Hemorrhagic disease of the newborn, also referred to as vitamin K deficiency bleeding (VKDB), is a totally preventable, potentially deadly condition that most of us pediatricians don’t give much thought. However, internet bloggers have once again apparently have made pediatricians unwitting victims of our success with the standard use of intramuscular (IM) vitamin K prophylaxis in every newborn since 1961 (Figure 1). That is more than 50 years of routine use in every newborn nursery, adding up to nearly 200 million doses in the United States alone. And for newborns, vitamin K delivered intramuscularly has shown almost no known adverse effects except possibly a total of seven dermatologic reactions. The only reported serious adverse effect I could find in the literature happened not in the United States, but in a newborn in Turkey only a few months ago. This was a single case of potentially severe anaphylaxis reaction from a dose given at birth. This is the only English-language report in any of the reputable medical literature that I could find, despite administration of probably more than a billion newborn IM doses. If this one in a billion occurrence should ever happen again, then what better place for it to happen than in the presence of a trained physician and at least two nurses?

I think that because the internet bloggers and parents posting in chat rooms may not have seen severe VKDB themselves, they have assumed cavalierly that severe VKDB must no longer exist. They are dead wrong, and they are gambling with some infants’ brains and lives in a dangerous game of intracranial roulette. No matter how much they want it to be true, VKDB is not a myth concocted by the medical establishment, which is a falsehood these bloggers try to perpetuate.

HISTORY IS DOOMED TO REPEAT ITSELF

For those young scientists and naive parents who claim that VKDB is a myth, I say not so fast. For example, we need only to look at four babies in Tennessee whose mothers declined vitamin K to see that the threat of devastating VKDB still lurks, as reported in the November 15, 2013, issue of Morbidity and Mortality Weekly Report. Three of these babies...
potentially had life-threatening blood clots evacuated from their cranium and will likely suffer from some form of permanent neurological damage.

And why did this happen? Let’s explore how something so tragic and preventable could still happen in these days of modern medicine. It must be remembered that VKDB is not caused by a lack of available medical care, but instead by a conscious parental decision to refuse customary known optimal care.

“DOCTOR, WE KNOW BETTER”

One of my older partners recently stormed into the office, notably upset about his current trip to our newborn nursery. The parents of a 12-hour-old newborn had just informed him that they were declining all “extraneous” medical interventions for their newborn boy. They desired that no “unnatural” substances be given to their newborn, and that their baby not be “unnecessarily disturbed or poked.” This included A) two state-mandated therapies: newborn metabolic screening (Figure 2) and prophylactic eye ointment (Figure 3); and B) two highly recommended prophylactic therapies: hepatitis B vaccination (Figure 4) and, for the first time in our experience, vitamin K1 injection (Figures 1 and 5).

My partner was totally flabbergasted by the hour-long discussion it required to explain the conventional pediatrician’s point of view about the importance of these potentially morbidity-sparing and mortality-saving interventions — only to casually hear the following rebuttals about his recommendations:

“We have read on the internet, etc … We want only the “natural way;” God does not want us to perform any unnecessary procedures... these newborn shots will cause permanent psychological and emotional damage... vitamin K has been associated with cancer...”

These last two objections were a first for our practice, and thus inspired us to...
perform further research into the recent voicing of these objections. With 17 key strokes in an internet search engine, we had our answer. The very first “hit” with a single search on Google under “newborn vitamin K” led us immediately to one source of such inspirations of medical paranoia about routine newborn care: Joseph Mercola, DO, and his website (http://www.mercola.com).

Why is there such pervasive parental anxiety about an “act of commission” or doing something preventively, no matter how bad the disease that this “something,” prevents and how well-known the safety of this “something” is documented? This is diametrically opposed to an “act of omission,” or merely passively letting mother nature wreak havoc by our doing nothing. Then, if the rare bad thing actually happens to our child, it would not be our fault, even though medical advances, such as vitamin K injection, could have prevented it.

