

Refusal of Intramuscular Vitamin K by Parents of Newborns: A Review

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In 2019, the American Academy of Pediatrics made public education about intramuscular vitamin K administration at birth a public health priority, partly in response to reports of refusal of intramuscular vitamin K by parents of newborns that led to vitamin K deficiency bleeding (VKDB). We reviewed the literature on the frequency of, reported reasons for, and factors associated with refusal of intramuscular vitamin K, incidence of VKDB in newborns who did not receive intramuscular vitamin K, and use of oral vitamin K to prevent VKDB. Without prophylaxis, estimates of the incidence per 100 000 births of VKDB range from 250 to 1700 for early VKDB and from 10.5 to 80 for late VKDB. The frequency of refusal of intramuscular vitamin K by parents ranged from 0% to 3.2% in US hospitals, up to 14.5% in home births, and up to 31.0% in birthing centers. Reported reasons for refusal were concern of harm from the injection, a desire to be natural, and a belief in alternative methods of prophylaxis. Parents who refused intramuscular vitamin K were more likely to refuse immunizations. Many different regimens were used for orally administered vitamin K; it is not clear which is best, but all are less effective than intramuscular vitamin K. VKDB is rare but can result in either neurologic sequelae or death. In addition to continued surveillance of the frequency of both refusal of intramuscular vitamin K and VKDB, a renewed focus on education of and collaboration with parents is needed to address this major public health threat.

ABSTRACT

www.hospitalpediatrics.org

DOI:<https://doi.org/10.1542/hpeds.2019-0228>

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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: Funded in part by a Yale University Department of Pediatrics Young Investigator Award (Dr Loyal), the Clinical and Translational Science Awards Program (grant UL1 TR000142 from the National Center for Advancing Translational Sciences), and the National Institutes of Health Roadmap for Medical Research (Dr Shapiro). The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health. Funded by the National Institutes of Health (NIH).

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

Dr Loyal conceptualized and designed the study, conducted the review, and reviewed and revised the manuscript; Dr Shapiro contributed to the conception and design of the study and interpretation of data and critically reviewed the manuscript; and both authors approved the final manuscript as submitted.



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TABLE 1 Frequency of Refusal of Intramuscular Vitamin K by Parents of Newborns

Study, Country	Study Design	Frequency of Refusal of Intramuscular Vitamin K, %
Marcewicz et al, ³ United States	Chart review of 5 hospitals and 5 birthing centers	3 (hospitals); 14.5 (home births); 31 (birthing centers)
Hamrick et al, ⁴ United States	Chart review of 5 community hospitals, 1 academic medical center, and 2 birthing centers	0.2–3.2 (community hospitals); 0.26 (academic center); 4.3–8.3 (birthing centers)
Sahni et al, ¹³ Canada	Review of birth documentation in a population-based cohort of live births	0.3
Loyal et al, ⁵ United States	Chart review of 35 well-newborn units	0.6 (range 0–2.3)
Bernhardt et al, ¹⁴ New Zealand	Chart review of 1 tertiary-level maternity and newborn care hospital	2.1
Burke et al New, ¹⁵ New Zealand	Chart review of 1 tertiary-level maternity and newborn care hospital	1.7
Danziger et al, ⁶ United States	1 academic medical center	2.3

In 2019, the American Academy of Pediatrics (AAP) made public education about intramuscular vitamin K administration at birth 1 of its top 10 public health priorities.¹ This response was partly due to an increase in the number of reports of parents who refuse intramuscular vitamin K for their newborns and a concomitant increase in reports of newborns with vitamin K deficiency bleeding (VKDB), a serious and potentially life-threatening condition, in recent years in the United States and other countries.^{2–12}

Newborns have low reserves of vitamin K, putting them at risk for VKDB. VKDB may present in the first week of life (classic VKDB) with bleeding from the gastrointestinal tract and/or from the umbilicus.^{2,12} Late VKDB presents between 2 and 12 weeks of life, and infants may present with intracranial bleeding.^{2,12} A 1-time, prophylactic, intramuscular injection of vitamin K administered shortly after birth that has been recommended by the AAP since 1961 virtually eliminated VKDB in the United States.² Although prophylaxis against VKDB with intramuscular vitamin K is universally recommended for newborns in the United States, this is not the case in many other countries.

