Khalifa, M. A., & Mahdi, Y. Yemeni J Med Sci. 2025; 19(7):108 -119
https://doi.org/10.20428/yjms.v19i7.3056
https://journals.ust.edu/index.php/yjms

OPEN ACCESS Review Article

Pharmacologic and Clinical Applications of Commonly Administered Medications to Neonates: Focus on Vitamin K, Vitamin D, and Hepatitis B Vaccine Un Updated Review

Mohammed Ali Khalifa[1,2]*, Yasameen Mahdi[1]

[1] *Department of Pharmacy, Faculty of Medicine and Health Sciences, University of Science and Technology, Aden, Yemen.*
[2] *Faculty of Pharmacy, Omdurman Islamic University, Khartoum, Sudan.*

ABSTRACT

Background: The neonatal period is highly susceptible, and early pharmacological treatments can significantly reduce morbidity and mortality. Three commonly used neonatal interventions—vitamin K, vitamin D, and the hepatitis B vaccine—are highlighted by this review as being pharmacological in nature, clinically used, having recommended doses, and being safe.
Methods: A systematic search was conducted in PubMed, ScienceDirect, Google Scholar, and the Cochrane Library using MeSH terms and keywords (e.g., "vitamin K in neonates"). The literature was restricted to that published in the English language during 2015–2025 and involving human neonates.
Results: Vitamin K: The world standard is intramuscular (IM) injection of 0.5–1 mg at birth to prevent vitamin K deficiency bleeding, although alternative oral administration is less uniform. Vitamin D: A daily dose of 400 IU is recommended for all neonates, with up to 1,000 IU in preterm or deficient infants, to prevent rickets and hypocalcemia. Hepatitis B vaccine: Early vaccination within 12–24 hours of birth is essential, especially for babies born to HBsAg-positive mothers, who should also receive hepatitis B immunoglobulin (HBIG). The vaccine is highly effective and safe.
Conclusion: Vitamin K, vitamin D, and the hepatitis B vaccine are essential components of neonatal preventive care. Strengthening health systems, improving parent and healthcare worker education, and increasing access are vital for optimal outcomes.

Keywords: Vitamin K, Vitamin D, hepatitis B vaccine, newborn, neonatal pharmacology.

**** Corresponding author address:*** *m.khalifa@ust.edu*

INTRODUCTION

The neonatal period, the first 28 days of life, represents a window of extreme need for pharmacologic interventions for morbidity and mortality associated with perinatal and congenital illnesses [1]. Because neonatestheirimmature body functions present special pharmacokinetic and pharmacodynamic challenges that require special attention in drug ordering [2]. Despite these obstacles, certain medications are routinely administered to nearly all infants of the world soon after birth in order to effect a smooth transition from fetal to postnatal life [3].

Among the most popular agents utilized within the neonatal setting are vitamin K, vitamin D, and the hepatitis B vaccine [4-6]. Such drugs are recommended by key health agencies like the World Health Organization (WHO), American Academy of Pediatrics (AAP), and Centers for Disease Control and Prevention (CDC) due to their established use in preventing serious disorders like vitamin K deficiency bleeding (VKDB), nutritional rickets, and perinatal hepatitis B virus (HBV) infection [7-9].

Vitamin K is required for activation of coagulation factors and is given intramuscularly to prevent hemorrhagic disease of the newborn, a condition that can be fatal if left untreated [10, 11]. Vitamin D is crucial in mineralization of bone and for calcium balance, and supplementation is especially warranted in exclusively breastfed infants since human milk is poorly supplied with the vitamin [12]. The hepatitis B vaccine, administered in most instances within the first 24 hours of life, provides early immunological protection against vertical spread of HBV, a possible etiology of chronic liver disease [13].

This review attempts to address the pharmacologic properties, modes of action, clinical applications, and safety profiles of these three key neonatal drugs. Understanding their roles within the context of neonatal physiology is important in a bid to optimize therapeutic gain and deliver safe and effective therapy at this vulnerable phase of life.

METHODS

This review was conducted to examine and summarize the pharmacological considerations, clinical utilization, and current recommendations for three medications most commonly administered to neonates: vitamin K, vitamin D, and the hepatitis B vaccine. The approach taken followed a systematic process of identification, selection, and synthesis of the literature.

Literature Search Strategy

A systematic literature search was performed using four electronic databases, including PubMed, ScienceDirect, Google Scholar, and the Cochrane Library. The Medical Subject Headings (MeSH) and keywords used in the search included "vitamin K in neonates," "neonatal vitamin D supplementation," "hepatitis B vaccine newborn," "pharmacokinetics in neonates," "neonatal pharmacology," and "guidelines for neonatal drug administration." Boolean operators such as "AND," "OR," and "NOT" were used to limit the search.

