

Infant & Young Child Feeding n Nutrition in Perspective

透視嬰幼兒餵哺與營養

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Breastfeeding and Gut Health: from Prematurity to Adulthood

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Introduction

Breastmilk is the best nutrition for infants. It has a myriad of health benefits for the infant and mother. There is an abundance of unique components in breastmilk which have tremendous beneficial effects for the growing infant. The gastrointestinal tract is one of the most important immune organs in the human body as 70% of the



immune cells are located there. **Breastmilk** does not only **affect the microbiota of the gut**, but also **the immune system and gut health**, both in the short and the longer terms. In this article, we review the health benefits of breastmilk on the gut, from prematurity to adulthood.

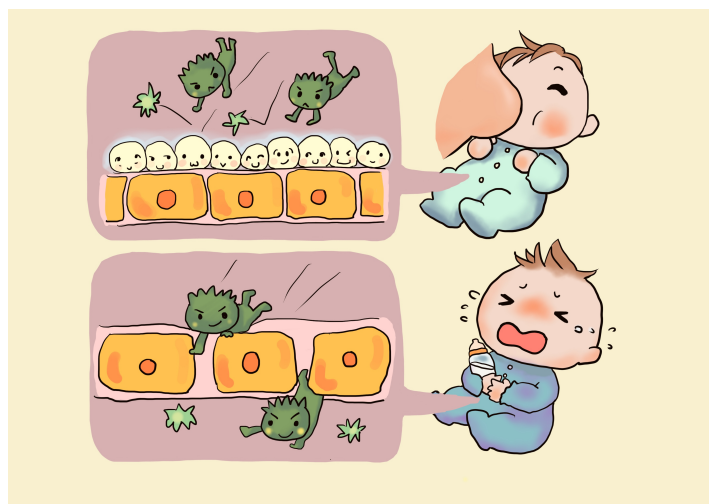
Necrotising Enterocolitis (NEC)

NEC is a severe inflammation of the gastrointestinal tract and the **commonest gastrointestinal emergency in prematurity**, affecting about 7% of premature babies. Patients can have multi-organ involvement which ends up with significant morbidity and mortality such as prolonged hospital stay, intestinal failure, short gut syndrome, etc. **Breastmilk feeding**, with its immunomodulating factors including human milk oligosaccharides, lactoferrin, antimicrobial peptides, and soluble IgA, is **the only proven nutritional strategy that contributes to a decreased risk of NEC**. The **protective effect** of breastmilk is also **dose dependent**, with a higher intake of breastmilk leading to higher protection against developing NEC¹. In a meta-analysis, for preterm and low birth weight infants whose mothers do not produce enough breastmilk, **donor breastmilk feeding also decreases the risk of NEC**. Formula

feeding increased the risk of necrotising enterocolitis by almost 2 folds (risk ratio (RR) 1.87, 95% confidence interval (CI) 1.23 – 2.85)². In sum, **breastmilk should be used to feed premature babies whenever possible**, as it provides the optimal nutrition and lowers the risk of NEC.

Gastroenteritis and Diarrhoea

Gastroenteritis and diarrhoea are common among children. Globally, between 3 and 5 billion children per year suffer from acute gastroenteritis, resulting in 1.3 million deaths because of its complications, especially in children younger than 2 years of age in developing countries. In Hong Kong, gastroenteritis and diarrhoeal illness are rare causes of mortality, but account for significant



economic burdens and societal losses. Rotavirus infection was associated with 3.4% (1 in 30) of hospital admissions in children under 5 years of age in Hong Kong³. **Breastmilk protects against diarrhoea by coating the intestinal lining and killing pathogens that can cause infections**. The risk of diarrhoea in infants under 6 months is lower in those who are breastfed (pooled relative risk (RR) 0.37, 95% CI 0.27 – 0.50)⁴. The estimated relative risk of hospitalisation for diarrhoea illness is elevated among infants not breastfeeding compared to those with any breastfeeding⁵. Not breastfeeding also results in an excess risk of diarrhoea mortality (RR 2.18, 95% CI 1.14-4.16) compared to breastfeeding, in children 6 to 23 months of age⁵.

Celiac Disease

Celiac disease is an immune-mediated inflammatory disease of the small intestine caused by sensitivity to dietary gluten and related proteins in genetically predisposed individuals. It affects 0.5 – 1% of the European and Northern American populations. However, it is not common in Chinese, especially those in the southern part of China. There is evidence suggesting that **never versus ever being fed human milk is associated with a higher risk of celiac disease**⁶. This **protective effect** of breastfeeding in Celiac disease is hypothesised to have been **mediated through different mechanisms**⁷, namely, (1) the presence of gluten-specific IgA antibodies and immune system modulators in breastmilk may influence gluten tolerance induction; (2) breast-fed children are more likely to ingest less amount of gluten; (3) breastfeeding may delay infants' encounter with cow's milk protein; and (4) human breastmilk

modulates infants' microbiome composition which has protective effects. However, the relationships between shorter versus longer durations of any breastmilk feeding, shorter versus longer durations of exclusive breastmilk feeding, feeding a lower versus higher intensity, proportion, or amount of breastmilk to mixed-fed infants and celiac disease outcomes are not well established.

