SPECIAL ARTICLE

Newborn Vitamin K Prophylaxis: A Historical Perspective to Understand Modern Barriers to Uptake

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ABSTRACT

Since its initial discovery almost a century ago, vitamin K has been labeled as both lifesaving and malignancy causing. This has led to debate of not only its use in general but also regarding its appropriate dose and route. In this article, we review through a historical lens the past 90 years of newborn vitamin K from its discovery through to its modern use of preventing vitamin K deficiency bleeding (VKDB). Although researchers in surveillance studies have shown considerable reductions in VKDB following intramuscular vitamin K prophylaxis, ongoing barriers to the universal uptake of vitamin K prophylaxis remain. Reviewing the history of newborn vitamin K provides an opportunity for a greater understanding of the current barriers to uptake that we face. Although at times difficult, improving this understanding may allow us to address contentious issues related to parental and health professional beliefs and values as well as improve overall communication. The ultimate goal is to improve and maintain the uptake of vitamin K to prevent VKDB in newborns.

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2018-0104

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HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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Dr Wheeler conceptualized and designed the review and revised the manuscript; Dr Majid and Ms Blackwell conducted the literature search and drafted the initial manuscript; Drs Broadbent, Barker, Edmonds, Al-Sallami, and Kerruish contributed to the review design and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

Vitamin K prophylaxis is one of the first health care interventions recommended for newborns, with the aim of preventing vitamin K deficiency bleeding (VKDB). This is an important area with numerous published studies and recent media attention, including that of 4 cases of VKDB in Nashville, Tennessee.[1] These infants in Nashville never received vitamin K and were developing normally until sudden bleeding occurred between 6 and 15 weeks after birth. Although all 4 infants survived, 3 suffered intracranial hemorrhage, and at least 1 was left with gross motor deficits.[1]

These cases illustrate that despite considerable scientific study in this field, barriers to universal prophylaxis remain. Given the potentially severe consequences of VKDB and the ease with which they can be prevented, in this review we provide a historical perspective on vitamin K prophylaxis. This perspective can be used to understand current barriers to acceptance and the challenges that remain in achieving universal prophylaxis and the prevention of VKDB.

VITAMIN K: DISCOVERY

The history of vitamin K dates back to 1929, when the Danish biochemist Henrik Dam (1895–1976) observed that chicks fed fat- and cholesterol-free diets developed subcutaneous and muscular hemorrhages.[2] He subsequently proposed that this fat-soluble active compound was different from the other known fat-soluble vitamins A, D, and E, and that this new anti-hemorrhagic factor should be named vitamin K (in reference to *koagulation* from the German and Scandinavian languages).[3]

Subsequently, in the early 1940s, Edward Doisy confirmed the structure and identity of the 2 naturally occurring forms of vitamin K, phylloquinone (vitamin K1) and menaquinone (vitamin K2; Fig 1).[4,5] For these discoveries, Dam[2] and Doisy were awarded the Nobel Prize in Physiology or Medicine (1943).[3]

VKDB

Vitamin K is found predominantly in green, leafy vegetables and plays a role in photosynthesis. In humans, it is a cofactor for some proteins involved in bone