Inclusion and Exclusion Criteria

The following criteria were met by the articles included: Published between the years 2015 and 2025 in the English language, they were on human neonates. had pharmacological properties, clinical guidelines, safety, or efficacy of the drugs under consideration and were randomized controlled trials, observational studies, review articles, or official guideline documents.

Exclusion criteria: non-neonate, non-human or animal studies, articles, and those with no full texts available.

Data Synthesis and Extraction

Qualitatively, the relevant information was extracted and synthesized. Significant themes such as drug mechanism of action, pharmacokinetics, dosing recommendations, clinical use, and safety profiles were extracted and compiled into coordinated sections. Global and regional guideline suggestions by WHO, CDC, and national pediatric societies were reviewed and compared.

RESULTS

Vitamin K

Pharmacologic Profile

Vitamin K_1 (phylloquinone) is the primary preparation employed for prophylaxis in neonates [14]. Pharmacokinetically, IM injection leads to rapid and sustained plasma levels, with a half-life of roughly 1.5 to 3 hours, and extensive hepatic storage that gives protection for weeks [17]. Oral administration is less reliable and requires dosing repetition [18]. As a fat-soluble vitamin, its

absorption in adults is [D2] dependent on bile salt and pancreatic enzyme [15]. Neonates have immature biliary and pancreatic function and a sterile gut, and therefore there is impaired absorption of oral vitamin K, particularly in infants who are exclusively breastfed [16].

Mechanism of Action

Vitamin K acts as a cofactor for the enzyme γ-glutamyl carboxylase, which carboxylates glutamic acid residues of the clotting factors to form γ-carboxyglutamate that can bind calcium and bind to phospholipid membranes. This enables activation of clotting factors II, VII, IX, and X, and proteins C and S [19].

Clinical Indications and Global Recommendations

The first-line use of vitamin K in neonates is the prevention of vitamin K deficiency bleeding (VKDB), formerly hemorrhagic disease of the newborn [20]. VKDB has three patterns of presentation: Early VKDB: ≤24 hours; associated with maternal drug intake (e.g., anticonvulsants, anti-tubercular drugs). Classic VKDB: Days 1–7; usually due to inadequate ingestion of vitamin K by the mother. Late VKDB: >2 weeks to 6 months; typically, severe with intracranial hemorrhage [20]. The WHO and AAP recommendation is an IM injection of 1 mg of vitamin K_1 in term neonates at birth. 0.5 mg IM in preterm or low-birth-weight neonates. Alternative oral administration (e.g., 2 mg at birth with repeated doses) is less potent but more prone to parental failure to comply [21]. See Table 1.

Variable intramuscular (IM) vitamin K availability and injection resistance across culture s in low-middle-income countries lead to the utilization of inferior oral regimens that put patients at risk of late-onset VKDB. Lack of good health system organization and suboptimal parental education also discourage universal coverage (22).

Table 1. Recommendation for Vitamin K Prophylaxis of the Newborn Infant

Population	Route	Dose & Schedule	Key Recommendation	Source
All term newborns	IM	0.5–1.0 mg once at birth	All newborn infants receive a single IM dose of 0.5 to 1.0 mg of vitamin K.	AAP (2022) NSH V4.0
All term newborns	Oral	1 mg once at birth	Effective against classic VKDB but fails to prevent late-onset unless multi-dose regimens are used	AAP (2022)
Term Infants (≥34 weeks)	IM	1mg	All healthy infants of 34 weeks and above should receive 1mg (0.1ml) Vitamin K (Konakion MM Paediatric) as soon as is practical after birth.	NSH V4.0
Preterm Infants (<34 weeks)	IM	0.5mg	All infants under 34 weeks gestation should receive 0.5mg (0.05ml via the included special syringe) Vitamin K (Konakion MM Paediatric) intramuscular (or intravenously on medical advice).	NSH V4.0
Preterm infants <1000 g	IM	0.3–0.5 mg/kg once at birth	The AAP has recommended a single IM dose of vitamin K of 0.3 to 0.5 mg/kg for preterm infants weighing less than 1000 g.	AAP (2022)
At Risk Infants	Oral	20mg	Mothers at high risk (taking potentially hepatic enzyme-inducing drugs during pregnancy, i.e., phenytoin, phenobarbitone,	NSH V4.0

			carbamazepine, primidone, topiramate, rifampicin, isoniazid, and warfarin) should be identified so that oral vitamin K 20 mg is given daily for 4 weeks prior to delivery.	
Breastfed infants	Oral	2 mg	In most countries with oral vitamin K supplementation policies, a late dose of oral vitamin K is recommended at 4 to 12 weeks to prevent late-onset VKDB in these infants.	AAP (2022) NSH V4.0

Adapted from AAP (2022) & NSH Neonatal Clinical Guideline V4.0 [23, 24].

