Newborn Nursery Controversies

CLOTA SNOW, MD, FAAP
PEDIATRIC HOSPITALIST, MAINEGENERAL MEDICAL CENTER

CLINICAL ASSISTANT PROFESSOR OF PEDIATRICS
UNIVERSITY OF NEW ENGLAND COLLEGE OF OSTEOPATHIC MEDICINE
Financial Disclosures

Nothing to disclose
AAP Section on Hospital Medicine

Celebrating 20 years!!
1999-2019
Objectives

- Topics selected from recent listserv discussions, informal poll of the neonatal hospitalist listserv

- Will review available evidence and guidelines

- Controversies for a reason - there are likely multiple opinions out there, not always one “right” approach

- Case Based
Topics

- Discharge timing
- Phototherapy – when to start, when to stop
- Vitamin K
Case #1

- 26 yo G2P1 presented in spontaneous labor at 40 2/7 weeks after an uncomplicated pregnancy. The mother is GBS positive but received multiple doses of penicillin before delivery. Membranes were ruptured for 48 hours before delivery. Mother had a Tmax of 100.3°F (37.9°C) just prior to delivery.

- A baby girl was born via a vaginal delivery complicated by a shoulder dystocia; APGAR scores were 7 and 8. Birth weight was 4140g, 89th percentile.

- Baby is now 24 hours old. Parents are requesting discharge. Is she safe to go home?
When Can Baby Go Home?

1. Clinical course and physical examination reveal no abnormalities that require continued hospitalization.
2. VS within normal range for 12 hours
3. Urine and stool output
4. At least 2 successful consecutive feeds
5. No significant bleeding at circumcision site
6. Risk of hyperbilirubinemia has been assessed, with appropriate follow-up arranged
7. Infant has been adequately evaluated and monitored for sepsis on the basis of maternal risk factors in accordance with current guidelines for prevention of perinatal GBS disease
8. Maternal blood test and screening results are available and have been reviewed (syphilis, hep B, HIV)
9. Initial hep B vaccine given
10. Newborn metabolic and hearing screens have been completed per hospital/state regulations
11. The mother’s knowledge, ability, and confidence to provide adequate care for her infant are documented
12. Knowledgeable support people are available to mother and infant after discharge
13. A medical home has been identified with appropriate follow-up arranged
14. Family, environmental and social risk factors and barriers to care have been addressed
7. Infant has been adequately evaluated and monitored for sepsis on the basis of maternal risk factors in accordance with current guidelines for prevention of perinatal GBS disease

- Guidance for management of babies at risk for EOS
  - Kaiser Neonatal Early-Onset Sepsis Calculator (data supporting current version published in 2014)
  - AAP Guidelines (new in 2018!)
CDC Guidelines (2010)
Kaiser Neonatal Early-Onset Sepsis Risk Calculator

- Provides a multivariate predictive model of sepsis risk for infants born at 34 weeks gestation or greater

- Based on data from a cohort of 608,014 infants in California and Boston (Puopolo et al, Escobar et al)

- Safety validated by several subsequent studies
  - Cohort of 204,485 infants in CA→ significant reduction in newborns receiving antibiotics without increase risk of adverse events (Kuzniewicz et al)
  - Another study included 11,782 infants in PA with similar conclusions (Dhudasia et al)

- Does not specifically comment on discharge timing
AAP Guidelines (2018)

- Supports three different approaches, recommends institutions develop approaches that are best suited to local resources and structures

- Categorical Risk Factor Assessment (aka CDC)

- Multivariate Risk Assessment using maternal risk factors and newborn condition (aka Kaiser)

- Risk Assessment Primarily Based on Newborn Clinical Condition

- Also does not directly comment on discharge timing
If baby is septic, how long before they look sick?

**TABLE 1. Characteristics of EOGBS Infection According to Maternal Risk Status and Intrapartum Antibiotic Treatment for Term Infants With Culture-Positive EOGBS Infection**

<table>
<thead>
<tr>
<th>Maternal Risk (+) Antibiotics (+)</th>
<th>Maternal Risk (+) Antibiotics (-)</th>
<th>Maternal Risk (-) Antibiotics (-)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n = 33 (%)</strong></td>
<td><strong>n = 48 (%)</strong></td>
<td><strong>n = 91 (%)</strong></td>
<td><strong>n = 172 (%)</strong></td>
</tr>
<tr>
<td><strong>Timing of onset of clinical signs of infection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 h</td>
<td>28 (84.9)</td>
<td>37 (77.1)</td>
<td>73 (80.2)</td>
</tr>
<tr>
<td>&gt;6-24 h</td>
<td>3 (9.1)</td>
<td>2 (4.2)</td>
<td>13 (14.3)</td>
</tr>
<tr>
<td>&gt;24-48 h</td>
<td>0 (0)</td>
<td>3 (6.3)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>&gt;48 h</td>
<td>0 (0)</td>
<td>1 (2.1)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>No symptoms</td>
<td>2 (6.1)</td>
<td>5 (10.4)</td>
<td>8 (4.7)</td>
</tr>
<tr>
<td>Median time (h)</td>
<td>.5</td>
<td>4</td>
<td>2.0</td>
</tr>
<tr>
<td>Range (h)</td>
<td>0-19.7</td>
<td>0-49.6</td>
<td>0-100.3</td>
</tr>
</tbody>
</table>