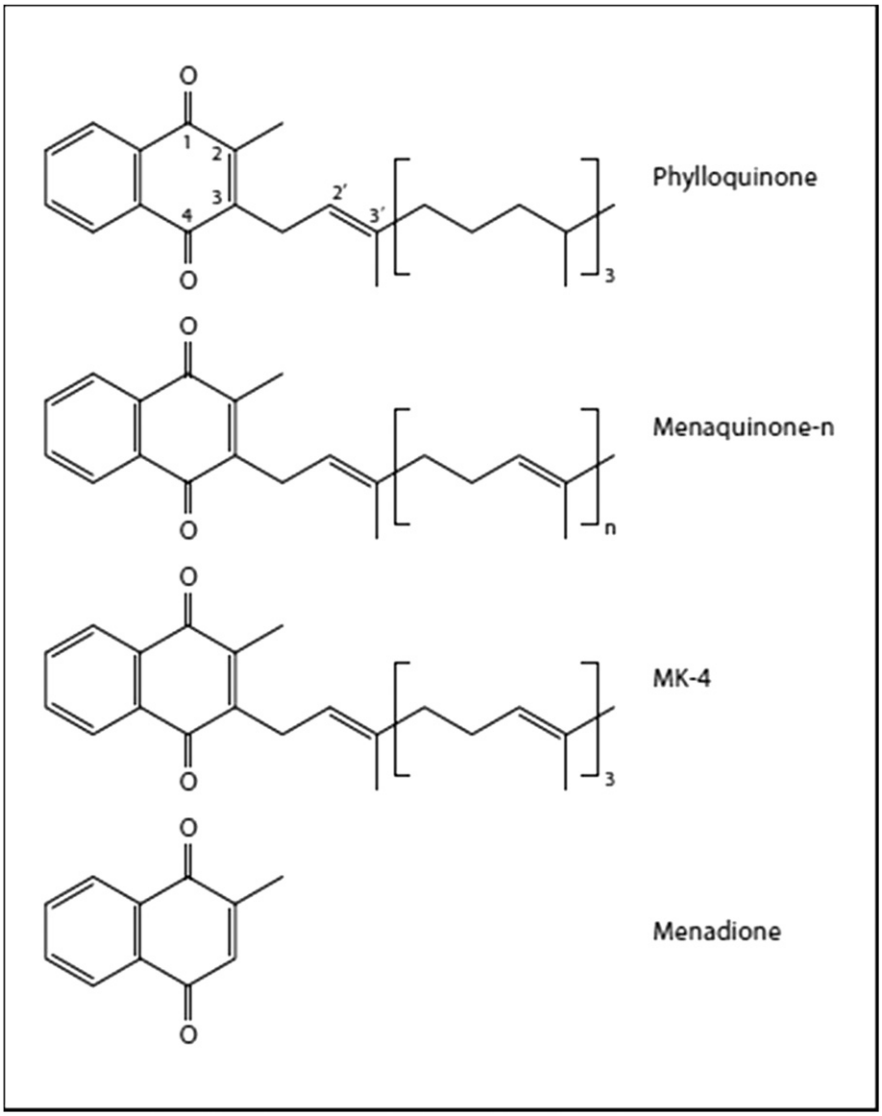

FIGURE 1 Chemical structures of phylloquinone, menaquinone-n, MK-4, and menadione. Adapted from MacCorquodale DW, Binkley SB, Thayer SA, Doisy EA. On the constitution of vitamin K1. *J Am Chem Soc.* 1939;61(7):1928–1929.

mineralization,[6] but primarily it is essential for the activity of several carboxylase enzymes within hepatic cells and the activation of the vitamin K–dependent coagulation factors VII, IX, X, and prothrombin. Therefore, deficiency can lead to an increased bleeding risk. This is a particular issue in newborns because they have naturally low levels of vitamin K, ~40% to 60% of normal adult values. These values slowly increase, and we attain adult values by 6 months of age.[7,8] Contributing factors for these low levels include the following: relatively poor placental transport of vitamin K; delays in the acquisition of vitamin K–producing gut microflora (such as *Bacteroides fragilis*)[9]; and insufficient intake, given that breast milk levels of vitamin K are low (as opposed to fortified formula) irrespective of maternal diet.

Rarely, an infant's relative and transient deficiency in vitamin K can lead to VKDB. This issue was first clinically appreciated in the 1930s, and it led to the experimental administration of oral vitamin K to infants with anemia and hemorrhage.[10] By the 1940s, prophylactic treatment of newborns

to prevent hemorrhage was being studied, as led by Jorgen Lehmann[11] from Sweden. He compared oral doses of 0.5 mg to up to 5 mg as well as oral doses with intramuscular (IM) administration. Lehmann concluded in these studies that 0.5 mg of oral vitamin K was as effective as a 5 mg dose, and oral and IM administration resulted in similar reductions in deaths due to hemorrhage. After this, all newborns at the women's clinic of Sahlgrenska Hospital were treated with vitamin K to prevent hypoprothrombinemia and hemorrhagic disease of the newborn.[11] Lehmann also concluded in his studies that the optimal dose of vitamin K for prophylactic treatments of newborns was 0.5 to 1 mg,[11] the dose that 78 years later we still use.

