Vitamin K in the Newborn

<table>
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<th>Full Title of Guideline:</th>
<th>E9 VITAMIN K IN THE NEWBORN: Prophylaxis against vitamin k deficiency bleeding in infants</th>
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</table>
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Midwifery staff on labour suite and postnatal wards |
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(Maternity and the Neonatal Unit) |
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| Summary of evidence base this guideline has been created from: | The current evidence base has been used in the development of this guideline. References are provided in the ‘Reference’ section. |

*This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.*

**Key points**

- VKDB is preventable
- All babies should be given Vitamin K at birth
- IM route is the best option but it can also be given orally
- Documentation is important
- Where the parents withhold consent neonatal support is available to have further discussion
Vitamin K occurs in two forms, vitamin K₁ whose source is dietary and vitamin K₂ (Menaquinone) that is produced by gut bacteria. Vitamin K₁ crosses the placenta poorly (maternal to fetal gradient, 30:1) resulting in low concentrations in the fetus. After birth, vitamin K status depends on dietary intake from milk. Human breast milk contains relatively lower concentrations of vitamin K₁ (1-2 micrograms/L) compared to supplemented formula milk (usually >30 micrograms/L). Hepatic menaquinones accumulate later in infancy and offer no additional protection until then. Therefore, babies exclusively breast fed; sick babies; babies slow to establish feeding and babies with cholestatic liver disease are at risk of Vitamin K Deficiency Bleeding (VKDB). Without prophylaxis, the risk of VKDB is 1 in 10,000.

Clinical and scientific evidence

Early VKDB, occurring on the first day of life, is rare and confined to infants born to mothers who have received medications that interfere with vitamin K metabolism. These include the anticonvulsants phenytoin, barbiturates or carbamazepam, the antitubercular drugs rifampicin or isoniazid and the vitamin K antagonists Warfarin or Phenprocoumon. It is prevented by giving vitamin K to the mother (except those that require ongoing anticoagulation) in the last weeks of pregnancy and ensuring that a dose of IM vitamin K is given to the baby.

Late VKDB can occur from the first week to up to 6 months, usually between 4 and 12 weeks. This form is more commonly associated with intracranial bleeds (30-50%) than classical VKDB and this can be fatal or leave permanent disability. It is almost completely confined to fully breast-fed babies. About half will have an underlying liver disease or other malabsorptive state. Late VKDB can be
optimally prevented by 1mg vitamin K IM at birth or significantly reduced by repeated doses of oral vitamin K.

The challenge for any vitamin K policy, advocating the oral route, lies in its attempt to prevent late VKDB. The department of health has an information leaflet for parents implying best practice. This policy incorporates the current practice, current evidence and drug licensing/formulation issues.

2. Clinical and scientific evidence

What is the best available prophylaxis?

Vitamin K, given intramuscularly, shortly after birth, is the best available prophylaxis. IM vitamin K significantly reduces the incidence of classical and late VKDB when compared to no prophylaxis or oral vitamin K prophylaxis (see Table 1).

A single 1mg IM dose provides almost complete protection, probably by providing a slow release, but a dose this large can cause some liver overload in the very preterm baby. Very low birth weight babies, therefore, are given a lower dose (see below). Oral vitamin K performs less well in protecting against late VKDB, unless it is given daily or weekly for the first 3 months. Variations in the reported efficacy of vitamin K may be due to differences in dose, formulation, regime or compliance.

Table 1: Risk for Late VKDB

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Incidence (per 100,000 births)</th>
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<tbody>
<tr>
<td>No prophylaxis</td>
<td>5.8 - 80</td>
</tr>
<tr>
<td>1 x 1mg IM dose</td>
<td>0 - 0.9</td>
</tr>
<tr>
<td>Daily low dose oral vitamin K for breast fed infants</td>
<td>0 - 1.3</td>
</tr>
<tr>
<td>3 x 1mg oral doses</td>
<td>1.1 - 4.8</td>
</tr>
<tr>
<td>2 x 2mg oral doses</td>
<td>0.7 - 10.6</td>
</tr>
<tr>
<td>3 x 2mg oral doses</td>
<td>0.33 – 0.9</td>
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What are the potential risks of intramuscular prophylaxis?

An association between the early preparations of IM vitamin K and childhood cancer was suggested in 1990 and 1992. The American Academy of Pediatrics Vitamin K Ad Hoc Task Force effectively dispelled concerns that IM administration of vitamin K was associated with childhood cancers such as leukemia. As a result, the intramuscular route is preferred in many countries. Other risks-the intramuscular route should not be used if there is active bleeding.

How can vitamin K be given?