**TABLE 2. Characteristics of EOGBS Infection According to Maternal Risk Status and Intrapartum Antibiotic Treatment for Term Infants With Clinically Suspected EOGBS Infection**

<table>
<thead>
<tr>
<th>Maternal Risk (+) Antibiotics (+)</th>
<th>Maternal Risk (+) Antibiotics (-)</th>
<th>Maternal Risk (-) Antibiotics (-)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n = 48 (%)</strong></td>
<td><strong>n = 15 (%)</strong></td>
<td><strong>n = 20 (%)</strong></td>
<td><strong>n = 83 (%)</strong></td>
</tr>
<tr>
<td><strong>Timing of onset of clinical signs of infection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 h</td>
<td>48 (100)</td>
<td>13 (86.7)</td>
<td>18 (90.0)</td>
</tr>
<tr>
<td>&gt;6-24 h</td>
<td>0 (0)</td>
<td>2 (13.3)</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>&gt;24-48 h</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&gt;48 h</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No symptoms</td>
<td>3 (6.1)</td>
<td>5</td>
<td>1.2</td>
</tr>
<tr>
<td>Median time (h)</td>
<td>0-13</td>
<td>0-17.9</td>
<td>0-9.0</td>
</tr>
</tbody>
</table>

Bromberger et al.
So is baby safe for discharge?

- Case-by-case decision evaluating:
  - AAP discharge criteria met
  - Sepsis risk score
  - Clinical appearance
  - Reliable follow-up/return to hospital
  - Provider’s own risk tolerance
Case #1a

- Same story except:
  - GBS negative
  - ROM x 5 hrs
  - Maternal Tmax 98.6°F (37.0°C)

- Family is requesting to go home 12 hours after delivery.

- What now?
Is baby safe for discharge before 24 hours?

- Newborn testing
  - Timing of newborn metabolic screen varies from state to state
  - More false positives of CCHD/hearing screen if done earlier

- Feeding?

- Follow-up?
Is baby safe for discharge before 24 hours?

- Multifactorial decision
  - Meets AAP guideline criteria
  - Risk-stratify when sepsis risk factors exist
  - Make institutional policy for discharges before 24 hours to ensure appropriate testing/follow-up
  - Medicolegal concerns?
Case #2

- Newborn Caucasian infant, 40 weeks gestation, now 36 hrs old, born via uncomplicated vaginal delivery. Breastfeeding well, multiple voids/stools. Weight is down 5% from birth weight. Physical exam shows no bruising or cephalohematoma.

- Mother is AB+, antibody negative, GBS negative, all other labs appropriate. No family history of neonatal jaundice or hemolytic disease.

- Serum total bilirubin at 36 hours of life is 13.0 mg/dL (direct bilirubin 0.4 mg/dL)

- The baby otherwise meets discharge criteria. What do you do?
Hour-Specific Nomogram for Risk Stratification

Infant age: 36 hours
Total bilirubin: 13 mg/dl
Risk zone: High Risk

Risk zone is one of several risk factors for developing severe hyperbilirubinemia.

Recommended Follow-up

<table>
<thead>
<tr>
<th>Hyperbilirubinemia Risk Level</th>
<th>Interval</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk (&lt;= 38 weeks and well)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
<td></td>
</tr>
<tr>
<td>Medium Risk (38 weeks + hyperbilirubinemia risk factors OR 35 to 37 6/7 weeks and well)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
<td></td>
</tr>
<tr>
<td>Higher Risk (35 to 37 6/7 weeks and hyperbilirubinemia risk factors)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
<td></td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Neurotoxicity Risk Level</th>
<th>Start phototherapy?</th>
<th>Approximate threshold at 36 hours of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk (&lt;= 38 weeks and well)</td>
<td>No</td>
<td>13.6 mg/dl</td>
</tr>
<tr>
<td>Medium Risk (38 weeks + neurotoxicity risk factors OR 35 to 37 6/7 weeks and well)</td>
<td>Yes</td>
<td>11.7 mg/dl</td>
</tr>
<tr>
<td>Higher Risk (35 to 37 6/7 weeks and neurotoxicity risk factors)</td>
<td>Yes</td>
<td>9.6 mg/dl</td>
</tr>
</tbody>
</table>

It is an option to provide conventional phototherapy in the hospital or at home at TSB levels 2-3 mg/dl (35-50 µmol/L) below those shown. Home phototherapy should not be used in infants with risk factors.