There is a growing body of literature about refusal of intramuscular vitamin K by parents of newborns and the implications of lack of prophylaxis in newborns, but many questions remain unanswered. Therefore, our objective was to review the current literature for original articles on what is known about the frequency of refusal, reported reasons and factors associated with refusal of intramuscular vitamin K,

reported outcomes of newborns who did not receive intramuscular vitamin K, and use of oral vitamin K against VKDB and identify what is still unknown to better direct future research efforts.

METHODS

We searched PubMed for original and relevant English-language studies on the following: the frequency of, reasons for, and factors associated with refusal of intramuscular vitamin K by parents of newborns, outcomes of those newborns, and use of oral vitamin K against VKDB that were published from January 1, 1950, through August 1, 2019. We chose 1950 as the start of our date range because we wanted to capture case reports and clinical presentations of infants with VKDB who did not receive vitamin K prophylaxis and because our institution's database collection started in 1950. Refusal of vitamin K by parents has become a popular subject for research, with many studies having been published in recent years. We manually searched the references of relevant articles for the frequency of and reasons for refusal of intramuscular vitamin K included the following terms: ((vitamin k[Title/Abstract]) AND newborns) AND refusal. Articles were excluded if the study was not original (eg, reviews) or if no information on either the frequency of or reasons for refusal of intramuscular vitamin K was provided in the article. For outcomes of newborns who did not receive IM vitamin K, the following terms were included in the search: (((vitamin K deficiency bleeding[Title/Abstract]) OR hemorrhagic disease of the newborn[Title/Abstract]) AND Humans[Mesh] AND English

[lang])) AND case. Articles were excluded if the primary etiology of the bleeding was not due to vitamin K deficiency or if the infant's age at presentation was missing. For oral vitamin K regimens to prevent VKDB, the following search terms were used: (((oral vitamin K[Title]) AND prophylaxis) AND newborns) AND bleeding. Addition of the word "hemorrhage" to the search string did not yield additional studies.

DISCUSSION

Frequency of Intramuscular Vitamin Refusal by Parents

We identified 7 original articles on the frequency of intramuscular vitamin K refusal by parents.^{3–6,13–15} Rates of refusal in these studies are shown in Table 1. In the hospital setting, most parents accept intramuscular vitamin K for their newborns with reported refusal rates that ranged up to 3.2%. Extrapolating a refusal rate of 3.2% to ~6 million live births in the United States, up to 192 000 newborns could be at risk for VKDB. Investigators in Canada also reported an increase in the frequency of refusal of intramuscular vitamin K, from 0.2% to 0.4%, from 1999 to 2005.¹³ Other than reports from single centers, there is a paucity of quantitative information about temporal changes in the frequency of refusal of intramuscular vitamin K, but there is a perception among clinicians that the frequency is increasing.⁷

In a 2014 report from the National Center for Health Statistics, the percentage of out-of-hospital births in the United States increased from 1.26% in 2011 to 1.36% in 2012, continuing an increase that began in 2004.⁸ Among out-of-hospital births in the