Safety and Adverse Effects

Vitamin K is usually well tolerated. Side effects occur infrequently and consist of reaction at the injection site, pain, and bruising. Anaphylactic and hypersensitivity reactions are extremely rare. Prior suggestions linking IM vitamin K with childhood leukemia have been refuted by large population-based studies [25].

Vitamin D

Pharmacologic Profile

Vitamin D_3 (cholecalciferol) is used due to greater potency and longer half-life [26]. It is converted in the liver after intestinal absorption by 25-hydroxylation to 25(OH)D, which is the major circulating form and index of vitamin D status. It is further metabolized in the kidneys to the active hormone $1,25(OH)_2D$ (calcitriol) [27]. Maternal status provides significant dependence of neonatal vitamin D status [28]. Premature birth, dark skin, lower sunlight exposure, and extended exclusive breastfeeding are risk factors for deficiency [29]. Pharmacokinetics: 25(OH)D half-life of 2–3 weeks. Fat-soluble and fat-stored in adipose tissue. Oral supplement preferable in neonates [26].

Mechanism of Action

Vitamin D is bound by vitamin D receptors (VDRs) in the intestine, bone, kidney, and immune cells [30]. It promotes the absorption of calcium and phosphate, enhances mineralization of the bone, and regulates immune function [31]. In neonates, adequate vitamin D is required to avoid nutritional rickets, skeletal deformities, hypocalcemia, and seizures [8].

Dosage and Clinical Use Recommendations

AAP and the Endocrine Society recommend 400 IU/day of vitamin D_3 from the initial days of life for all babies, including those breastfed solely [32]. Preterm infants, especially when they have limited sun exposure or low birth weight, may require 800–1,000 IU/day [32]. WHO advises vitamin D supplementation specifically in areas of high prevalence of deficiency [33]. Deficiency in Sudan and sub-Saharan Africa in general is underreported, presumably because of maternal deficiency and cultural restrictions of sun exposure [34]. See Table 2 about recommendations for the treatment of low vitamin D in newborn infants.

Vitamin D: Motherly deficiency and limited supplementation programs in LMICs are accountable for rates of neonatal vitamin D deficiency that are overwhelmingly high. Cultural restrictions in sun exposure and poor healthcare infrastructure in rural areas aggravate the problem. (35)

Safety and Adverse Effects

Vitamin D has a wide therapeutic range. Its toxicity is rare but may be seen with prolonged high doses and causes hypercalcemia, irritability, vomiting, polyuria, and nephrocalcinosis. Preterm and formula-fed babies on multiple preparations of vitamin D must be monitored [36].

https://doi.org/10.20428/yjms.v19i7.3056
https://journals.ust.edu/index.php/yjms

Table 2. Recommendation for Treatment of low vitamin D In Newborn Infant

Category	Age / Population	Replacement Dosing	Maintenance / Prevention Dosing
Preterm Infants	≥ 1,500 g	Mild–Mod (20–29 ng/mL)400–800 IU/day	400 IU/kg/day (max 400 IU)
	< 1,500 g	All levels200–400 IU/day via enteral feeds	
	< 37 weeks gestation	Deficient (< 20 ng/mL)800 IU/day for 1 month then reassess	
Term Infants (< 3 months)	All feeding types	Deficient / Severe1,000 IU/day × 3 months	400 IU/day
		Mild–Mod (20–29 ng/mL) 400 IU/day × 3 months	
Infants (3–12 months)	All feeding types	Deficient / Severe1,000 IU/day × 3 months OR 50,000 IU "stat" once then reassess in 1 month	400 IU/day
		Mild–Mod400 IU/day × 3 months	400 IU/day

Adapted from (RCH). Vitamin D deficiency CPG [36, 37].

Hepatitis B Vaccine

Composition of the vaccine and pharmacologic profile

The hepatitis B vaccine is a non-live, recombinant vaccine prepared from yeast cells genetically modified to secrete hepatitis B surface antigen (HBsAg) [39]. It is preserved in aluminum-based adjuvants to enhance immunogenicity [40]. Pharmacokinetically, it is administered intramuscularly and produces an adaptive immune response in weeks with the development of neutralizing anti-HBs antibodies [41].

Mechanism of Action

Upon administration, the HBsAg is digested by antigen-presenting cells (APCs) and presented to helper T cells, leading to B cell proliferation and the generation of antibodies [42]. The development of anti-HBs antibodies (>10 mIU/mL) is considered to be protective against HBV infection [43].

