **vitamin B** helps downregulate pro-inflammatory cytokines, alleviate respiratory distress and potentially prevent or reduce COVID-19 symptoms[13]. **Vitamin C** promotes anti-viral cytokines and free radical synthesis, more, its administration improved the survival rate of COVID-19 patients via the attenuation of excessive immune response activation[14]. **Selenium** helps maintain T cell maturation, functioning and T-cell dependent antibody production[14]. **Human milk oligosaccharides (HMOs)** are unique glycans found in human milk which can mimic the receptor sites of many viruses and therefore inhibit their cell entry and replication[15]. Of note, biosynthesized HMO analogues, namely 2'-fucosyllactose (2'-FL) and Lacto-N-neotetraose (LNnT), have been clinically proven to reduce the rate of parental reported morbidities including bronchitis and lower respiratory tract infection throughout the first year of life[15].

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Connecting the dots:
From infant dietary components to microbiota and allergies

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Key messages

- The 20-year follow-up results of the GINI study confirm that early nutritional intervention involving hydrolysed proteins in at-risk infants has a preventive effect for eczema that lasts until adulthood
- A local study found bacterial strains of the class Clostridia in the gut were associated with eczema risk in infants
- HMOs have been postulated to potentially impact on allergy risk via the gut microbiota, while *in vitro* studies have shown they reduce adhesion of clostridial strains to the intestinal epithelium

The German Infant Nutritional Intervention (GINI) study has recently published the 20-year follow-up data, continuing to evaluate the long-term effects of hydrolysed formulae on allergic diseases in at-risk children[1]. With more than 50% retention in the study groups, intention-to-treat (ITT) analyses of the 20-year follow-up data showed different protective effects of partially hydrolysed whey (pHF-W), extensively hydrolysed casein (eHF-C) formulae and extensively hydrolyzed whey formula (eHF-W), in comparison to formula based on intact cow's milk (CMF) **(Table 1)**.

Table 1 - Different formulae feeding with significant effects on allergic diseases after ITT analyses (in blue)[1]

	CMF	pHF-W	eHF-W	eHF-C
ITT, number of followed children (n = 2,252)	556	557	559	580
Asthma prevalence, 16 to 20 yrs, aOR (95% CI)	1	**0.44 (0.23-0.85)**	0.64 (0.35-1.16)	**0.46 (0.24-0.87)**
Eczema prevalence, 16 to 20 yrs,	1	0.60 (0.32-1.13)	0.94 (0.53-1.66)	**0.49 (0.25-0.94)**
Eczema cumulative incidence, birth to 20 yrs,	1	**0.73 (0.57-0.94)**	0.86 (0.68-1.10)	**0.61 (0.47-0.78)**

Note: aOR = adjusted odds ratio; RR = relative risks; CI = confidence interval

These findings confirm that early nutritional intervention involving hydrolysed proteins has a preventive effect that lasts until adulthood for both eczema and allergic airway manifestation, among at-risk infants when breastfeeding is not available. Authors of the GINI study suggested these effects may depend on the specific hydrolyzation processes and their effectiveness in reducing potentially allergy-inducing epitopes[1,2]. It was also highlighted that indirect effects on the immune system such as via the gut microbiota cannot be excluded[1].

The importance of gut microbiota is reflected in a local study by Chan *et al.* (2021), where it was identified as a potential risk factor for eczema development[3]. From birth to one year of age, the increased levels of Clostridia (Class) and *Hungatella hathewayi* (species) in the gut were significantly greater in the eczema group (n = 24) than the control group (n = 36) (p = 0.027 and p = 0.004, respectively)[3]. Multivariate analyses showed changes in the abundance of *Hungatella hathewayi* were significantly associated with an increased risk of developing eczema at one years old (p = 0.005)[3]. These results demonstrated that bacterial strains of the class Clostridia were associated with eczema risk[3].