Have we as a society become that distrusting of our medical scientific methods and of our pediatricians that we would rather trust the unsubstantiated unscientific innuendos and claims of a single person or group of naysayers? I think that most pediatricians would welcome an open-minded question from the parents and a chance to explain the science and to provide credible internet sites, rather than dooming a baby to potentially devastating, substandard care.

NEWBORN INTRACRANIAL ROULETTE

Without standard IM (or even oral) supplemental vitamin K during the immediate newborn period, the totally healthy infant is at notable risk for significant hemorrhaging during three specific time periods:

1) Early-onset hemorrhagic disease (within the first 24 hours), which is usually associated with cephalohematoma, gastrointestinal bleeding, or intracranial bleeding, such as subarachnoid bleeding that we have all seen.

2) “Classic” hemorrhagic disease (days 2 to 7), which occurs with a staggering incidence (reportedly as high as 0.25% to 1.7%) during the first week of life. This bleeding tends to be milder and more often from the umbilicus, gastrointestinal, and at puncture sites.

3) “Late” hemorrhagic disease (2 weeks to 6 months), which occurs with an incidence ranging from 4.4 to 7.2 per 100,000 live births from ages 2 to 12 weeks, based on reports from Europe and Asia. However, an even more alarming statistic is that late VKDB can develop in 1 in 15,000 to 1 in 20,000 infants who are exclusively breast-fed. Infants who do not receive IM vitamin K at birth are estimated to have an 81-times greater risk for late VKDB than those who receive the shot. And 50% of infants with late VKDB present with intracranial hemorrhage with a 20% mortality.

Overall, the typical sites of VKDB or hemorrhaging include intracranial (usually late disease), subarachnoid bleeding and extracranial cephalohematoma (usually early disease), gastrointestinal (usually classic disease), epistaxis, intrathoracic, circumcision, and skin. More subtle, milder bleeds and infant failure to thrive may herald the more catastrophic events.

RISK FACTORS FOR VKDB

Certain maternal medications are major risk factors for early VKDB. These include anti-seizure medications, such as phenytoin, phenobarbital, carbamazepine, or primidone; anticoagulants such as warfarin and aspirin; and maternal antibiotics, particularly cephalosporins. Early VKDB (first 24 hours) will develop in 6% to 12% of infants whose mothers have ingested these vitamin K–inhibitor drugs. Thus, there really is a critical urgency to substantially increase the vitamin K levels in the newborn to normal or higher as quickly as possible in the first hour or so after birth, which can definitely be accomplished with an IM dose of vitamin K. Otherwise, the newborn is particularly at risk for both early-onset and classic VKDB with their cutaneous, gastrointestinal, or intracranial bleeding.

Breast-feeding is a major risk factor for both classic and late VKDB. Other risk factors for late VKDB include malabsorption syndromes, such as celiac disease and cystic fibrosis, and liver diseases, such as biliary atresia and alpha-1 antitrypsin deficiency.

Also note that late VKDB mostly occurs in breast-fed infants who are healthy. Who are the parents most likely to decline the birth dose of vitamin K? The breast-feeding mother, whose infant remains highly deficient in vitamin K for a month or longer.

ACHIEVING PROTECTIVE NEWBORN VITAMIN K LEVELS

Due to vitamin K’s critical role in clotting factor production, vitamin K deficiency, particularly during the newborn period, can lead to significant hemorrhage and bleeding into the internal organs and brain. Vitamin K concentrations in the newborn are precarious.
low in the first week of the infant’s life, almost regardless of how much vitamin K the mother ingests during the pregnancy. Trans-placental transfer of vitamin K is minimal. The newborn infant’s liver is also too immature to efficiently use vitamin K. In the breast-fed infant, the normal gut bacteria that convert vitamin K into its active form are not available until several weeks of life. Newborns also do not have any vitamin K stored in the liver until age 2 to 3 months. Thus, only supplemental infant vitamin K can alter the young newborn’s levels of vitamin K. Most experts think that increasing the maternal ingestion of vitamin K-rich foods will likely be insufficient for protection of the breast-feeding newborn. However, maternal supplementation with high doses of vitamin K (5 mg/day) for 12 weeks has been shown to increase breast milk concentrations from the usual 0.1 mg/dL to 4.5 to 6 mg/dL. No clinically important protection has ever been demonstrated with this approach. Furthermore, these breast milk concentrations are still much lower than the protective amount of vitamin K received with infant formula (50 mg/dL). Remember that formula-fed babies are at almost no risk for classic or late VDKB, and no toxicity from the higher levels of vitamin K in formula has ever been reported.