If phototherapy threshold is exceeded, please also review AAP Guidelines for Exchange Transfusion.
Don’t get in a BIND!

- Bilirubin-induced neurologic dysfunction (BIND)
  - Acute bilirubin encephalopathy (ABE) → kernicterus/chronic bilirubin encephalopathy (CBE), ~1/100,000 births

- Prospective data from the Canadian Paediatric Surveillance Program (Sgro et al):
  - 32 of 258 infants (12.4%) with severe hyperbilirubinemia (>24.8 mg/dL) were diagnosed with ABE
  - Infants with ABE had higher peak TB levels than those without ABE (29.7 vs 27.3 mg/dL)

- 525,409 infants in northern California; 47 infants with TsB ≥30 mg/dL (Kuzniewicz et al)
  - No cases of ABE with bilirubin levels <35 mg/dL
Retrospective cohort study of 25,895 newborns ≥35 weeks gestation

Newborns with total serum bilirubin level 0.1-3.0 mg/dL below AAP threshold, never exceeded threshold

Assessed readmission for phototherapy within 15 days of discharge

Compared infants who received sub-threshold phototherapy to those who did not
-19.1% of newborns received subthreshold phototherapy

-Associated with a 22-hour longer length of stay

<table>
<thead>
<tr>
<th></th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Population</td>
<td>14.1 (11.2 – 19.0)</td>
</tr>
<tr>
<td>Patients at highest risk of readmission</td>
<td>6.3 (5.1-8.3)</td>
</tr>
<tr>
<td>Patients at lowest risk for readmission</td>
<td>60.8 (44.5-95.8)</td>
</tr>
</tbody>
</table>

-High risk for readmission: lower gestational age, closer to phototherapy threshold, younger age at time of bilirubin level, exclusive breast feeding

<table>
<thead>
<tr>
<th>Formula feedings per day</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>10.3 (8.4-13.4)</td>
</tr>
<tr>
<td>≥6</td>
<td>32.4 (25.8-43.5)</td>
</tr>
</tbody>
</table>
So...do we start lights?

<table>
<thead>
<tr>
<th>Potential Harms</th>
<th>Potential Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased LOS</td>
<td>Prevent readmission</td>
</tr>
<tr>
<td>Resources used unnecessarily</td>
<td>Prevent BIND?</td>
</tr>
<tr>
<td>Disruption to bonding/breastfeeding</td>
<td></td>
</tr>
<tr>
<td>Vulnerable child syndrome?</td>
<td></td>
</tr>
<tr>
<td>Increased cancer risk?</td>
<td></td>
</tr>
<tr>
<td>Increased seizure risk?</td>
<td></td>
</tr>
</tbody>
</table>
Is readmission an appropriate quality metric?

“In the US health care system, hospital readmissions soon after discharge are often considered a negative indicator of quality. However, because 80% of newborns develop jaundice and TSB levels often peak after newborns are discharged, some readmissions for hyperbilirubinemia should be expected and should not be considered a negative quality indicator. Efforts to avoid these readmissions could lead to overtreatment of hyperbilirubinemia during the birth hospitalization and to more newborns receiving phototherapy overall.”

– Wickremasinghe et al.
Case #2a

- Newborn Caucasian infant, 40 weeks gestation, now 36 hrs old, born via uncomplicated vaginal delivery. Breastfeeding well, multiple voids/stools. Weight is down 5% from birth weight. Physical exam shows no bruising or cephalohematoma.

- Mother is AB+, antibody negative, GBS negative, all other labs appropriate. No family history of neonatal jaundice, hemolytic disease.

- Serum total bilirubin at 36 hours of life was 14.0 mg/dL (direct bilirubin 0.4 mg/dL), and phototherapy was initiated.

- When can you stop?
Hour-Specific Nomogram for Risk Stratification

<table>
<thead>
<tr>
<th>Infant age</th>
<th>36 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin</td>
<td>14 mg/dl</td>
</tr>
<tr>
<td>Risk zone</td>
<td><strong>High Risk</strong></td>
</tr>
</tbody>
</table>

Risk zone is one of several risk factors for developing severe hyperbilirubinemia.