Inflammatory Bowel Disease (IBD)

IBD is a disease of chronic inflammation of the gastrointestinal tract. It can be classified as Crohn's disease (CD) and ulcerative colitis (UC). The incidence of IBD has increased dramatically over the past few decades. In Hong Kong, there is a 30-fold increase in the age-adjusted incidence of IBD from 0.10 (95% CI 0.06 – 0.16) per 100,000 in 1985 to 3.12 (95% CI 2.88 – 3.38) per 100,000 in 2014. The overall crude prevalence of IBD was 45.81 per 100,000 (95% CI 44.04 – 47.58) in 2015⁸. IBD has a significant impact on the quality of life of the patients and poses an economic burden to the health care system. About 15.3% of CD and 1.6% of UC patients require expensive anti-tumour necrosis factor treatment. In addition, the 5-year actuarial bowel resection rates for patients with CD and UC are 25.7% and 2.1 % respectively. Moreover, IBD is also a risk factor for developing colorectal cancers, which cause significant mortality. Environmental factors play significant roles in the development of IBD. Having been breastfed for more than 12 months decreases the odds for CD (adjusted Odds Ratio (aOR) 0.10, 95% CI 0.04 – 0.30) and UC (aOR 0.16, 95% CI 0.08 – 0.31) in Asia⁹. In a meta-analysis comprising 7536 patients with CD, 7353 with UC and 330 222 controls¹⁰, **ever-breastfeeding is associated with a lower risk of CD (OR 0.71, 95% CI 0.59 – 0.85) and UC (OR 0.78, 95% CI 0.67 – 0.91). The association between breastfeeding and risks of IBD is dose dependent.** The risk further decreases when breastfeeding for at least 12 months is compared to that for 3 to 6 months. This **protective effect** is observed in all ethnic groups, and the magnitude of protection is **significantly greater among Asians** (OR 0.31, 95% CI 0.20 – 0.48).

There are several mechanisms involved in the protective effects of breastfeeding on the risk of developing CD or UC. First, non-breastfed infants have an abundance of peptostreptococci in the gastrointestinal tract, such as *Clostridium difficile*, which predisposes to immune-mediated diseases. Second, breastfeeding protects against childhood infections, which in turn, decrease antibiotic exposure. Both childhood infections and antibiotics exposure increase the risk of IBD. Third, components of breastmilk, such as the epidermal growth factor, insulin-like growth factor, leptin and adiponectin, modulate inflammatory response and reduce the risk of immune-mediated diseases.

Conclusions

Breastfeeding is the optimum mode of feeding for the newborn and confers immense health benefits to the developing infant. Its positive health impacts are not limited to the gastrointestinal system but a range of organs, systems and functions, e.g., better neuro-behavioural outcomes, protective effects in respiratory infection, otitis media, urinary infection and sepsis, as well as the sudden infant death syndrome. In addition to macro and micronutrients and bioactive compounds, now we also understand that **breastmilk contains a plethora of bacterial species with its own unique microbiome, which plays a vital role in inoculating the infant gut with favourable bacteria after birth.** With further research, we will certainly learn more about the implications on the development of the immature immune system, and its impact on the health of the individual, from infancy to adulthood.

Key Messages:

1. The unique components in breastmilk not only affect the microbiota of the gut, but also the development of the immune system, which impact health from infancy to adulthood.
母乳中的獨特成分不只影響孩子腸道菌叢的生長，亦有助免疫系統的發育，對從嬰兒到成年期的健康都有深遠的影響。
2. Breastmilk protects against diarrhoea by coating the intestinal lining and killing pathogens that can cause infections.
母乳在嬰兒的腸道建立一道保護塗層，並消滅可引起感染的病原體，以減低患腹瀉的機會。
3. Breastmilk should be used to feed premature babies whenever possible, as it provides the optimal nutrition and lowers the risk of necrotising enterocolitis.
母乳可為早產兒提供最佳營養，和減低患壞死性小腸結腸炎的風險。所以，應盡可能以母乳餵養早產兒。
4. Breastfeeding is associated with a lower risk of inflammatory bowel disease, with the magnitude of protection significantly greater among Asians.
母乳餵哺可減低孩子日後患炎症性腸病的機會，這保護在亞洲人尤其顯注。

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