That leaves us with one trusted means of protecting the breast-feeding newborn from devastating classic or late VKDB: infant supplementation. This can be readily accomplished via a single IM injection, or potentially by multiple oral doses. Oral ingestion, however, leaves us with several caveats.

ORAL VITAMIN K VERSUS INTRAMUSCULAR VITAMIN K

The consensus of most experts in the U.S. is to routinely use a single dose of IM vitamin K1 (0.5 mg to 1 mg) for all newborns, which is administered immediately after birth. No other method of delivery of vitamin K has been shown to be as nearly uniformly reliable or simple or to provide 100% adherence with the regimen. Furthermore, the IM route is much more likely to be protective against VKDB in uncommon diseases in the U.S. general population, such as alpha-1 antitrypsin deficiency (1 in 1,600), biliary atresia (1 in 10,000 to 1 in 20,000), and cystic fibrosis (1 in 3,000 white children).

For the healthy, full-term, breast-feeding infant, multiple oral doses of vitamin K1 (1 or 2 mg) have been used as an alternative to the IM approach for decliners and as routine practice in some countries. However, the following caveats to oral dosing must be addressed:

- In one recommended regimen, the higher dose (1 mg) of oral vitamin K must be given with the first feeding and at 1, 4, and 8 weeks of life. Note that some experts state that a single dose of oral vitamin K at birth fails to prevent late VDKB.
- No approved oral formulation exists in the U.S., so multiple vials of the parenteral formulation must be ordered. This is expensive and can be challenging for some parents. Babies tend to spit out non-milk substances.
- For the newborn, onset of action and normalization of poor clotting occurs within 4 to 6 hours with oral vitamin K and in 1 to 2 hours for IM vitamin K.
- Adherence to the four-dose schedule of oral vitamin K is only 93%. Thus, many babies will not be fully protected during their high-risk period. Also, two cases of VDKB were reported in children with alpha-1 antitrypsin deficiency treated orally. For example, in my practice, despite my strong recommendation at the hospital stay and at the first newborn office visit to administer daily vitamin D to the breast-feeding newborn, I still frequently encounter many mothers who have not initiated the vitamin D by 2 weeks. This is a scary thought if one imagines the omission were vitamin K instead.
- One study confirmed that among the different oral schedules for 1 mg of vitamin K prophylaxis in Australia, Germany, The Netherlands, and Switzerland, each was less effective than the single IM dose. Many countries have subsequently switched back to a policy of routine newborn IM vitamin K.
- In breast-feeding children with cholestatic liver disease, such as biliary atresia, or with malabsorption syndromes, the rates of VDKB are typically much higher when using oral schedules versus a single IM dose. One study in children with biliary atresia showed that a single daily dose of 25 mcg for months was much less effective than prophylaxis with either an oral 1-mg weekly dose of vitamin K or a single IM dose. Formula feeding provided the most effective protection in this high-risk population. Rarely, late VDKB can occur in infants who are given IM vitamin K, but only in those with cholestasis or malabsorption syndromes, who should always be given vitamin K IM.
- VDKB failures occur much more commonly with single daily doses of 0.25 mg vitamin K, and this regimen should possibly be avoided in breast-fed infants.
- Aspiration pneumonia in a newborn has been reported with oral vitamin K ingestion.

HOW COMMONLY DO PARENTS DECLINE VITAMIN K?