A similar policy was soon widely adopted elsewhere, although many were unable to replicate his findings.[12] The argument, as Ethel Dunham[13] put it in 1948, was that "since the vitamin does no harm and may do good, it is probably best to give it to all premature infants immediately after birth." When a 1 mg dose did not stop some infants from bleeding (likely because of other causes), physicians started using larger doses. This practice was eventually put to a halt when researchers in 1956 established that these high doses (>5 mg/day) could lead to hemolysis, severe jaundice, and kernicterus.[14] By the 1950s, the water-soluble product (Synkavit) started replacing the fat-soluble, natural plant form of vitamin K. This product was suggested to not cause hemolysis,[15] and it has since dominated European and American markets.

In 1985, Lane and Hathaway[16] further categorized VKDB into the following 3 common patterns: early, classic, and late. These are still widely accepted and used today (Table 1).[17] Several countries participating in surveillance programs for VKDB, including the Netherlands, Germany, Australia, and Switzerland, have subsequently agreed on standardized case definitions of VKDB to allow for international comparison (Table 2).[18]

After the Swedish experiments of the 1940s, it was not until 1961 that the American Academy of Pediatrics first recommended IM vitamin K prophylaxis immediately after birth for all newborns.[19] Now, nearly all developed countries have implemented vitamin K prophylaxis programs, usually recommending 1 mg of IM vitamin K (Konakion MM) at birth or 0.5 mg in preterm infants. If parents decline an IM injection, an alternative option is 2 mg of Konakion MM orally at birth and again at 3 to 5 days, followed by an additional dose at 4 to 6 weeks of age.[20] This option is likely less effective than IM[21] and certainly more complicated. Because of this efficacy issue (as well as availability), the American Academy of Pediatrics, in contrast to some countries, still does not have a policy statement on the use of oral prophylaxis.[22]

Minimal international data on adherence rates to vitamin K prophylaxis are available, with only single region data from New Zealand, Australia, and Canada published. Data from a single tertiary birthing unit in Otago, New Zealand revealed a 92.9% rate of IM prophylaxis and a 5.4% rate of oral prophylaxis, with 1.7% declining any prophylaxis.[23] In New Zealand, there is also evidence that oral vitamin K may be becoming more popular, with its use potentially more than doubling since 2008.[24] Data from New South Wales, Australia, revealed a higher rate of IM prophylaxis than New Zealand at 96.3%, with only 2.6% opting for oral prophylaxis and 1.2% declining any prophylaxis.[25] The highest uptake reported is from Alberta, Canada, with IM prophylaxis at 99.3% and oral prophylaxis at 0.4%, with only 0.3% declining.[26]

TABLE 1 The 3 Patterns of VKDB

Pattern[a]	Definition
Early	Defined as bleeding caused by vitamin K deficiency in the first 24 h of life, usually because of vitamin K deficiency in the mother. Early VKDB is rare, and it is typically seen in conjunction with maternal use of drugs that interfere with vitamin K metabolism such as anticoagulants (warfarin), anticonvulsants (phenytoin), and antituberculosis drugs (rifampicin and/or isoniazid).[10] It is frequently life-threatening because common bleeding sites include the head (cephalohematoma, intracranial, and subgaleal), intrathoracic and/or abdominal cavities, and the gastrointestinal tract.[8]
Classic	Occurs during the first wk of life, and the most common bleeding sites are gastrointestinal sites, umbilical sites, the skin, nose, and wounds (eg, postcircumcision). Intracranial hemorrhage may occur, but it is rare.[8]
Late	Late VKDB encompasses bleeding that occurs between 8 d and 6 mo,[9] with the peak incidence generally occurring between 3 and 8 wk of age.[11,12] Late VKDB occurs almost exclusively in breastfed infants.[13] Late VKDB can have similar etiology to classic VKDB (low milk intake and low vitamin K content of milk), and it can also be precipitated by fat malabsorption caused by gastrointestinal or hepatobiliary disease, such as biliary atresia.[14,15]

[a] It is also usual to distinguish between idiopathic and secondary VKDB. Secondary VKDB has a known underlying cause (eg, congenital hepatobiliary or malabsorptive disorders) or results as a consequence of medications given to the mother or infant.[8]

