



Background and Transparency: This short report was commissioned by Biofloratech Ltd, who manufacture Labinic® drops, which contain *Lactobacillus Acidophilus NCFM*, *Bifidobacterium infantis Bi-26* and *Bifidobacterium bifidum Bb-06*. Labinic is completely stable at room temperature for at least 2 years, is allergen-free and contains no animal products.

American Gastroenterological Association August 2020: Lactobacillus and Bifidobacterium combination significantly reduces severe NEC

Preidis GA, Weizman AV, Kashyap PC, Morgan RL. AGA Technical Review on the Role of Probiotics in the Management of Gastrointestinal Disorders. *Gastroenterology*, 2020;159(2):708-738.e4. doi:10.1053/j.gastro.2020.05.060

With commentary on the paper by renowned Neonatologist Keith Barrington

<https://neonatalresearch.org/2020/08/24/probiotics-save-the-lives-or-preterm-infants-find-a-reliable-source/>

This month the AGA published a systematic review/network analysis covering 63 trials in over 15,000 babies. The review showed that probiotics were safe and there was a substantial reduction in severe NEC (OR 0.35(0.2-0.59).

Keith Barrington comments that “all at risk babies should be receiving probiotics” and specifically a mixture of Lactobacilli and Bifidobacteria. The importance of a high quality manufacturing process, which includes being produced to GMP standards.

Labinic is produced in bespoke GMP-standard facilities with microbiological testing for purity, dosing and contaminants as well as stability data. As Barrington says “there is reason to believe what is in the bottle is actually what it says on the label”.

** DISCLAIMER: This short review was produced for Biofloratech Ltd who manufacture and supply Labinic Drops, a multispecies liquid bio-flora food supplement. This review is written in technical language and is only intended for professional use. The content is not intended to advertise nor to describe any health claim for Labinic Drops, and all words including “probiotic” are used purely in their scientific WHO-approved forms. The purpose of the review is to stimulate discussion, debate and formulate research questions for the future. www.biofloratech.com



Probiotics reduce NEC and mortality in 23-29 week population

Gray, A., Messina JA., Cortina C.c et al Probiotic Use and Safety in the Neonatal Intensive Care Unit: A Matched Cohort Study. J. Peds 2020;222:59-64

In [this recent paper](#), the authors tackle the use of probiotics in a premature population from 23 to 29 weeks gestation. With the known relationship of risk from NEC and mortality to immaturity, this is a relevant population and the data was collected over 19 years. Only 5% of babies received probiotics. Those who did had reductions in NEC (OR 0.62) and death (OR 0.52). There was however an increase in Candida infection (OR 2.23) but not in sepsis/meningitis.

The most frequently used species were Lactobacillus and Bifidobacteria. The association with increased Candida infection is in contrast to previous publications showing reductions in such infections in babies given probiotics. The absolute difference, however, is <1% and may be a chance finding. It is certainly something to be vigilant for, but it is likely than antibiotic stewardship has improved over the years in addition to ventilation, hygiene and feeding practices, which may also account for differences.

Overall the authors felt that the data supported the safety profile of probiotics and the reductions in NEC and death are similar proportions to that previously reported in other meta-analyses.

Dysbiosis due to antibiotic exposure associated with allergies

Zven, SE., Susi A., Mitre E., Nyland CM. Association Between Use of Multiple Classes of Antibiotic in Infancy and Allergic Disease in Childhood. Jama Pediatrics (2019)

A [recent paper](#) examined outcomes from nearly 800,000 children in the US, between 2001 and 2013 who had been exposed to antibiotics in the first 6 months of life. The data showed a strong association with allergic disease, and the greater the antibiotic exposure the greater the risk. The inference is that disturbance of the microbiome is a risk factor for developing allergies. The authors said that there was an association of an 8% risk for food allergies up to 47%

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Not just antibiotics that can cause dysbiosis

Mitre E, Susi A, Kropp LE, Schwartz DJ, Gorman GH, Nylund CM. Association between use of acid-suppressive medications and antibiotics during infancy and allergic diseases in early childhood. *JAMA Pediatr.* 2018;172(6)

An association between antacids and necrotising enterocolitis led to Neonatologists stopping the use of drugs such as ranitidine and omeprazole in preterm babies. The hypothesis from [this paper](#) is that the dysbiosis caused by the antacids is implicated in the development of allergies too.

It is also interesting that, with regard to the neonatal concerns about H2-blockers and NEC, one of the earliest papers was published in 2006 <https://pubmed.ncbi.nlm.nih.gov/16390920/>

They noted that their retrospective data showing increased incidence of NEC was “in agreement with a previous RCT of acidification of infant feeds, that showed a reduction in NEC”. This was back in 1990, by Carrion and Egan, and they added HCl to infant feeds to test the hypothesis that gastric pH affected the colonisation by enteric bacteria. They found, despite the small sample size of 34 babies, a significant reduction in NEC.

Acidification of the gut appears to be important. *L. Acidophilus* NCFM, one of the components of Labinic Drops, produces L- and D-lactate (predominantly L-lactate) and the acidification properties of this bacteria may play a key role in the reduction of NEC and mortality in babies on Labinic noted in the study by Robertson et al. <https://pubmed.ncbi.nlm.nih.gov/31666311/>

Artificial Sweeteners – Also bad for the microbiome....

Suez J, Korem T, Zeevi D, Zilberman-Schapira G, Thaïss CA *et al.* Artificial Sweeteners induce glucose intolerance by altering the gut microbiota. *Nature* 2014;514:181

Whilst looking at dysbiosis, we found this paper from Nature in 2014. This research group examined the impact of artificial sweeteners on the intestinal microbiome. In studies of humans and mice, they convincingly show that intake of artificial sweeteners have a

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detrimental effect on the microbiome, which in turn leads to impairment of glucose tolerance. This adverse effect could be transferred by faecal transplantation.

The dysbiotic microbiome was associated with Type-2 diabetes and obesity. There was variability between subjects in their responses to artificial sweeteners, leading the authors to speculate that the individual dysbiotic pattern could be associated with clinical disease variation. They wonder if, paradoxically, sweeteners are in fact a driver for the increases in diabetes seen since their introduction.

We therefore wondered if breastfeeding mothers, and milk bank donors, be asked to stop using artificial sweeteners in their diets, given the sensitivity of the neonatal microbiome, and the risks of early adverse programming? We don't know the levels of artificial sweeteners in breast milk, and we know that some probiotic mixtures contain sweeteners (Labinic doesn't).

Thank you for reading this, we hope you found it interesting. Please feel free to share with healthcare professional colleagues.

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