Clinical Indications and WHO Recommendations

Hepatitis B is the leading cause of chronic liver disease globally. Neonatal infection, especially from vertical (mother-to-child) transmission, has a 90% probability of evolving into chronic infection [44]. WHO recommends a birth dose (0.5 mL IM) within the first 24 hours of life, ideally within 12 hours. And three additional doses at 6, 10, and 14 weeks with the pentavalent vaccine schedule. In neonates of HBsAg-positive mothers: Administer hepatitis B vaccine and HBIG (0.5 mL each) at separate sites within 12 hours of birth. And finish with a complete vaccine schedule [45]. See Table 3 about hepatitis B vaccine schedules for infants.

Hepatitis B Vaccine: Delayed birth doses and poor screening rates of pregnant women for HBsAg in LMICs limit the effectiveness of the vaccine. Challenges of cold chain storage and far-flung delivery sites contribute to the barriers in receiving timely administration. (46)

Safety and Adverse Effects

The hepatitis B vaccine is highly safe. Local pain, erythema, or low-grade fever are frequent side effects. Severe reactions such as anaphylaxis occur very rarely (estimated <1 per million doses), and there is no causal relation between vaccines and autism or neurodevelopmental disorders, as concluded by multiple studies [47].

Table 4. Hepatitis B vaccine schedules for infants, by infant birthweight and maternal HBsAg status

Birthweight	Maternal HBsAg status	Single-antigen vaccine		Single-antigen + combination vaccine	
		Dose	Age	Dose	Age
≥2,000 g	Positive	1	Birth (≤12 hrs)	1	Birth (≤12 hrs)
		HBIG	Birth (≤12 hrs)	HBIG	Birth (≤12 hrs)
		2	1–2 months	2	2 months
		3	6 months	3	4 months
				4	6 months

https://doi.org/10.20428/yjms.v19i7.3056
https://journals.ust.edu/index.php/yjms

	Unknown*	1	Birth (≤12 hrs)	1	Birth (≤12 hrs)
		2	1–2 months	2	2 months
		3	6 months	3	4 months
				4	6 months
	Negative	1	Birth (≤24 hrs)	1	Birth (≤24 hrs)
		2	1–2 months	2	2 months
		3	6–18 months	3	4 months
				4	6 months
<2,000 g	Positive	1	Birth (≤12 hrs)	1	Birth (≤12 hrs)
		HBIG	Birth (≤12 hrs)	HBIG	Birth (≤12 hrs)
		2	1 month	2	2 months
		3	2–3 months	3	4 months
		4	6 months	4	6 months
	Unknown	1	Birth (≤12 hrs)	1	Birth (≤12 hrs)
		HBIG	Birth (≤12 hrs)	HBIG	Birth (≤12 hrs)
		2	1 month	2	2 months
		3	2–3 months	3	4 months
		4	6 months	4	6 months
	Negative	1	Hospital discharge or age 1 month	1	Hospital discharge or age 1 month
		2	2 months	2	2 months
		3	6–18 months	3	4 months
				4	6 months

adapted from CDC [47].

HBIG = hepatitis B immune globulin; HBsAg = hepatitis B surface antigen.

The final dose in the vaccine series should not be administered before age 24 weeks (164 days).

DISCUSSION

This review critically examined pharmacokinetics, mode of action, and clinical practice guidelines for neonatal administration of vitamin K, vitamin D, and the hepatitis B vaccine. While these interventions are still the pillars of neonatal practice, examination also revealed disparities in access, variability in practice, and systemic barriers to timely and proper use. Through a blend of pharmacological evidence and real-life challenges, this review highlights not just the science underpinning these interventions but also the need for improved implementation plans and policy advocacy so that there can be universal and equitable neonatal coverage (48-50).

Vitamin K prophylaxis is generally advocated across the globe for the evident prevention of vitamin K deficiency bleeding (VKDB) in the form of potentially fatal late-onset VKDB [20, 51]. Intramuscular (IM) injection proved more bioavailable and longer in duration of protection compared to oral regimens, as confirmed through several comparative studies [21]. Nonetheless, some countries continue to administer oral vitamin K due to cultural opposition towards neonatal injections, which carries the risk of enhanced noncompliance and decreased efficacy [52].

Similarly, vitamin D supplementation in neonates, particularly those who are being exclusively breastfed, plays a crucial role in the prevention of rickets and complications of hypocalcemia [8]. Pharmacological reasoning has been supplied by the low level of vitamin D in human milk and high prevalence of maternal deficiency in the majority of low- and middle-income nations [53]. But the dose variation of recommendations from 400 IU/day to as much as 1,000 IU/day among preterm infants implies the lack of consensus concerning the optimal regimens for specific neonatal subgroups [32].