THE EMERGENCE OF BARRIERS TO VITAMIN K PROPHYLAXIS

Why parents would refuse this apparently safe and effective medical intervention often puzzles us as health professionals. Gaining an increased understanding of barriers to adherence and their origins is therefore essential, and it allows us to continue to promote vitamin K and fully participate in the VKDB debate. However, addressing these barriers can be challenging because it often requires us to combine professional views about child welfare with an appropriate respect for parental autonomy. Achieving an

TABLE 2 Diagnostic Criteria for VKDB

Criteria
PT ≥4 times the control value
At least 1 of the following:
Platelet count normal or raised
Normal fibrinogen with absent fibrin degradation products
PT returns to normal after vitamin K administration
Concentration of PIVKA proteins exceeds normal controls

PIVKA, proteins induced by vitamin k antagonists; PT, prothrombin time.

appropriate balance between these 2 issues is essential because parents who perceive health professionals as overly coercive or manipulative may disengage not only with vitamin K prophylaxis but also with other subsequent medical services.[27] Therefore, we detail in the following paragraphs the known barriers to vitamin K prophylaxis and how these have evolved over time.

As with any medical intervention, vitamin K prophylaxis has both potential benefits and risks, with concerns based on child welfare issues raised by researchers as potential barriers to adherence in several recent studies.[28,29] The most important and prominent of these concerns was the association of vitamin K prophylaxis with childhood leukemia. This has its origins in a 1990 study published by Golding et al[30] in the *British Journal of Cancer*, in which the authors examined factors associated with childhood cancer and found an unexpected association with vitamin K administration. Little was made of this finding until 2 years later, when Golding et al's[30] findings gained more traction in the media.[31] After this attention, researchers in another study published in 1992 reported that the odds of leukemia in children given IM vitamin K at birth were almost doubled (odds ratio 1.97), but they noted no increased risk when it was given orally.[32] In response, the British Pediatric Association recommended the routine use of oral vitamin K prophylaxis in healthy newborns, with IM prophylaxis reserved for those thought to be at a particularly high risk of VKDB.[33] Not surprisingly, this led to a subsequent decrease in the use of IM prophylaxis in Britain, with a rate of 58% IM use in 1988 falling to 38% in 1993.[33]

Golding et al's[30] study was the catalyst for further studies in numerous countries in which researchers tested this association between vitamin K and cancer. In 1999, a working group of the World Health Organization's International Agency for Research on Cancer reviewed the available literature and concluded that there was "inadequate evidence in humans and experimental animals for the carcinogenicity of vitamin K substances."[34] In 2002, Roman et al[35] combined data from 6 major case-control studies. In total, 2431 children with cancer and 6338 children without cancer were included, with the authors concluding that the "analysis provides no convincing evidence that intramuscular vitamin K is associated with childhood leukaemia." In 2003, Fear et al[36] published additional data, which included 2530 children with cancer (1174 of whom had leukemia) and 4487 children without cancer. Again, the authors of this study concluded "that there is no convincing evidence that neonatal vitamin K administration, irrespective of the route by which it is given, influences the risk of children developing leukaemia or any other cancer." Although these fears surrounding leukemia and IM vitamin K have eased since Golding et al's[30,32] original articles, recently published studies have revealed that some health professionals and parents maintain concerns that prophylaxis may be associated with cancer.[37,38] This reveals how influential previously refuted data can be, and the vitamin K–leukemia story strongly parallels the ongoing fears and misconceptions seen between autism and the vaccination of measles, mumps, and rubella.

Likely stemming from the above cancer concerns, other, less specific concerns regarding possible side effects have more recently been raised. These include nonspecific fears that ingredients in the injection are synthetic and/or toxic and the impression that the dose of vitamin K may be excessive and therefore harmful.[28,29] Some parents and health professionals have also questioned the efficacy of and actual need for vitamin K prophylaxis. In 1 study, a parent stated, "For us it was the risks from Vitamin K were higher because he was such a normal, easy birth,"[29] which was paralleled by findings from Gosai et al[37] in which 45% of midwives felt only those who were "at risk" should receive prophylaxis.