TABLE 2 Reasons for Refusal of Intramuscular Vitamin K by Parents of Infants

Authors, Country	Study Type and Participants	Reasons for Refusal of IM Vitamin K
Marcewicz et al, ³ United States	Telephone interviews of 74 parents who refused intramuscular vitamin K for their newborns	Parent's perception that intramuscular vitamin K is not necessary (53%); parents desired natural birthing process (36%); concern about preservatives or ingredients (19%); concern about adverse reactions (14%); concern about harmful effect of pain for infant (11%); concern about dose being too high (11%); concern that injection causes cancer (8%); concern about potentially overwhelming infant's immune system (1%)
Hamrick et al, ⁴ United States	Cross-sectional survey of 54 parents who refused intramuscular vitamin K for their newborns	Concern about synthetic or toxic materials (37%); concern about excessive dose (28%); concern about side effects (24%); preference for natural sources of vitamin K (24%); views as unnecessary or no benefit (21%); concern about pain (13%); personal reason (11%); religious reason (11%); concern about cancer (7%)
Loyal et al, ⁵ United States	Cross-sectional survey of 85 newborn nursery directors in a national network of newborn nurseries	Parents' perceptions that intramuscular vitamin K is unnecessary (69%); lack of knowledge regarding the role of intramuscular vitamin K in preventing VKDB (69%); concern about preservatives in the intramuscular injection (53%); concern about damaging effects of pain from injection (51%); concern about the association of intramuscular vitamin K with leukemia (32%); perception that vitamin K is a vaccine (31%); perception that dose of intramuscular vitamin K is too high (12%)
Centers for Disease Control and Prevention, ¹⁶ United States	Case report of 4 infants with late-onset VKDB who did not receive intramuscular vitamin K because of refusal by parent	Concern about an increased risk for leukemia; impression that the injection was unnecessary; desire to minimize their infant's exposure to "toxins"
Miller et al, ¹⁷ New Zealand	Qualitative study of 15 parents who refused intramuscular vitamin K for their newborns	Parents' beliefs and values: preference for alternative or natural lifestyle; questioning of mainstream medicine or science; religious reasons Child welfare: perceived risk outweighs benefits; amount given via intramuscular; changing mind depending on outcomes External influences: Health care professionals; information sources; celebrities; family; friends
Weddle et al, ¹⁸ United States	Case report of a newborn whose parents refused intramuscular vitamin K	Concern about dose being too high; concern about pain from injection and a potential entry for germs; concern about metal and preservatives in the injection; oral vitamin K was recommended by a chiropractor
Levin et al, ¹⁹ United States	Case reports of 6 infants who did not receive intramuscular vitamin K because of refusal by parent	Parents identified with an alternative lifestyle; religious reason; concern about harm from "toxic ingredients" in injection; wanting to be "natural"; and desire to delay shots
Eventov-Friedman et al, ²⁰ Israel	Survey of a convenience sample of 217 expectant parents	Of parents who were not sure or not intending to give their newborns intramuscular vitamin K, perceptions were influenced by recommendations from the pediatrician, spiritual leaders, family members, friends, and the Internet; some parents were concerned about pain from the injection, and some parents were opposed to "medications" or immunizations and injections

TABLE 2 Continued

Authors, Country	Study Type and Participants	Reasons for Refusal of IM Vitamin K
Loyal et al. ⁶¹ United States	Qualitative study of 19 parents who refused intramuscular vitamin K for their newborns	<p>Risk/benefit ratio: parents who refused intramuscular vitamin K perceived risk to their newborns from preservatives, for example</p> <p>“Natural” approaches: leading to seeking oral vitamin K or increasing the mother’s own prenatal dietary vitamin K intake</p> <p>Placement of trust and mistrust: mistrust of the medical and pharmaceutical community with overlapping concerns about vaccines and trust of self, likeminded allopathic and nonallopathic health care providers, the social circle, the Internet, and social media</p> <p>Informed by experiences: includes hospital experiences with previous pregnancies and communication with health care providers</p>

United States, the frequency of refusal of intramuscular vitamin K has been reported to be as high as 14.5% among home births and 31% in birthing centers.³ Using the previous estimation of 6 million live births in the United States per year and a refusal rate of 1.36%, we can expect ~81 000 out-of-hospital births per year, of which ~12 000 to 25 000 may be at risk for VKDB if prophylactic vitamin K is not administered.

Reasons for Refusal of Intramuscular Vitamin K

We identified 9 original articles on reasons for intramuscular vitamin K refusal by parents.^{3,4,7,8,16–19} Details on data collection and results are shown in Table 1. There were 3 major categories of reasons for refusal of intramuscular vitamin K by parents of newborns.

Concern of Harm From the Injection

For many parents who refused intramuscular vitamin K, the perceived risk of the injection outweighed the perceived benefit. Parents reported concerns about the preservative in the injection^{2,4,7,8,16–20} or that pain to the infant from the injection could be harmful.^{3,4,7,8,16,19} Additional reported concerns were a perception that intramuscular vitamin K is a “vaccine,”^{7,18–20} that the dose of intramuscular vitamin K was too high,^{3,4,7,8,16,19,20} that there was a potential for adverse reactions to an injection,^{4,7,16–19} that the injection created a potential entry for germs,⁷ that intramuscular vitamin K causes cancer,^{3,4,7,8}

and that intramuscular vitamin K may overwhelm the newborn’s immune system.³

Desire To Be Natural

Some parents who refused intramuscular vitamin K for their newborns desired to be more “natural” and believed that intramuscular vitamin K was unnecessary for their infants.^{3,4,6–8,17,19,20} Additional drivers of the desire to be natural included parents’ religious beliefs and a belief that vitamin K deficiency is to be expected for infants.^{3,4,8,17–20}