The hepatitis B vaccine is still one of the most successful interventions in neonatal care, and early vaccination has been shown to greatly reduce vertical transmission [54]. The use of both vaccine and hepatitis B immunoglobulin (HBIG) in infants whose

mothers are HBsAg-positive is an extremely effective combination strategy [55]. In practice, however, it has been shown that early use, particularly in the first 12 hours, remains low in the majority of resource-limited settings [55].

Despite shared clinical consensus regarding their efficacy, several controversies persist; vitamin K: the safety of IM injection, once linked (although disproven) to leukemia, remains an influence upon parental preference [56]. Secondly, the lack of a single-dose regimen that is as effective as IM dosing, taken orally, persists as a significant gap in our understanding [57].

Vitamin D: Large, randomized trials are extremely limited in neonates from geographically widespread areas [58]. Such trials are lacking from Africa and Southeast Asia, which are likely to have a high prevalence of deficiency but where reporting is poor [58]. The ideal dose in very-low-birth-weight infants and in comorbid patients is under-researched [59].

Hepatitis B Vaccine: The challenge of ensuring maternal screening for HBsAg status and integration of on-time HBIG administration into routine delivery care poses logistic hurdles. Additionally, the emergence of HBV variants might have implications for future vaccine efficacy, an issue not yet sufficiently examined in neonates [5].

The early pharmacologic interventions depicted early are not only preventive; they are crucial in the prevention of infant morbidity and mortality [61-63]. Their universal use reflects an investment by a system in public health, maternal-child integration of care, and practice based on evidence. Universal coverage, however, is thwarted in rural or underserved settings by logistical, educational, and cultural barriers. Neonatologists, midwives, and public health workers should be well-trained and well-equipped to employ these agents early and appropriately [61-63].

CONCLUSION

Pharmacologic and clinical use of vitamin K, vitamin D, and hepatitis B vaccine among newborns is a reflection of urgent, evidence-based interventions that significantly reduce the risk of potentially life-threatening conditions such as VKDB, nutritional rickets, and vertical hepatitis B transmission. Despite their proven efficacy, there remains a challenge to guarantee equal application, particularly where low resources and ethnic diversity prevail.

Intramuscular prophylaxis with vitamin K remains the gold standard for VKDB prevention, but diverse oral dosing practices and parent resistance highlight the need for improved communication and alternative regimens. Vitamin D supplementation is critical in exclusively breastfed infants and preterm infants, but divergent dosing recommendations and underreporting of deficiency necessitate stronger data in different populations. The hepatitis B vaccine, especially in combination with HBIG in infants of HBsAg-positive mothers, is the cornerstone of infection prevention, but delays in making the birth dose available restrict its best utilization in most settings.

In order to optimize neonatal outcomes, there is a need for concerted systemic effort towards optimizing the education of healthcare professionals, parents' education, and policy advocacy. Additional research is also required in order to standardize dosing in special populations as well as improve access to adequate delivery systems. These early interventions are not only life-saving pharmacologic interventions but also integral parts of long-term public health agendas.

Recommendations

Promote universal administration of vitamin K, vitamin D, and the hepatitis B vaccine as a routine procedure of neonatal care. Promote education and awareness among parents and health workers regarding the importance and safety of the medicines. Enhance national policy and guidelines to enable timely administration, especially in low-resource settings. Encourage further studies on individualized dosing and pharmacokinetics in special neonatal populations (e.g., preterm or low birth weight infants).

Conflict of Interest

The authors declare that no conflict of interest

REFERENCES

[1] Dol J, Hughes B, Bonet M, Dorey R, Dorling J, Grant A, Langlois EV, Monaghan J, Ollivier R, Parker R, Roos N. Timing of neonatal mortality and severe morbidity during the postnatal period: a systematic

review. JBI evidence synthesis. 2023 Jan 1;21(1):98-199.

[2] Thigpen JC, Odle BL, Harirforoosh S. Opioids: a review of pharmacokinetics and pharmacodynamics in neonates, infants, and children. European Journal of Drug Metabolism and Pharmacokinetics. 2019 Oct; 44:591-609.

[3] Loureiro CV, Fonteles MM, Mascarenhas MB, Chaves EF, Firmino PY. Medication follow-up in newborns with extremely low birth weight. Pharmacy Practice (Granada). 2019 Dec;17(4).

[4] Hand I, Noble L, Abrams SA. Vitamin K and the newborn infant. Pediatrics. 2022 Mar 1;149(3): e2021056036.

[5] Elsori DH, Hammoud MS. Vitamin D deficiency in mothers, neonates, and children. The Journal of Steroid Biochemistry and Molecular Biology. 2018 Jan 1;175:195-9.