Parental fears of perceived infant pain also appear to be a strong driver toward opting for oral vitamin K as opposed to the recommended IM route. Again, this parallels parental fears seen in the context of pediatric immunization[39] and newborn screening.[40] Parental fears of newborn pain may be 1 possible contributing factor in an association linking Asian and Indian ethnicities to increased uses of oral vitamin K,[23] a speculation supported by Asian and Indian parent responses in a recent qualitative study in which researchers examine why parents decline vitamin K for their newborns.[29]

Researchers in recent literature have identified instances in which parental beliefs and values were incompatible with the use of vitamin K for reasons such as a strong identity with an alternative lifestyle, a belief that birth is a natural process that needs little interference, or religious or evolutionary values. These factors have all been linked to vitamin K refusal and are some of the hardest barriers to counteract,[29,41] contrasting with the above issues regarding pain or cancer, which, if adequately addressed, may lead to parental reassurance. The following factors aligned to a parental wish for a natural birth process or less medicalization have also been linked to parental refusal of IM vitamin K: having a vaginal delivery, delivery in a birth center as opposed to a hospital, greater gestational age, and having a planned home birth.[23,25] These infants are also more likely to have older mothers and analgesia-free deliveries.[25] In a recent study, up to 36% of parents who refused vitamin K prophylaxis quoted the reason for their refusal as being the desire to have a natural birthing process.[28] Researchers in 2 additional studies have also noted that a minority of parents and midwives promote the use of maternal diets to increase vitamin K levels in human breast milk[28,37] despite evidence that human milk does not contain enough vitamin K to be protective against VKDB.[25,42] In addition to the above, declining vitamin K prophylaxis has been associated with parents who identify as anticonformist or who are questioning of mainstream medicine.[29] These beliefs are also associated with refusals of other related public health initiatives such as immunization,[25,26,41,43] newborn screening,[29] and erythromycin eye drops.[41] Again, these beliefs are extremely hard to shift, with the majority of parents in 1 study unwilling to consider alternative, scientifically accurate information and remaining steadfast in their decision to decline.[28] When information

is made available, consistency in message and the need for availability in multiple languages have also been identified as potential aids to uptake.[44]

Family pressure and choices made by other pregnant women in the social circles of parents may also be barriers to vitamin K.[29] These psychosocial factors as well as inaccurate media portrayal[29] have all been shown to have an effect on subsequent parental decision-making. A lack of awareness of the possibility for intracranial hemorrhage or death is also present.[28,45] Ensuring awareness of the serious risks appears essential, with researchers in a recent study from the United States finding that >69% of parents cited a lack of awareness of importance as a reason for vitamin K prophylaxis refusal.[46]

Interestingly, there are also health professional factors associated with refusals of vitamin K prophylaxis. In a recent study in which researchers examined health professionals' attitudes toward vitamin K prophylaxis in New Zealand, it was found that 100% of the doctors surveyed thought vitamin K should be given to all infants, compared with 55% of the surveyed midwives.[37] In addition, 26% of midwives in this study reported that they would not give vitamin K to their own children, and they highlighted personal concerns about safety and interference in the natural birth process.[37] This finding is supported by data from a Canadian study in which births attended by midwives were 8 times more likely to be associated with vitamin K refusal compared with physician-attended deliveries (risk ratio, 8.4).[26] These persisting fears from a minority of health professionals are particularly concerning because these sorts of negative views may also influence subsequent immunization uptake.[41]

CONCLUSIONS

Vitamin K is not only an important public health intervention but also an indicator of future parental health care decision-making behavior such as that concerning immunization. All prospective parents and the health professionals guiding them should be aware of the benefits of vitamin K prophylaxis, the risks of not receiving it, and of the lack of evidence for any serious harms. Recent research efforts highlighted in this review have revealed multiple barriers to vitamin K adherence. Moving forward, researchers in future studies need to address the current lack of data on how to successfully mitigate these fears and concerns.