NICE guidance published in 2006 and updated in 2015 recommends that vitamin K prophylaxis should be administered as a single IM dose as the most clinically and cost effective method. Should parents decline IM vitamin K, then oral vitamin K should be offered as a second line, whilst advising parents that oral vitamin K is less effective and will require multiple doses. This is the guidance that NUH is following.

Konakion® MM Paediatric is the licensed product for use. When 3 oral doses of Konakion® MM Paediatric were compared with an IM dose of Konakion® MM Paediatric, no significant differences in coagulation and PIVKAII production were found in the first 8 weeks of life. The main concerns with delivery by the oral route are compliance and protecting the baby with liver disease or malabsorption. If it is given IV, without a prior IM dose, then further oral doses should be given when the baby is well (Table 2).

The fourth BPSU study on VKDB, undertaken on cases between 2006-2008, demonstrated the sustained decrease in cases of VKDB since the implementation of vitamin K prophylaxis. Eleven cases were identified during this period, 6 of which received no vitamin K, and 2 had incomplete oral courses. The remaining 3 had IM vitamin K – but two of these babies were determined to have
biliary atresia. Of the 217 UK centres included in the study, 69% recommended IM, 9% recommended oral and 21% gave a choice.\textsuperscript{21}

**What is the best oral regime for preventing late VKDB?**\textsuperscript{4, 5, 8, 9, 22}

Clearly a single oral dose of vitamin K does not protect against late VKDB. Comparable protection to the IM regime has been achieved by daily or weekly doses of vitamin K given for up to 3 months. Shorter regimes have been more popular, but associated with some cases of late VKDB in well breast fed babies and those with liver disease. The current licensed regime is to give 2 or 3 doses of 2mg Konakion\textsuperset{®} MM Paediatric, depending on what feeds is infant is receiving breast or formula.

3. **Prevention of vitamin K deficiency bleeding in infants**

Giving vitamin K after birth to all babies can reduce the risks of developing both classical and late VKDB. **Intramuscular vitamin K offers the best protection.**

4. **Patient groups and their management**

- Vitamin K prophylaxis should be discussed and decided upon antenatally
- **All babies admitted to the NNU** should have IM vitamin K, unless contraindicated
- Outside of NICU, the **recommended route** of administration is IM
- If parents decline IM, the alternative route of administration is oral
- Midwives are able to give vitamin K (licensed or unlicensed) without medical prescription at NUH as part of their midwife exemptions
- All infants with a suspected bleeding disorder should have **intravenous** vitamin K (will need further doses- see Table 2)
- **If Vitamin K is given IV, without a prior IM dose, then further oral doses should be given when the baby is well**
- If an oral dose is vomited within three hours, this can be repeated, as advised by the manufacturer and BNFc
- The administration of vitamin K should be documented immediately to avoid confusion regarding whether it has been given. If there is uncertainty regarding whether a baby has received vitamin K, this needs discussion with the neonatal team and reviewed on a case by case basis
- If less than 36 weeks gestation, the license is for IM or IV dosing. **The licensed dose for babies <2.5kg is 0.4mg/kg (maximum 1mg). Due to the difficulty of drawing up very small volumes, we will use the most practical dosing regime, as outlined below**

5. **Vitamin K Dosing (Table 2)**\textsuperscript{23, 24}

<table>
<thead>
<tr>
<th>Route</th>
<th>1\textsuperscript{st} Dose (at birth)</th>
<th>2\textsuperscript{nd} Dose (1 week)</th>
<th>3\textsuperscript{rd} Dose (1 month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM (if &gt;1.5kg)</td>
<td>1mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IM (if &lt;1.5kg)</td>
<td>0.5mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Oral (breast or mixed fed)</td>
<td>2mg</td>
<td>2mg</td>
<td>2mg</td>
</tr>
<tr>
<td>Oral (formula fed)</td>
<td>2mg</td>
<td>2mg</td>
<td>-</td>
</tr>
<tr>
<td>IV prophylaxis dose with NO prior IM dose (NICU only)</td>
<td>1mg</td>
<td>2mg oral</td>
<td>2mg oral</td>
</tr>
<tr>
<td>For Treatment of VKDB</td>
<td>IV with a prior IM dose: (only on NICU)</td>
<td>First dose 1mg- repeated 8 hourly, if required</td>
<td></td>
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Please note the following:

- If prophylactic vitamin K is administered IV instead of IM, due to a contraindication with the IM route, then further oral doses of vitamin K should be administered, as above, in order to avoid late VKDB
- If IV Vitamin K is given as treatment for VKDB, in addition to a prior IM dose, the IV dose can be repeated 8 hourly, if required. No further oral doses are required in this circumstance

Please refer to the Neonatal Vitamin K Monograph for further details of dosing.

6. Consent

All parents will receive information about the need for postnatal vitamin K in the antenatal period. Those taking consent must have understanding of local policy. Documentation is of importance. The use of vitamin K should be recorded in the maternal notes (stamp). Similarly, if parents withhold consent, this should also be documented. The neonatal team can be contacted if further support is required.