Belief in Alternative Prophylaxis To Prevent VKDB

Some parents preferred natural sources of vitamin K, and this preference included increasing the mother’s own dietary intake of vitamin K during the pregnancy.^{4,20} Some parents thought that oral vitamin K was effective in preventing VKDB.^{16,18–20} For some parents, their beliefs or values included a strong identification with an alternative lifestyle that factored into their decision-making.^{8,17} This alternative lifestyle included questioning norms and not immediately accepting recommendations by physicians. In some instances, parents’ refusal of intramuscular vitamin K for their infants was a result of a lack of knowledge about the risk of VKDB to their infants and the role of intramuscular vitamin K in preventing VKDB.^{6,18–20}

Some parents would have only considered intramuscular vitamin K in the event of a potential injury to the infant or if the birth

required another intervention.⁹ Decisions about the refusal of intramuscular vitamin K were influenced by the opinions of other mothers or family members; statements of celebrities and health professionals, including midwives and chiropractors; as well as written information (information sheets) and Internet blogs.^{8,16,18–20}

Factors Associated With Refusal of Intramuscular Vitamin K

Seven studies that examined the factors associated with refusal of intramuscular vitamin K are shown in Table 2. Parents who refused intramuscular vitamin K tended to refuse other preventive measures, including the hepatitis B vaccine at birth, prophylaxis against gonococcal ophthalmia, and subsequent routine vaccinations.^{3–5,13–15} Investigators from Canada found that refusal of intramuscular vitamin K was significantly associated with planned home births, deliveries in birthing centers, midwife-assisted deliveries, and the child subsequently not receiving any recommended childhood vaccines at 15 months of age.¹³ Investigators in New Zealand found that mothers with midwife-assisted deliveries, who have planned home births, and of Asian ethnicity were more likely to refuse intramuscular vitamin K for their newborns.¹⁵ The association between intramuscular vitamin K refusal by parents and midwife-assisted deliveries was replicated by investigators in Michigan.⁶ In a cross-sectional survey of mothers in the United States, investigators found that

TABLE 3 Factors Associated With Refusal of Intramuscular Vitamin K

Study, Country	Study Design (No. Participants)	Risk Factors Associated With Refusal of Intramuscular Vitamin K	Statistics ^a
Marcewicz et al, ³ United States	Cross-sectional survey (<i>N</i> = 74)	Refusal of erythromycin eye ointment	<i>N</i> = 50 (68%)
		Refusal of hepatitis B vaccine	<i>N</i> = 69 (93%)
		Refusal of vitamin K injection, erythromycin eye ointment	<i>N</i> = 49 (66%)
		Neonatal hepatitis B vaccine	—
Hamrick et al, ⁴ United States	Cross-sectional survey (<i>N</i> = 54)	White race	<i>N</i> = 42 (78%)
		>30 y of age	<i>N</i> = 31 (57%)
		Intention to exclusively breastfeed	<i>N</i> = 54 (100%)
		Refusal of hepatitis B vaccine	<i>N</i> = 49 (90%)
		Refusal of erythromycin eye ointment	<i>N</i> = 42 (77%)
Sahni et al, ¹³ Canada	Cohort study (<i>N</i> = 282 378)	Planned home birth	RR 4.9 (95% CI 3.8–6.4)
		Deliveries in birthing centers	RR 3.6 (95% CI 2.3–5.6)
		Midwife-assisted deliveries	RR 8.4 (95% CI 6.5–11.0)
		No childhood vaccines at 15 mo	RR 14.6 (95% CI 13.9–15.3)
Loyal et al, ⁵ United States	Nested case-control study (<i>N</i> = 102 878)	Exclusive breastfeeding	aOR 3.4 (95% CI 2.1–5.5)
		Infant's non-Hispanic white race and/or ethnicity	aOR 1.7 (95% CI 1.2–2.4)
		Female sex	aOR 1.6 (95% CI 1.2–2.3)
		Increased gestational age	aOR 1.2 (95% CI 1.1–1.4)
		Increased mother's age	aOR 1.05 (95% CI 1.02–1.08)
		Refusal of both ocular prophylaxis and hepatitis B vaccine	aOR 88.7 (95% CI 50.4–151.9)
Bernhardt et al, ¹⁴ New Zealand	Cohort study (<i>N</i> = 3575)	Nonimmunization	RR 14.1 (95% CI 7.8–25.9)
		Incomplete immunization in childhood	RR 5.4 (95% CI 3.5–8.3)
Burke et al, ¹⁵ New Zealand	Cohort study (<i>N</i> = 7089)	Asian ethnicity	OR 5.87 (95% CI 3.61–9.53)
		Vaginal delivery	OR 2.85 (95% CI 1.83–4.43)
		Increased gestational age (per week)	OR 1.24 (95% CI 1.10–1.39)
Danziger et al, ⁶ United States	Cohort study (<i>N</i> = 3758)	Delivery by certified midwife compared with physician	OR 6.2 (95% CI 3.3–11.6)

aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; RR, risk ratio.