There have also been postulations that human milk oligosaccharides (HMOs) such as 2'-fucosyllactose (2'-FL) may impact allergy risk via their influence on early microbiota establishment[4]. Interestingly, in vitro studies have demonstrated the selectivity of different gut bacteria on utilizing HMOs as substrates[5,6]. While bifidobacteria and bacteroides strains can metabolise HMOs, strains such as clostridia were not able to grow on HMOs[5,6]. In addition, it was found that HMOs can act as receptor decoys and reduce the adhesion of clostridial strains to the intestinal epithelium, which is an important factor influencing the colonization of the gut microbiota[7]. Current research shows the potential of gut microbiota as a linkage between infant dietary components and allergy risk, presenting an opportunity for early intervention.

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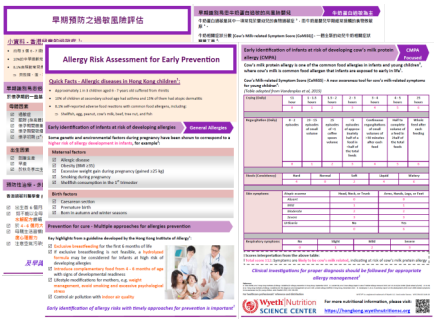
ADDITIONAL READING...

WNSC HK Factsheet on Allergy Risk Assessment for Early Prevention

https://hongkong.wyethnutritionsc.org/allergies-immunity/wnsc-hong-kong-info-card-allergy-risk-assessment-early-prevention



Genetic variation in fatty acid metabolism and its health influences

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

Quick facts on fatty acid desaturases[1,2]

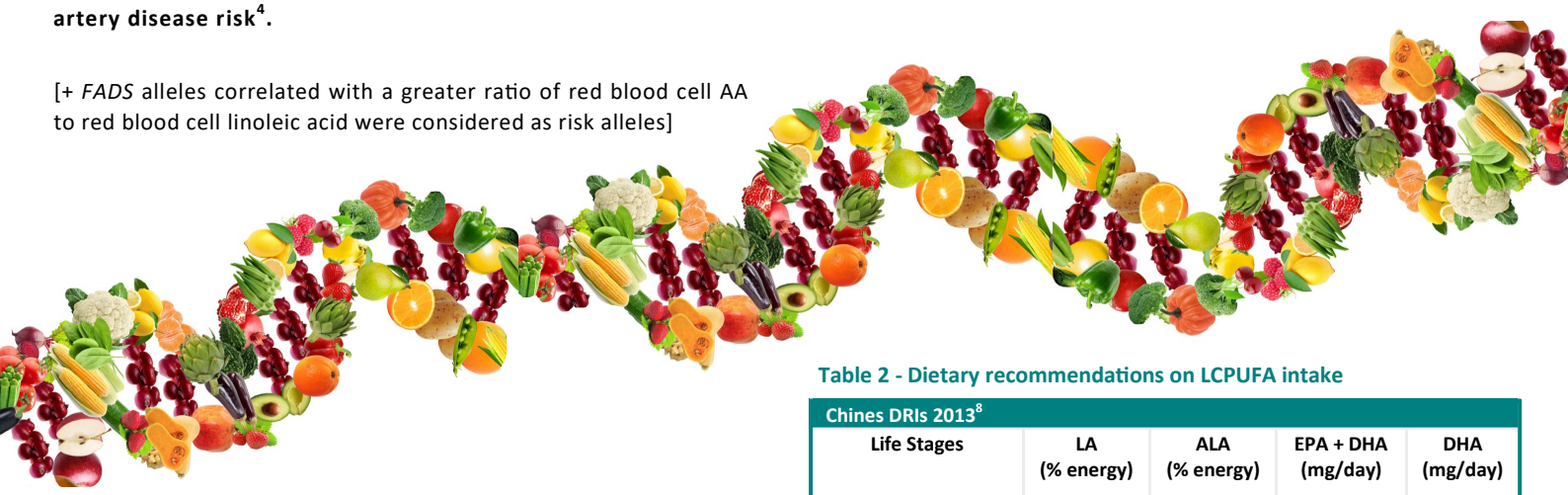
- The human body can synthesize long-chain polyunsaturated fatty acids (LCPUFAs) from essential fatty acids [i.e. DHA from alpha-linolenic acid (ALA)] through a series of desaturation and elongation processes
- Fatty acid desaturases (FADSs) are enzymes involved in the desaturation step