All babies admitted to the Neonatal Unit will receive intramuscular vitamin K as part of their treatment. Specific parental consent is not sought but parents are informed.

7. Vitamin K preparations

1. Vitamin K (Phytomenadione) is administered as Konakion® MM Paediatric within the hospital setting. Konakion MM Paediatric is a mixed micellar preparation, which is well absorbed orally. It is licensed for IM, IV and oral use, and supplied in glass ampoules with an oral filter straw. The preparation is 2mg in 0.2ml, therefore a 1mg dose is 0.1ml. There is also an unlicensed product called Konakion MM, which is the same strength as the licenced product 2mg/0.2mL and may be used where the licensed product is not available. However, when the unlicensed product is used, the product details such as baby’s name, K number, batch number and expiry date must be recorded in the relevant pharmacy approved documentation.

2. Upon discharge, if requiring further oral doses, phytomenadione 1mg in 1mL unlicensed suspension is given, which is made up by pharmacy.

3. An alternative oral preparation is Neokay drops- 200 microgram/ml, where 0.25ml = 50 micrograms. This is often referred to by GPs and suggested as a lower daily dose.

8. Side effects

Vitamin K is generally very well tolerated, however, some risks or side effects can be as follows:

- "May induce haemolysis in erythrocyte G6PD deficiency or low concentrations of alphatocopherol in the blood" 15
- There are a few unconfirmed cases of anaphylaxis after IV administration of Konakion® MM Paediatric
- Local irritation and inflammation after IM use have been reported, but thought less likely with the smaller volume
- Parenteral administration to premature babies <2.5kg may theoretically increase the risk of jaundice because of the effect of glycocholic acid (one of the excipients) in displacing bilirubin from protein binding sites

Neonatal Alert: Infants of mothers taking medication interfering with vitamin K metabolism, such as Warfarin, Phenobarbitone, Phenytoin and Carbamazepine

Mothers require vitamin K at the end of their pregnancy. Mothers requiring on going anticoagulation do not receive vitamin K, as it counters the effect of their warfarin. The baby must receive vitamin K soon after birth as 1mg IM (Konakion® MM Paediatric). In the event of significant trauma and bleeding, IV vitamin K should be given by slow intravenous injection. FFP at 10-15ml/Kg will raise the clotting factors by 10-20iu/dL and should be considered.
9. **Audit points**

Differed parental consent for Vitamin K IM versus Oral route of Vitamin K administration
Complications / side effects of Vitamin K

10. **References**


18. Joint statement and recommendations on vitamin K administration to newborn infants to prevent vitamin K deficiency bleeding in infancy. NHMRC, RACP (Paediatric division), RANZCOG, RACGP, ACM.

19. NICE guidance CG37 2006 and 2015: Postnatal care: Routine postnatal care of women and their babies


24. British National Formulary for Children
In Nottingham, we aim to give Vitamin K (also called Konakion) to all babies soon after birth to protect against a disease called vitamin K deficiency bleeding (VKDB). This is a rare bleeding disorder (5-20 per 100,000 births or 1-2 babies per year in Nottingham), which can be fatal or produce long-term disability if bleeding occurs into the brain. This disorder can be almost entirely prevented by giving Vitamin K soon after birth.

**Vitamin K prophylaxis can be given as an injection or be given into the mouth.**

The best protection is provided by the injection and many babies receive it in this way in the UK and around the world. In 1990 and 1992, some published research suggested a possible link between Vitamin K given by injection and childhood cancer, but this finding has not been conclusively supported in reviews of subsequent research studies. Australian and American Paediatricians recommend giving vitamin K as an injection.

**In Nottingham we strongly advise all parents to agree to their babies receiving Vitamin K.**

Vitamin K by intramuscular injection offers the best protection (reduces incidence of VKDB to 0.3 per 100,000 cases).

In Nottingham, in recent years, Vitamin K given by mouth has been found to be consistently safe and effective, provided all the 2 or 3 doses of 2 mg are given, depending on whether breast or formula fed (3 oral doses reduces incidence to 0.9 per 100,000 cases).

Parents are always asked to give verbal consent before their babies are given Vitamin K prior to discharge from labour suite, unless admitted to NICU at birth, in which case all babies receive IM vitamin K.

When given by oral route, breast feeding mothers should take home two further doses to give by mouth to their babies - at one week and one month after birth. Bottle feeding babies take home only a second dose (given at 1 week). Full instructions on how to give subsequent doses at home are given before discharge.

We strongly recommend that all babies be given Vitamin K. More information can be obtained from your midwife. If you have any further questions or concerns, please feel free to ask your midwife or the paediatrician.