REFERENCES

1. Wilemon T. More babies hemorrhaging after parents refuse vitamin K shots. *The Tennessean*. May 2, 2014. https://www.tennessean.com/story/news/health/2014/05/02/babies-hemorrhaging-parents-refuse-vitamin-k-shots/8610155/. Accessed March 5, 2018
2. Dam H. The antihæmorrhagic vitamin of the chick.: occurrence and chemical nature. *Nature*. 1935;135(3417):652–653
3. Ferland G. The discovery of vitamin K and its clinical applications. *Ann Nutr Metab*. 2012;61(3):213–218
4. MacCorquodale DW, Binkley SB, Thayer SA, Doisy EA. On the constitution of vitamin K1. *J Am Chem Soc*. 1939;61(7):1928–1929
5. Binkley SB, McKee RW, Thayer SA, Doisy EA. The constitution of vitamin K2. *J Biol Chem*. 1940;133:721–729
6. Lippi G, Franchini M. Vitamin K in neonates: facts and myths. *Blood Transfus*. 2011;9(1):4–9
7. Andrew M. The relevance of developmental hemostasis to hemorrhagic disorders of newborns. *Semin Perinatol*. 1997;21(1):70–85
8. Shearer MJ. Vitamin K metabolism and nutriture. *Blood Rev*. 1992;6(2):92–104
9. Zipursky A. Prevention of vitamin K deficiency bleeding in newborns. *Br J Haematol*. 1999;104(3):430–437
10. Waddell WW, Guerry D. The role of vitamin K in the etiology, prevention, and treatment of hemorrhage in the newborn infant: part II. *J Pediatr*. 1939;15(6):802–811
11. Lehmann J. Vitamin K as a prophylactic in 13,000 infants. *Lancet*. 1944;243(6294):493–494
12. Grontoft O. Intracranial haemorrhage and blood-brain barrier problems in the new-born; a pathologico-anatomical and experimental investigation. *Acta Pathol Microbiol Scand Suppl*. 1954;100:8–109
13. Dunham EC. *Premature Infants: A Manual for Physicians*. Washington, DC: US Government Printing Office; 1948
14. Allison AC. Danger of vitamin K to newborn. *Lancet*. 1955;265(6865):669
15. Asteriadou-Samartzis E, Leikin S. The relation of vitamin K to hyperbilirubinemia. *Pediatrics*. 1958;21(3):397–402
16. Lane PA, Hathaway WE. Vitamin K in infancy. *J Pediatr*. 1985;106(3):351–359
17. Sutor AH, von Kries R, Cornelissen EA, McNinch AW, Andrew M. Vitamin K deficiency bleeding (VKDB) in infancy. ISTH Pediatric/Perinatal Subcommittee. International Society on Thrombosis and Haemostasis. *Thromb Haemost*. 1999;81(3):456–461
18. McNinch AW, Tripp JH. Haemorrhagic disease of the newborn in the British Isles: two year prospective study. *BMJ*. 1991;303(6810):1105–1109
19. American Academy of Pediatrics, Committee on Nutrition. Vitamin K compounds and the water-soluble analogues: use in therapy and prophylaxis in pediatrics. *Pediatrics*. 1961;28(3):501–507
20. Darlow PB; Fetus and Newborn Committee of the Paediatric Society of New Zealand, The New Zealand College of Midwives, The New Zealand Nurses Organisation, The Royal New Zealand College of General Practitioners, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Vitamin K prophylaxis in the newborn: a consensus statement. 2001. Available at: http://www.medsafe.govt.nz/profs/PUarticles/vitk.htm. Accessed February 3, 2018
21. Ipema HJ. Use of oral vitamin K for prevention of late vitamin K deficiency bleeding in neonates when injectable vitamin K is not available. *Ann Pharmacother*. 2012;46(6):879–883

22. American Academy of Pediatrics Committee on Fetus and Newborn. Controversies concerning vitamin K and the newborn. American Academy of Pediatrics Committee on Fetus and Newborn. *Pediatrics*. 2003;112(1 pt 1): 191–192

23. Burke M, Bernhardt H, Reith DM, Barker D, Broadbent RS, Wheeler BJ. Perinatal influences on the uptake of newborn Vitamin K prophylaxis–a retrospective cohort study. *Aust N Z J Public Health*. 2015;39(6):573–576

24. Darlow BA, Phillips AA, Dickson NP. New Zealand surveillance of neonatal vitamin K deficiency bleeding (VKDB): 1998-2008. *J Paediatr Child Health*. 2011;47(7): 460–464

25. Khambalia AZ, Roberts CL, Bowen JR, Nassar N. Maternal and infant characteristics by mode of vitamin K prophylaxis administration. *J Paediatr Child Health*. 2012;48(8):665–668