mothers who refused intramuscular vitamin K were more likely to be white, >30 years of age, college graduates, or breastfeeding.² In a study of a national network of US nurseries, exclusive breastfeeding, non-Hispanic white race and/or ethnicity, female sex of the newborn, gestational age, increasing mother's age, and refusal of ocular prophylaxis, hepatitis B vaccine, or both were associated with refusal of intramuscular vitamin K.⁵

Outcomes of Newborns Who Did Not Receive Intramuscular Vitamin K

There were no systematic reports of the frequency of either classic or late VKDB. There are numerous case reports and case series of VKDB in infants who did not receive intramuscular vitamin K at birth.^{11,21–60} Most

infants with VKDB were exclusively breastfeeding, and most of the case reports were from countries where administration of intramuscular vitamin K is not routine. Because administration of intramuscular vitamin K at birth became routine after the AAP recommendation in 1961, reports of VKDB in the United States are almost always associated with refusal of intramuscular vitamin K by a parent. Most case reports were of infants who had late VKDB. Signs and symptoms at the time of presentation varied widely. Infants had nonspecific findings (fussiness, poor feeding, vomiting, pallor, fever, or jaundice), signs of bleeding (blood in the stool, ecchymosis, epistaxis, hematuria, bleeding from an injection site, umbilicus, or mucosa), neurologic signs and symptoms (altered mental status, lethargy,

posturing, fixed dilated pupils, bulging fontanelle, hypotonia, or seizures), or respiratory issues (increased work of breathing or cyanosis).^{21–58} Rarely, children with late VKDB presented with bleeding either in the vitreous of the eye or in the thymus.^{10,31,53} Intracranial bleeding occurred commonly in infants with late VKDB. Reported outcomes of VKDB ranged from no significant effect to severe developmental delays and death. In 40 case reports and case series, of 1486 infants with VKDB in the absence of prophylaxis, there were 305 deaths (20.5%) and 146 infants (9.8%) had significant neurologic sequelae (hemiparesis, seizures, or developmental delay). The latter number is likely an underestimate because this information was not included in some studies. Case

TABLE 4 Oral Vitamin K Regimens and VKDB Cases

Study, Country	Methods	Oral Vitamin K	No. Live Births	Incidence of VKDB
Laubscher et al, ⁶² Switzerland	Survey of cases recalled by pediatricians	3 doses × 2 mg: 4 h of life, day 4, week 4	458 184	Overall incidence: 1.09 in 100 000 (95% CI 0.4–2.6); late VKDB incidence: 0.87 in 100 000 (95% CI 0.24–2.24)
Hansen et al, ⁶³ Denmark	Survey of parents and survey of cases recalled by pediatricians	Multiple doses: 2 mg at birth, 1 mg weekly until 3 mo of age	507 850	Incidence: 0–0.9 per 100 000
von Kries et al, ⁶⁴ Germany	Survey of cases recalled by pediatricians	3 doses × 2 mg: birth, week 1, and week 4	3 138 695	Incidence: late VKDB 0.44 in 100 000 (95% CI 0.19–0.87)
Wariyar et al, ⁶⁵ United Kingdom	Chart review, survey of parents, and survey of cases recalled by pediatricians	4 doses × 1 mg: birth, (breastfed infants) week 2, week 4, and week 6	182 000	Incidence: late VKDB 2.2 in 100 000
Strehle et al, ⁶⁶ United Kingdom	Survey of midwives	Multiple doses: 1 mg given at birth, 50 µg for 3 mo (breastfed infant)	—	Outcomes were acceptability of regimen by parents and midwives; investigators did not track cases of VKDB
Schubiger et al, ⁹ Switzerland	Monthly survey of pediatric hospitals on VKDB cases	2 doses × 2 mg: day 1 and day 4	247 000	Incidence: late VKDB 2.8 in 100 000 live births
Von Kries et al, ¹⁰ Germany	Monthly survey of pediatric hospitals on VKDB cases	3 doses × 2 mg: birth, days 4–10, weeks 4–6	3 200 000	Incidence: late VKDB ranged from 0.44 to 0.72 in 100 000 live births

CI, confidence interval.

series of >40 infants with VKDB were all published in countries outside the United States, where vitamin K prophylaxis is not routine. In case reports from the United States, of 33 infants with VKDB, 3 died (9%).