[6] Lu Y, Liang XF, Wang FZ, Yan L, Li RC, Li YP, Zhu FC, Zhai XJ, Li J, Zhuang H. Hepatitis B vaccine alone may be enough for preventing hepatitis B virus transmission in neonates of HBsAg (+)/HBeAg (−) mothers. Vaccine. 2017 Jan 3;35(1):40-5.

[7] Araki S, Shirahata A. Vitamin K deficiency bleeding in infancy. Nutrients. 2020 Mar 16;12(3):780.

[8] Charoenngam N, Ayoub D, Holick MF. Nutritional rickets and vitamin D deficiency: Consequences and strategies for treatment and prevention. Expert Review of Endocrinology & Metabolism. 2022 Jul 4;17(4):351-64.

[9] Cheung KW, Seto MT, Lao TT. Prevention of perinatal hepatitis B virus transmission. Archives of gynecology and obstetrics. 2019 Aug 1;300:251-9.

[10] Ahmed MA, Alamoodi AA, Muthanna FM. Strategies for the Use of Antithrombotic Drugs in Atrial Fibrillation Patients Undergoing Percutaneous Coronary Intervention. A review article. Yemeni Journal for Medical Sciences. 2025;19(1):70-83.

[11] Nowak-Göttl U, Limperger V, Bauer A, Kowalski D, Kenet G. Bleeding issues in neonates and infants—update 2015. Thrombosis Research. 2015 Feb 1;135:S41-3.

[12] Goltzman D. Functions of vitamin D in bone. Histochemistry and Cell Biology. 2018 Apr;149(4):305-12.

[13] World Health Organization. Hepatitis B vaccines: WHO position paper, July 2017–Recommendations. Vaccine. 2019 Jan 7;37(2):223-5.

[14] Jullien S. Vitamin K prophylaxis in newborns. BMC pediatrics. 2021 Sep;21:1-7.

[15] Emekli-alturfan eb. Fat-soluble vitamins. A guide to vitamins and their effects on diseases. 2023 Mar 28;36.

[16] Indrio F, Neu J, Pettoello-Mantovani M, Marchese F, Martini S, Salatto A, Aceti A. Development of the gastrointestinal tract in newborns as a challenge for appropriate nutrition: a narrative review. Nutrients. 2022 Mar 28;14(7):1405.

[17] Sugandhi VV, Pangeni R, Vora LK, Poudel S, Nangare S, Jagwani S, Gadhave D, Qin C, Pandya A, Shah P, Jadhav K. Pharmacokinetics of vitamin dosage forms: A complete overview. Food Science & Nutrition. 2024 Jan;12(1):48-83.

[18] Afanasjeva J. Administration of injectable vitamin K orally. Hospital Pharmacy. 2017 Oct;52(9):645-9.

[19] Berkner KL, Runge KW. Vitamin K-dependent protein activation: normal gamma-glutamyl carboxylation and disruption in disease. International Journal of Molecular Sciences. 2022 May 20;23(10):5759.

[20] Okubo R, Shirota C, Wada M, Shinkai M, Tomita H, Umeda S, Miyake H, Matsuura T, Fumino S, Odaka A, Hibi T. Vitamin K deficiency bleeding and optimal prophylaxis methods in biliary atresia: A surveillance study in Japan. Pediatrics International. 2025 Jan;67(1):e70075.

[21] Ng E, Loewy AD. Guidelines for vitamin K prophylaxis in newborns. Pediatrics & child health. 2018 Aug 16;23(6):394-7.

[22] Coffey PS, Gerth-Guyette E. Current perspectives and practices of newborn vitamin K administration in low- and middle-income countries. Research and reports in neonatology. 2018 Apr 5:45-51.

[23] Hand I, Noble L, Abrams SA. Vitamin K and the newborn infant. Pediatrics [Internet]. 2022 Mar;149(3):e2021056036 [cited 2025 May 25]. Available from: https://publications.aap.org/pediatrics/article/149/3/e2021056036/184866/Vitamin-K-and-the-Newborn-Infant

[24] Royal Cornwall Hospitals NHS Trust. Vitamin K administration—neonatal clinical guideline [Internet]. Cornwall (UK): RCHT; 2020 [cited 2025 May 25]. Available from: https://doclibrary-rcht.cornwall.nhs.uk/DocumentsLibrary/RoyalCornwallHospitalsTrust/Clinical/NewbornCare/VitaminKAdministrationNeonatalClinicalGuideline.pdf

[25] Simes DC, Viegas CS, Araújo N, Marreiros C. Vitamin K as a powerful micronutrient in aging and age-related diseases: pros and cons from clinical studies. International Journal of Molecular Sciences. 2019 Aug 25;20(17):4150.