26. Sahni V, Lai FY, MacDonald SE. Neonatal vitamin K refusal and nonimmunization. *Pediatrics*. 2014;134(3):497–503

27. Kerruish NJ, McMillan J, Wheeler BJ. The ethics of parental refusal of newborn vitamin K prophylaxis. *J Paediatr Child Health*. 2017;53(1):8–11

28. Hamrick HJ, Gable EK, Freeman EH, et al. Reasons for refusal of newborn vitamin K prophylaxis: implications for management and education. *Hosp Pediatr*. 2016;6(1):15–21

29. Miller H, Kerruish N, Broadbent RS, Barker D, Wheeler BJ. Why do parents decline newborn intramuscular vitamin K prophylaxis? *J Med Ethics*. 2016;42(10): 643–648

30. Golding J, Paterson M, Kinlen LJ. Factors associated with childhood cancer in a national cohort study. *Br J Cancer*. 1990; 62(2):304–308

31. Shearer MJ. Vitamin K deficiency bleeding (VKDB) in early infancy. *Blood Rev*. 2009;23(2):49–59

32. Golding J, Greenwood R, Birmingham K, Mott M. Childhood cancer, intramuscular vitamin K, and pethidine given during labour. *BMJ*. 1992;305(6849):341–346

33. Barton JS, Tripp JH, McNinch AW. Neonatal vitamin K prophylaxis in the British Isles: current practice and trends. *BMJ*. 1995;310(6980):632–633

34. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Vitamin K substances. In: *Some Antiviral and Antineoplastic Drugs, and Other Pharmaceutical Agents*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol 76. Lyon, France: IARC Press; 2000:417–482

35. Roman E, Fear NT, Ansell P, et al. Vitamin K and childhood cancer: analysis of individual patient data from six case-control studies. *Br J Cancer*. 2002;86(1): 63–69

36. Fear NT, Roman E, Ansell P, Simpson J, Day N, Eden OB; United Kingdom Childhood Cancer Study. Vitamin K and childhood cancer: a report from the United Kingdom Childhood Cancer Study. *Br J Cancer*. 2003;89(7):1228–1231

37. Gosai S, Broadbent RS, Barker DP, Jackson PM, Wheeler BJ. Medical and midwifery attitudes towards vitamin K prophylaxis in New Zealand neonates. *J Paediatr Child Health*. 2014;50(7): 536–539

38. Schulte R, Jordan LC, Morad A, Naftel RP, Wellons JC III, Sidonio R. Rise in late onset vitamin K deficiency bleeding in young infants because of omission or refusal of prophylaxis at birth. *Pediatr Neurol*. 2014;50(6):564–568

39. Kennedy A, Basket M, Sheedy K. Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey. *Pediatrics*. 2011;127(suppl 1):S92–S99

40. Nicholls SG, Southern KW. Parental decision-making and acceptance of newborn bloodspot screening: an exploratory study. *PLoS One*. 2013;8(11): e79441

41. Marcewicz LH, Clayton J, Maenner M, et al. Parental refusal of vitamin K and neonatal preventive services: a need for surveillance. *Matern Child Health J*. 2017;21(5):1079–1084

42. Greer FR. Vitamin K in human milk–still not enough. *Acta Paediatr*. 2004;93(4): 449–450

43. Bernhardt H, Barker D, Reith DM, Broadbent RS, Jackson PM, Wheeler BJ. Declining newborn intramuscular vitamin K prophylaxis predicts subsequent immunisation refusal: a retrospective cohort study. *J Paediatr Child Health*. 2015;51(9):889–894

44. Miller H, Wheeler B, Kerruish N. Newborn vitamin K prophylaxis: an analysis of information resources for parents and professionals. *N Z Med J*. 2016;129(1446): 44–52

45. Eventov-Friedman S, Vinograd O, Ben-Haim M, Penso S, Bar-Oz B, Zisk-Rony RY. Parents' knowledge and perceptions regarding vitamin K prophylaxis in newborns. *J Pediatr Hematol Oncol*. 2013;35(5):409–413

46. Loyal J, Taylor JA, Phillipi CA, et al. Refusal of vitamin K by parents of newborns: a survey of the better outcomes through research for newborns network. *Acad Pediatr*. 2017; 17(4):368–373

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Hospital Pediatrics 2019;9;55
DOI: 10.1542/hpeds.2018-0104 originally published online December 28, 2018;

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