From January to October 2013 in three Nashville-area hospitals, an alarming 3.4% of 3,080 newborns did not receive vitamin K by time of discharge. Even more disturbing, 28% of 218 neonates from Tennessee “birthing centers,” run primarily by midwives did not receive a birth dose of vitamin K. A similar rate of refusal has been reported at a birthing center in Missouri.

Some experts think that the rates of
VKDB are grossly under-reported because it is always assumed that any young infant with gastrointestinal bleeding, or with a subdural or other brain bleed, who enters an emergency department or intensive care unit has received the birth dose of vitamin K. According to these recent data, we could be totally wrong.

I cannot begin to estimate the notable number of exclusively breast-feeding, otherwise healthy young babies with some significant hematochezia who were seen in our practice during the past few years. Like many pediatricians, our practice had always just assumed that they had an atypical “cow’s milk allergy” from milk proteins being transferred through the breast milk.14

We have usually switched the breast-feeding infant to one of the casein hydrolysate formulas, and then noted remarkable amelioration of the hematochezia in the next few days to weeks. Perhaps recently, many of these infants had not received the birth dose of vitamin K, and their ingestion of the larger concentration of daily oral vitamin K manufactured into the formula was the cure instead.

ARE THERE ANY VALID CONCERNS WITH VITAMIN K INJECTION FOR THE NEWBORN?

Let’s explore the alleged issues with vitamin K injection of the newborn.

Parental Reports to the US Centers for Disease Control and Prevention

According to the CDC’s report in 2013,3 three reasons were attributed to vitamin K refusal by parents. The first was that IM vitamin K doubles the risk for leukemia. This idea was first touted in a case-control study from Great Britain. For multiple reasons, including lack of plausibility and reproducibility, this theory has since been totally debunked. Even the website of Dr. Mercola has acknowledged this as pure mythology. And as for triggering leukemia, why would an IM injection be much different than oral ingestion of either small daily doses or weekly small boluses of vitamin K? Each method achieves some improved levels in the bloodstream.

The second reason was that parents felt the injection was unnecessary. Thus, they allege that they were not made fully aware of the possibility of late VKDB by our ‘experts’ or by our website.

Another part of their concerns may revolve around the list of adverse reactions in the package insert.

The third reason was that parents wanted the “all natural” method, and desired that no artificial substances be injected into their newborn. Many worried about exposure to toxins (see below from Dr. Mercola). The only possible worrisome ingredient in the aqueous vitamin K injection is 9 mg of benzyl alcohol used as a preservative. Mostly in preterm infants has benzoyl peroxide been reported to cause problems of kernicterus and brain hemorrhage, but only when given in relatively high volumes of preservative-containing intravenous saline flushes — not the miniscule dose received with IM vitamin K.15 Furthermore, for our IM vitamin K product, the U.S. Food and Drug Administration (FDA) has written: “There is no evidence to suggest that the small amount of benzyl peroxide contained in the Vitamin K injection when used as recommended, is associated with toxicity.”16

Personally, I think that another part of their concerns may revolve around the list of adverse reactions in the package insert that says that “deaths have occurred.” However, families were unaware that these have never been reported in infants. Rather, they primarily occur extremely rarely in adults, and mostly with the intravenous form and not the IM form.

Mercola.com: “The Potential Dark Side of the Routine Vitamin K Shot”

Dr. Mercola, a mass marketer of multiple diverse, controversial, and unproven homeopathic products, does acknowledge the lack of any link between IM vitamin K and leukemia. He also acknowledges that vitamin K is essential to prevent VDKB.

However, www.Mercola.com has three additional complaints about IM vitamin K. He argues that the multiple oral doses are better than a single IM dose, that a single shot will cause psychological problems in the newborn and may “jeopardize breastfeeding,” and that an IM injection within the hospital may create a site for infection. None of these claims are based on scientific data.