[26] Deb S, Reeves AA, Lafortune S. Simulation of physicochemical and pharmacokinetic properties of vitamin D3 and its natural derivatives. Pharmaceuticals. 2020 Jul 23;13(8):160.

[27] Fleet JC. Differences in the absorption and metabolism of vitamin D2, vitamin D3, and 25-hydroxyvitamin D. The Journal of Steroid Biochemistry and Molecular Biology. 2025 May 1;249:106718.

[28] Ni M, Zhang Q, Zhao J, Shen Q, Yao D, Wang T, Liu Z. Relationship between maternal vitamin D status in the first trimester of pregnancy and maternal and neonatal outcomes: a retrospective single-center study. BMC pediatrics. 2021 Dec;21:1-4.

[29] Bezabih AS, Eshetu D, Yohanis N, Hirigo AT. Knowledge and practice of infants exposure to sunlight among lactating mothers attending at Yirgalem Hospital, Sidama Regional State. Clinical Medicine Insights: Pediatrics. 2021 Sep;15:11795565211041348.

[30] Goltzman D. Functions of vitamin D in bone. Histochemistry and Cell Biology. 2018 Apr;149(4):305-12.

[31] Fleet JC. Regulation of intestinal calcium and phosphate absorption. In Vitamin D 2018 Jan 1 (pp. 329-342). Academic Press.

[32] Abrams SA. Vitamin D in preterm and full-term infants. Annals of Nutrition and Metabolism. 2020 Nov 27;76(Suppl. 2):6-14.

[33] Cashman KD. Vitamin D deficiency: defining, prevalence, causes, and strategies of addressing. Calcified Tissue International. 2020 Jan;106(1):14-29.

[34] Martin CA, Gowda U, Renzaho AM. The prevalence of vitamin D deficiency among dark-skinned populations according to their stage of migration and region of birth: A meta-analysis. Nutrition. 2016 Jan 1;32(1):21-32.

[35] Cashman KD, Sheehy T, O'Neill CM. Is vitamin D deficiency a public health concern for low-middle-income countries? A systematic literature review. European Journal of Nutrition. 2019 Feb 1;58:433-53.

[36] Corsello A, Spolidoro GCI, Milani GP, Agostoni C. Vitamin D in pediatric age: current evidence, recommendations, and misunderstandings. Front Med (Lausanne). 2023 Mar 16;10:1107855. doi: 10.3389/fmed.2023.1107855. PMID: 37007781; PMCID: PMC10060648.

[37] Royal Children's Hospital (RCH). Vitamin D deficiency [Internet]. Melbourne: RCH; [date unknown] [cited 2025 May 24]. Available from https://www.rch.org.au/clinicalguide/guideline_index/Vitamin_D_deficiency/

[38] Rizzoli R. Vitamin D supplementation: upper limit for safety revisited?. Aging clinical and experimental research. 2021 Jan;33(1):19-24.

[39] Tulenko SE. Evaluating Immunogenicity of a Hepatitis B Birth Dose Vaccine in the Democratic Republic of Congo and of Measles Vaccination in the Context of Malaria Infection in Kenya (Doctoral dissertation, The University of North Carolina at Chapel Hill).

[40] Moni SS, Abdelwahab SI, Jabeen A, Elmobark ME, Aqaili D, Gohal G, Oraibi B, Farasani AM, Jerah AA, Alnajai MM, Mohammad Alowayni AM. Advancements in vaccine adjuvants: the journey from alum to nano formulations. Vaccines. 2023 Nov 9;11(11):1704.

[41] Di Lello FA, Martínez AP, Flichman DM. Insights into induction of the immune response by the hepatitis B vaccine. World Journal of Gastroenterology. 2022 Aug 21;28(31):4249.

[42] 42 Grillo M. Study the dynamics of HBsAg-specific B cells in a mouse model of HBV pathogenesis.

[43] Mastrodomenico M, Muselli M, Provvidenti L, Scatigna M, Bianchi S, Fabiani L. Long-term immune protection against HBV: Associated factors and determinants. Human Vaccines & Immunotherapeutics. 2021 Jul 3;17(7):2268-72.

[44] Veronese P, Dodi I, Esposito S, Indolfi G. Prevention of vertical transmission of hepatitis B virus infection. World Journal of Gastroenterology. 2021 Jul 14;27(26):4182.

[45] Accrombessi M, Adetola CV, Bacharou S, Dossou Y, Avokpaho E, Yakoubou A, Koumakpai-Adeothy S, Lozes E, Issifou S. Assessment of the anti-HBs antibody response in Beninese infants following 4 doses of HBV vaccine, including administration at birth, compared to the

standard 3-dose regimen: a cross-sectional survey. Vaccine. 2020 Feb 11;38(7):1787-93.

