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### Letter to the Editor:

## Vitamin K – missed at peril: the case for extra supplementation to prevent deficiency in breastfed preterm infants

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Vitamin K deficiency bleeding (VKDB) is a rare but potentially-devastating disease which is essentially preventable by prophylactic vitamin K (VK) at birth, and adequate dietary VK intake thereafter. The ultimate consequence of missing prophylaxis, especially for exclusively-breastfed preterm babies, was highlighted by the tragic death of a 34-week gestation boy who suffered catastrophic intracranial VKDB 4-weeks post discharge.<sup>1</sup> The hospital's omission of VK at birth - despite parental wishes - was deemed "*gross failure in medical care amounting to neglect*" by the Coroner.<sup>1</sup>

Parents have the right to decline VK prophylaxis against medical advice and are not deemed neglectful, even though this places their newborns at risk of serious harm. Parental refusal of VK prophylaxis, and thus number of babies at risk of VKDB, is increasing.<sup>2,3</sup> Conflation of the VK 'shot' with anti-vaccine rhetoric on social media may be further contributing.<sup>4</sup>

Recognising the devastation caused by late VKDB, we wish to emphasise the importance of assuring both VK prophylaxis at birth *and* adequate ongoing VK intakes, particularly for breastfeeding preterm babies. In ex-preterm babies given routine VK prophylaxis at birth, late-onset VKDB cases are reported in large epidemiological surveys,<sup>2,3</sup> and in our recent experience,<sup>5</sup> with exclusive breastfeeding/human milk-only diet the sole identifiable risk factor. For very preterm babies, by the time of discharge, the large prophylactic VK dose given at birth is distant and its protective efficacy will have waned substantially such that they have become completely reliant upon adequate ongoing dietary VK intake for sustained protection.

A preterm infant on full exclusive-breastmilk feeds (150mL/kg/day) receives only a thirtieth of their currently recommended VK intake of 8–10µg/kg/day.<sup>6</sup> A prospective observational study in exclusively-breastfed preterm infants who all received intramuscular prophylaxis at birth showed that some already had undetectable VK<sub>1</sub> (phyloquinone) concentrations prior to discharge; importantly, the majority who remained exclusively breastfed post-discharge had compelling biochemical evidence of functional subclinical VK deficiency by 2-3 months corrected age.<sup>6</sup>

Current multivitamin supplements (Abidec/Dalivit) given to breastfed preterm infants throughout infancy provide recommended vitamin D intake (also supplementary A, B, C vitamins), but contain no VK. VK is the forgotten vitamin. Until a more-complete VK-containing multivitamin supplement is commercially available, we recommend routine additional VK<sub>1</sub> supplementation of preterm infants from the time of exclusive, unfortified breastmilk feeding/discharge to improve intakes in early infancy and guard against subsequent deficiency.

We suggest supplementation continues until at least 3 months corrected age. Options could include: i) NeoKay oral drops (Neoceuticals Ltd; 200µg/mL VK<sub>1</sub>) dose 50µg (0.25mL via dropper) once daily to provide daily VK<sub>1</sub> intake comparable to that from formula milks which are supplemented to meet current recommendations (VK<sub>1</sub> content typically 60-80µg/L); ii) Neokay oral capsules (Neoceuticals Ltd) 1mg VK<sub>1</sub> (one capsule) once weekly; iii) oral Konakion MM Paediatric (phytomenadione 2mg in 0.2mL; Neon Healthcare Ltd) capsules, 2mg once monthly; iv) intramuscularly, a single further Konakion MM Paediatric 1mg injection at discharge - this should protect for up to 3 months and would avoid compliance issues but may be far less acceptable to parents and babies. Any chosen intervention merits surveillance but all should prevent subclinical VK deficiency in early infancy and abolish the very small but real risk of clinical VKDB in otherwise-healthy breastfed preterm infants. This would potentially save lives, including those who missed prophylaxis at birth.

Regarding exclusively breastfed *term* infants: a recent observational study suggests that they too should be given daily oral VK<sub>1</sub> supplementation during their first 3 postnatal months to avoid the risk of VK insufficiency.<sup>7</sup>

The National Institute for Health and Care Excellence (NICE) has made recommendations for vitamin D supplementation to prevent deficiency. We request that NICE now reviews the need for wider practice change for VK supplementation to protect all future preterm and term breastfed infants from another entirely-preventable essential micronutrient deficiency.

**Author contributions:** PC wrote the first and last manuscript draft. All authors contributed to manuscript revisions and approved the final version.

**Competing interests/ Conflict of interest statement:** AP and NM are the parents of a preterm baby who died due to vitamin K deficiency bleeding after missed prophylaxis at birth. MJS has previously acted as an expert witness to the Court in medico-legal cases involving vitamin K deficiency bleeding. PC, DJH and MJS have provided intellectual input to AP who is developing a PIVKA-II test which may have diagnostic utility for diagnosis and prevention of vitamin K deficiency. NDE and MF previously served on the ESPGHAN Committee on Nutrition and were co-authors of the 2016 ESPGHAN Position Paper ‘Prevention of Vitamin K Deficiency Bleeding in Newborn Infants’. There are no other relevant competing interests or conflicts of interest to declare in relation to this work.

**Ethics approval:** Not required.

**Dedication:** This contribution is dedicated in memoriam William Moris-Patto.

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