In addition to dietary intake, genetic variation in the fatty acid desaturase (*FADS*) gene cluster has marked influences on LCPUFAs status that is related to numerous health outcomes[1,2]:

CARDIOVASCULAR HEALTH

A significant difference in the incidence of coronary heart artery disease of 84.1% and 65.8% for people with 6-7 versus 2-3 risk alleles[+] was noted ($p < 0.05$)[3]. A higher AA to linoleic acid (LA) ratio was identified as an independent risk factor for cardiovascular diseases whereas FADS genotypes leading to a greater desaturase activity may contribute to an increased risk of cardiovascular disease through proinflammatory responses favoring atherosclerotic vascular damage[3]. A review analysis has summarized that ***FADS* genotypes associated with decreased desaturase activity were linked to lower inflammation, total cholesterol, LDL-cholesterol and coronary artery disease risk[4].**

[+ *FADS* alleles correlated with a greater ratio of red blood cell AA to red blood cell linoleic acid were considered as risk alleles]



PREGNANCY OUTCOMES

Pregnant women with *FADS* genotypes associated with decreased desaturase activity had lower level of DHA in red blood cell phospholipids[5]. Moltó-Puigmartí *et al.* has also demonstrated that **maternal *FADS* genotypes (rs174556 single nucleotide polymorphism, SNP) was related with pregnancy duration and birth weight that were positively influenced by maternal DHA intake[6]** while no involvement of fetal genotype was observed6. Women who were homozygous for the *FADS* alleles associated with decreased desaturase activities (i.e. minor alleles) had 2-day shorter pregnancies ($p = 0.035$) and infants with ~140 g lighter ($p = 0.006$) compared with those who were homozygous for the *FADS* alleles associated with increased desaturase activities (i.e. major alleles)[6].

HUMAN MILK CONTENT

A Taiwanese study has elucidated that **dietary intake and genotype are two key factors influencing DHA proportion in human milk[7]**. There was a positive association between total DHA intake and DHA level in human milk[7]. A 0.28% (% fatty acid) decline in DHA content in human milk from mothers with high versus low genetic risk (stratified by whether minor allele numbers were ≥ 3 in rs1535 and rs174448) was noted[7]. Dietary DHA conferred benefits to mothers with a low genetic risk while increasing DHA intake did not impact DHA content in human milk among mothers with a high genetic risk[7].

Emerging evidence on the role of *FADS* genotypes could open new opportunities on personalized precision nutrition and it would be beneficial to follow expert recommendations on LCPUFA intake **(Table 2)**:

Table 2 - Dietary recommendations on LCPUFA intake

Chines DRIs 2013[8]				
Life Stages	**LA (% energy)**	**ALA (% energy)**	**EPA + DHA (mg/day)**	**DHA (mg/day)**
0 to < 6 months	7.3	0.87	ND	100
6 months to < 1 year	6.0	0.66	ND	100
1 year to < 4 years	4.0	0.60	ND	100
4 to < 18 years	4.0	0.60	ND	ND
18 to 80 years	4.0	0.60	250-2000	ND
Pregnant women	4.0	0.60	250	200
Lactating women	4.0	0.60	250	200

Remarks:

- ND = Not determined
- WHO recommends adults should have 250 mg of DHA and EPA daily[9]
- An expert group stated that higher DHA intake (600 - 800 mg) during pregnancy may provide greater protection against early preterm birth[10]