[46] de Villiers MJ, de Villiers E, Nayagam S, Hallett TB. Direct and indirect effects of hepatitis B vaccination in four low- and middle-income countries. Epidemics. 2024 Dec 1;49:100798.

[47] Centers for Disease Control and Prevention (CDC). Vaccine administration: hepatitis B [Internet]. Atlanta (GA): CDC; 2023 [cited 2025 May 25]. Available from https://www.cdc.gov/hepatitis-b/hcp/perinatal-provider-overview/vaccine-administration.html.

[48] Pattyn J, Hendrickx G, Vorsters A, Van Damme P. Hepatitis B vaccines. The Journal of Infectious Diseases. 2021 Oct 1;224(Supplement_4):S343-51.

[49] Chamia JM. Uptake of Neonatal Vitamin K Prophylaxis in the Postnatal Wards of Kenyatta National Hospital (Doctoral dissertation, Uon).

[50] Wagner CL, Hollis BW, Kotsa K, Fakhoury H, Karras SN. Vitamin D administration during pregnancy as prevention for pregnancy, neonatal, and postnatal complications. Reviews in Endocrine and Metabolic Disorders. 2017 Sep;18:307-22.

[51] Costa B, Gouveia MJ, Vale N. Safety and Efficacy of Antiviral Drugs and Vaccines in Pregnant Women: Insights from Physiologically Based Pharmacokinetic Modeling and Integration of Viral Infection Dynamics. Vaccines. 2024 Jul 16;12(7):782.

[52] Coffey PS, Gerth-Guyette E. Current perspectives and practices of newborn vitamin K administration in low- and middle-income countries. Research and reports in neonatology. 2018 Apr 5:45-51.

[53] Cashman KD. Vitamin D deficiency: a public health issue in high- and low-income countries or just hype? . Hidden Hunger: Strategies to Improve Nutrition Quality. 2018 Jan 1;118:206-14.

[54] Bradshaw C, DiFrisco E, Schweizer W, Pavsic J, Demarco K, Weckesser J, Gold-VonSimson G, Rosenberg RE. Improving birth dose hepatitis B vaccination rates: a quality improvement intervention. Hospital pediatrics. 2020 May 1;10(5):430-7.

[55] Wei KP, Zhu FC, Liu JX, Yan L, Lu Y, Zhai XJ, Chang ZJ, Zeng Y, Li J, Zhuang H. The efficacy of two different dosages of hepatitis B immunoglobulin combined with hepatitis B vaccine in preventing mother-to-child transmission of hepatitis B virus: a prospective cohort study. Vaccine. 2018 Jan 4;36(2):256-63.

[56] Phillippi JC, Holley SL, Morad A, Collins MR. Prevention of vitamin K deficiency bleeding. Journal of Midwifery & Women's Health. 2016 Sep;61(5):632-6.

[57] Afanasjeva J. Administration of injectable vitamin K orally. Hospital Pharmacy. 2017 Oct;52(9):645-9.

[58] Mo M, Wang S, Chen Z, Muyiduli X, Wang S, Shen Y, Shao B, Li M, Chen D, Chen Z, Yu Y. A systematic review and meta-analysis of the response of serum 25-hydroxyvitamin D concentration to vitamin D supplementation from RCTs from around the globe. European Journal

of Clinical Nutrition. 2019 Jun;73(6):816-34.

[59] Bilezikian JP, Formenti AM, Adler RA, Binkley N, Bouillon R, Lazaretti-Castro M, Marcocci C, Napoli N, Rizzoli R, Giustina A. Vitamin D: dosing, levels, form, and route of administration: does one approach fit all?. Reviews in Endocrine and Metabolic Disorders. 2021 Dec;22(4):1201-18.

[60] Tan J, Liu X, Mao X, Yu J, Chen M, Li Y, Sun X. HBsAg positivity during pregnancy and adverse maternal outcomes: a retrospective cohort analysis. Journal of viral hepatitis. 2016 Oct;23(10):812-9.

[61] Mailhot G, White JH. Vitamin D and immunity in infants and children. Nutrients. 2020 Apr 27;12(5):1233.

[62] Rai RK, Luo J, Tulchinsky TH. Vitamin K supplementation to prevent hemorrhagic morbidity and mortality of newborns in India and China. World Journal of Pediatrics. 2017 Feb;13:15-9.

[63] Pattyn J, Hendrickx G, Vorsters A, Van Damme P. Hepatitis B vaccines. The Journal of Infectious Diseases. 2021 Oct 1;224(Supplement_4):S343-51.