Oral Vitamin K To Prevent VKDB

We identified 7 original articles about oral vitamin K to prevent VKDB in newborns.^{9,61–66} Specific regimens and incidences of VKDB are shown in Table 3. The reported incidence of VKDB in infants who had received prophylaxis with oral vitamin K is shown in Table 4. For most studies, these numbers were derived from periodic surveys of clinicians and their recall about cases of VKDB, confirmation with national registries of hospital discharge diagnoses (when possible), and surveys of parents.^{9,61–66} Oral vitamin K is not used routinely in the United States and is not approved by the US Food and Drug Administration to use for the prevention of VKDB. In Europe, several different regimens are used, and the most effective regimen is still unclear.

Regimens reported in European studies included 3-dose series of oral vitamin K (given at birth, either day 4 or week 1, and week 4),^{61,63} multiple-dose series (at birth and then either daily or weekly until

3 months of age),^{62,65} 2-dose series (at birth and day 4),⁶⁶ and 4-dose series (at birth and at weeks 2, 4, and 6 [in breastfed neonates]).⁶⁴ The incidence of VKDB after oral vitamin K prophylaxis in these studies was up to 2.8 per 100 000. Investigators concluded that although oral vitamin K was not as effective as a single intramuscular dose, oral regimens can provide an alternative prophylaxis against VKDB in otherwise healthy newborns.

Ensuring compliance by parents is an important problem for oral regimens.⁶¹ Of parents surveyed, 93% to 94% reported compliance with the prescribed oral regimen.^{62,64} Investigators in the United Kingdom surveyed midwives and had a 25% response rate to an anonymous e-mail survey about the midwives' experiences with the oral vitamin K supplement, and most respondents found oral vitamin K acceptable but expressed concerns about parents' compliance with the regimen.⁶⁵

A limitation of these large-scale, population-based studies is the potential underreporting of cases of VKDB by clinicians. Although reported compliance with prescribed oral regimens was >90% in surveys of parents, there is the potential for both recall and reporting bias. A factor contributing to good compliance was

routine administration of the oral doses in the pediatrician's office. In the United States, the availability of oral preparations of vitamin K, ability to both store and administer oral doses of vitamin K in outpatient clinics, and willingness of clinicians to perform this additional task are unknown. Despite the increased out-of-hospital births and higher rates of refusal of intramuscular vitamin K among those parents, little is known about what oral regimens, if any, are being used by US midwives in these settings. It is also unknown if and which multiple-dose regimens are being offered, how are they obtained, and if either parents or pediatric clinicians are administering the follow-up doses.

Finally, national surveillance for VKDB in these European countries is noteworthy. Regular surveys of both clinicians and hospitals and, when possible, confirmation through review of registries of both discharge diagnoses and medical records are routinely performed. No such surveillance for VKDB is done in the United States at either the national or state level.

CONCLUSIONS

Refusal of intramuscular vitamin K by parents of newborns has serious

implications for the health of children. In our review, the frequency of intramuscular vitamin K refusal by parents was higher in out-of-hospital births compared with in-hospital births, and refusal of vitamin K was associated with refusal of other preventive practices, including immunizations. There is an understanding about why parents refuse intramuscular vitamin K, and there are opportunities to use this information to inform educational efforts in the public. More information about the association of vitamin K with out-of-hospital births is needed to better understand the gap and greatly improve collaboration with midwife colleagues. More information is needed on the use of oral vitamin K to prevent VKDB in the United States, and there is a need for systematic surveillance of the outcomes of newborns who do not receive intramuscular vitamin K to monitor this emerging threat to the health of newborns.

Acknowledgments

We acknowledge John Leventhal for his comments on the article.

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Hospital Pediatrics 2020;10;286

DOI: 10.1542/hpeds.2019-0228 originally published online February 4, 2020;

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