Dr. Mercola states that the oral doses avoid the toxic preservatives and will reduce the “excessive” amount of vitamin K the child receives, but this makes no sense. First, note that no oral liquid preparation is commercially available that is regulated by the FDA. So, by default, one needs to give a regulated pure vitamin K preparation orally (at the same dose of 1 mg that he recommends, as well). Thus, the child must receive a minimum of three to four doses of the same IM vitamin K — with its “20,000 times needed dose,” and the same “toxic preservatives” — and then with three to four doses at least. How is this better than a single IM dose? Studies show that there are more, albeit rare, breakthrough cases of VDKB with the oral doses than with the single IM dose.6

He obviously dislikes the notion of any shots for the newborn (Figure 6). I agree that the avoidance of pain in any child or newborn is an admirable goal. But preventing all tears in a baby is just not practical for the routine care that is
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required. As anyone knows who works or lives with babies, babies will cry, and they will often act like babies. No matter how gently anyone tries, crying often also accompanies our newborn examination or care while trying to check their red reflex, hip dislocation, femoral pulses, posterior pharynx, temperature, or even when diapering, bathing, and unclothing them. Are babies really that fragile?

Yet, in our hospital, we actually do quite well without fussing or tears with the vitamin K injection during the “kangaroo care” time period. Sometimes, we even give the injection using the calming effects of the feeding itself to prevent any crying. To say that one or two shots or heel sticks (Figure 7) will cause permanent psycho-emotional trauma is perhaps ludicrous. This objection is not based on any credible science. Again, we are not talking about weeks or days of necessary heel sticks every 2 hours for glucose, blood gas, or bilirubin in a sick infant, which truly is a pain-management problem.

As for iatrogenic site infection being caused by a routinely and correctly done single IM injection into a newborn, no data support this allegation, either in the literature or in my daily practice of 31 years. Perhaps he is referring to an unrelated iatrogenic intravenous catheter site infection? To call an IM injection of morbidity-sparing or life-saving medications or immunizations “damaging” is inflammatory and has no merit.

CONCLUSION

We must now be ever-vigilant about whether each of our patients younger than 6 months has received vitamin K in some form at birth or beyond, especially if the child is breast-feeding. For any child who presents to your office, emergency department, or intensive care unit with any bleeding diathesis, the parents must now be interrogated as to whether

Figure 6. An infant receiving the newborn injection of vitamin K to prevent hemorrhagic disease of the newborn. Could this be a cause of permanent psycho-emotional damage?

Figure 7. Recipient of a total of three tiny “sticks” during the first 48 hours of life, each of which is well-documented to prevent permanent liver damage from hepatitis B; prevent hemorrhagic disease of the newborn during the first 6 months of life, particularly for the breast-fed infant; and assess for numerous genetic and metabolic treatable disorders that could otherwise be deadly or devastating. Will the “sticks” into his skin and muscle themselves lead to purported long-term psycho-emotional damage?
supplemental vitamin K was administered IM or orally during the newborn period. The 3% to 25% chance of not receiving vitamin K is terrifying. I would personally not perform a circumcision in a breast-feeding boy during the first 6 months of life who has not received IM vitamin K. (Think: possible not-yet-identified rare liver or intestinal problems, or even more common medication adherence issues.) Also, have you ever witnessed the terrifying “free bleeding” circumcision site?) The optimal dose of IM vitamin K in premature infants is still debated, and some have recommended using a lower dose of 0.2 mg IM.7

Back to our newborn case: We were finally able to convince the baby’s family that it was in the best interest of their child’s future health to at least proceed with the metabolic screening and prophylactic eye ointment. Sadly, we were unable to convince them to give their child the hepatitis B shot or the newborn vitamin K by injection or orally.

I hope that their spin of the intracranial roulette wheel is a lucky one. They will be seeking their care outside of our practice.

I continue to be amazed at how a single person or group with a medical or postgraduate degree, an internet site, and incredulous speculation(s) can totally undermine the standard of care and recommendations of an entire legion of medical experts and massive credible scientific data. Such is the power of the internet today. ■

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