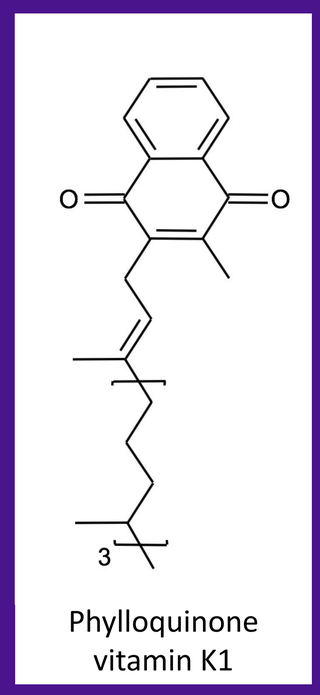
Preterm infants who remain exclusively **human milk fed** post NICU discharge are at **high risk** of developing **vitamin K deficiency** in early infancy



Phylloquinone
vitamin K1

HIGH PREVALENCE OF SUBCLINICAL VITAMIN K_1 DEFICIENCY AMONG HUMAN MILK-FED PRETERM INFANTS IN EARLY INFANCY

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BACKGROUND

- Vitamin K (VK) status of preterm infants post-NICU discharge and in early infancy is unknown
- Exclusive breast milk feeding is often the only factor identifiable in cases of idiopathic VK deficiency bleeding
- Despite the low VK content of human milk, VK supplements are not routinely given to human milk-fed preterm infants after NICU discharge; in contrast, vitamins A, B, C, D, and E are widely given

AIM

To examine the VK status of breast milk fed preterm infants nearing discharge and in early infancy.

HYPOTHESIS

In the absence of extra VK supplementation at/after discharge home, preterm babies who remain exclusively or predominantly human milk fed will have a high prevalence of subclinical VK deficiency in early infancy.

METHODS

Design: Prospective, multicentre, observational cohort study with ethics approval
Included: preterm infants born <33 weeks' gestation and exclusively or predominantly human milk fed, approaching NICU discharge.
Excluded: infants with cholestasis.
Measures of VK status: serum concentrations of vitamin K_1 (VK_1) and PIVKA-II (Protein Induced by Vitamin K Absence/antagonism of blood clotting factor II; undercarboxylated prothrombin)
Timing of assessment: Samples taken at two time-points: ~35 weeks postmenstrual age (PMA) for baseline VK status, and at ~2 months corrected age (CA) (primary outcome).

Definitions used for 'Satisfactory' and 'Deficiency' of vitamin K status

Satisfactory VK status: normal PIVKA-II (<50.9 mAU/mL)
VK deficiency: raised PIVKA-II (≥51.0 mAU/mL)

MAIN RESULTS:

VK status approaching NICU discharge
Of n=45 infants assessed prior to discharge (at median PMA 35+1): **only 1/45 (2%) was VK deficient**, an exclusively breast fed 23+6-week gestation baby.

VK status in early infancy:
N=37 completed the study, at median CA 8 weeks. By this time only 12/37 (32%) remained exclusively breast milk (BM) fed. Overall by 8 weeks CA, 9/37 (24%) infants had developed VK deficiency (as shown by ↑PIVKA-II).
But **of BM-fed infants 8/12 (67%) were VK deficient** vs. only 1/25 (4%) FM/mixed feeding babies, p=0.0001 **(Figure)**.

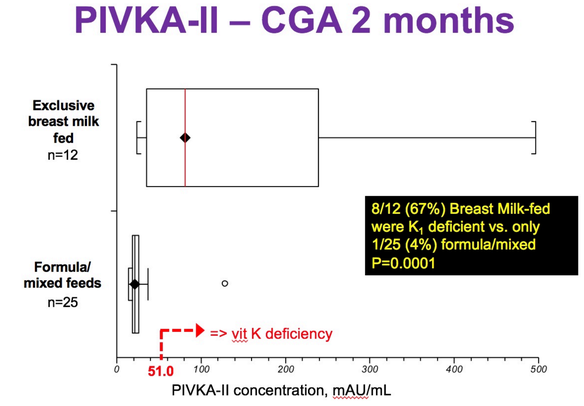

Figure *PIVKA-II concentrations at ~8 weeks corrected age according to mode of milk feeding since discharge*

VK_1 concentrations were significantly lower and PIVKA-II concentrations higher in exclusive BM vs FM/mixed fed babies, **Table**.

Table: Measures of vitamin K status of preterm infants in early infancy according to mode of feeding.

	Exclusive breast milk fed, n=12	Formula/mixed fed, n=25	P-value
Vitamin K_1 (µg/L)*	0.15 (<0.10–0.59) [IQR: 0.11–0.24]	1.91 (0.16–5.31) [IQR: 1.29–2.32]	<0.0001
PIVKA-II (mAU/mL)	80.8 (23.6–496.6) [IQR: 36.2–232.7]	21.2 (14.1–129.1) [IQR: 18.8–25.9]	<0.0001

Data are median (range) [IQR, interquartile range]
*VK_1 reference range: 0.15-1.55 µg/L

CONCLUSIONS:

- The majority of exclusively breast milk fed babies had evidence of mild vitamin K deficiency by 2-3 months CA
- Preterm infants who remain exclusively human milk fed post NICU discharge are at a high risk of developing mild vitamin K_1 deficiency in early infancy without additional K_1 supplements
- Routine post-discharge K_1 supplementation may prevent subclinical K_1 deficiency in breast-fed babies in early infancy

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