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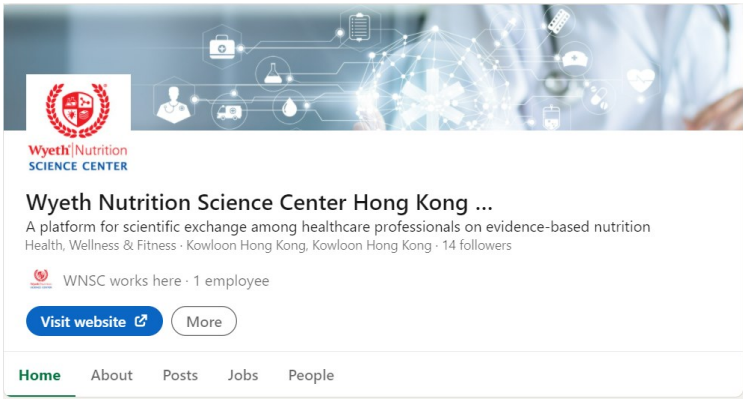

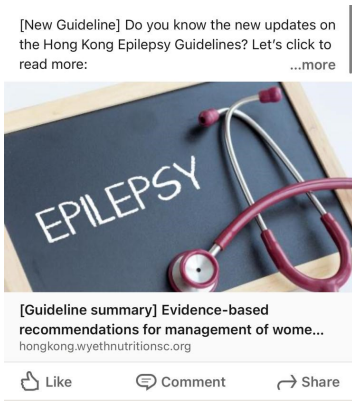

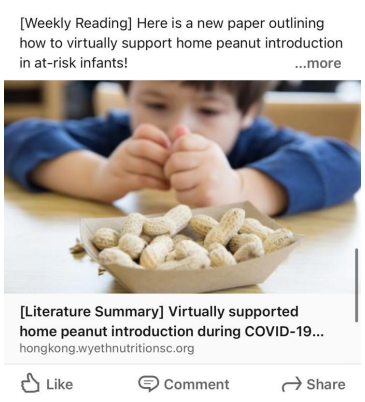

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Bitesize Nutrition

NUTRITION MYTH BUSTER...

"Prebiotics such as galacto-oligosaccharide (GOS), fructo-oligosaccharides (FOS) and inulin are all oligosaccharides naturally found in human milk."

MYTH! While being commonly used as ingredients for food products such as milk formula for their prebiotic properties, **these non-digestible carbohydrates are structurally very different from oligosaccharides naturally found in human milk (i.e. human milk oligosaccharides, HMOs).** For example, galacto-oligosaccharides (GOS) are synthetic mixtures of oligosaccharides derived from the enzymatic glycosylation of lactose which typically consist of two to ten molecules of galactose and one molecule of glucose; whereas HMOs are characterized by having a lactose backbone bounded to various types of residues such as a fucose molecule at the galactose terminal end (to form 2'-fucosyllactose, 2'-FL). Since most of the functional properties of HMOs are thought to be structure-specific, it is unlikely that the above prebiotic ingredients can provide similar health benefits as described for HMOs.

Reference: **1.** *Bode L et al. Adv Nutr. 2012;3:383S-391S.*

More on our website!

NUTRITION A TO Z...

R for Recommended Dietary Allowance (RDA):

Established by the Food and Nutrition Board of the Institute of Medicine, **Recommended Dietary Allowance (RDA)** is the set of nutrient-based reference values which represent the average daily level of intake sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals. For example, the RDA of folate for pregnant women of all ages is 600 mcg per day.

S for *sn*-2 palmitate:

Palmitic acid constitutes 20-25% of total fatty acids in human milk, of which 70% is esterified to the *sn*-2 position of the milk triacylglycerols (***sn-2* palmitate**) and is well absorbed. In contrary, palmitic acid esterified to the *sn*-1 or *sn*-3 positions will result in intestinal calcium binding, forming fatty acid calcium soaps that are excreted in feces, leading to hard stools and calcium loss.

References: **1.** *National Institutes of Health. Dietary Supplement Fact Sheets: Folate. Available at: https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/. Accessed on 19Feb2021.* **2.** *Innis SM et al. Lipids. 1994; 29:541-545.* **3.** *Yao M et al. J Pediatr Gastroenterol Nutr. 2014;59:440-448.*

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