Recommended Follow-up

<table>
<thead>
<tr>
<th>Hyperbilirubin Risk Level</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk (6-8 weeks and well)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
</tr>
<tr>
<td>Medium Risk (6-8 weeks + hyperbilirubin risk factors OR 35 to 37 weeks and well)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
</tr>
<tr>
<td>Higher Risk (35 to 37 weeks and hyperbilirubin risk factors)</td>
<td>Evaluate for phototherapy and check TSB in 4-24 hours</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Neurotoxicity Risk Level</th>
<th>Start phototherapy?</th>
<th>Approximate threshold at 36 hours of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Risk (6-8 weeks and well)</td>
<td><strong>Yes</strong></td>
<td>13.6 mg/dl</td>
</tr>
<tr>
<td>Medium Risk (6-8 weeks + neurotoxicity risk factors OR 35 to 37 weeks and well)</td>
<td><strong>Yes</strong></td>
<td>11.7 mg/dl</td>
</tr>
<tr>
<td>Higher Risk (35 to 37 weeks and neurotoxicity risk factors)</td>
<td><strong>Yes</strong></td>
<td>9.6 mg/dl</td>
</tr>
</tbody>
</table>

It is an option to provide conventional phototherapy in the hospital or at home at TSB levels 2-3 mg/dl (35-50 µmol/L) below those shown. Home phototherapy should not be used in infants with risk factors.

If phototherapy threshold is exceeded, please also review AAP Guidelines for Exchange Transfusion.

Links

- Hour-specific nomogram
- Phototherapy nomogram
- Exchange nomogram

Hyperbilirubinemia Risk Factors

- TSB/T/H in high-risk zone
- Jaundice in first 24 hours
- ABO incompatibility with positive direct Coombs, known hemolytic disease, or elevated ETCO
- Gestational age 35-36 weeks
- Prior sibling had phototherapy
- Cephalohematoma or bruising
- Exclusive breastfeeding, esp. with poor feeding or weight loss
- East Asian Race

Neurotoxicity Risk Factors

- Isoimmune Hemolytic Disease
- G6PD deficiency
- Asphyxia
- Significant lethargy
- Temperature instability
- Sepsis
- Acidosis
- Albumin < 3.0 g/dL
Phototherapy – When to Stop?

- Cohort of 7048 infants treated with phototherapy before 14 days
- Attempted to determine predictors of “rebound,” defined as return to treatment threshold levels within 72 hours discontinuation of the first round of phototherapy
- Data were used to create a score to help clinicians decide when to stop phototherapy

- Uses 3 variables: gestational age, age at phototherapy initiation, and “relative” total serum bilirubin (related to AAP phototherapy threshold)

A Clinical Prediction Rule for Rebound Hyperbilirubinemia Following Inpatient Phototherapy

\[ \text{Score} = 15 \times (\text{if gestational age} < 38\text{ weeks}) - 7 \times (\text{age in days at phototherapy initiation}) - 4 \times (\text{AAP phototherapy threshold} - \text{TSB at phototherapy termination}) + 50 \]
Score of $< 20 \implies < 4\%$ probability of rebound hyperbilirubinemia

Use of the score could have resulted in a 1-day shorter hospital stay for approx. $1/3$ of babies treated with phototherapy.
33 yo G3P3 presented in labor at 40 3/7 weeks. Pregnancy was uncomplicated.

A healthy baby girl is born via NSVD

The nurse notifies you that the mother plans to refuse all newborn medications, including IM vitamin K

When asked why, the mother states “I prefer a holistic approach,” and “None of my other kids got vitamin K and they are fine.” You attempt to provide education about the benefits of IM vitamin K, and she states “No thank you, I have done my research and I am very well informed. The shot is not necessary.”
Poor placental transfer of vitamin K → neonatal levels much lower than maternal levels
Vitamin K levels continue to drop in the first days of life
Lactobacillus (primary breastfed gut flora) does not synthesize vitamin K; gut-flora of formula fed babies can generally produce vitamin K
Breastmilk contains <5 mcg/L of vitamin K; formula contains 50-60 mcg/L
Vitamin K Deficiency Bleeding

- Early onset disease – within first 48 hrs
  - Maternal anti-seizure meds, anticoagulants, antibiotics (cephalosporins)
  - Vitamin K given at birth may not help, but ante-partum maternal K may
  - Often severe

- Classic disease – between day 2 and 7
  - 250 -1500/100,000 births
  - Exclusive breastfeeding with no vitamin K given
  - Usually milder than late onset bleeding

- Late onset disease – between 2 weeks and 6 months
  - 4.4-10.5/100,000 births in Europe, 72/100,000 in Asia
  - Exclusively breastfeeding babies with no vitamin K or on some oral vitamin K regimens
  - Exclusive breastfeeding, fat malabsorption (CF, biliary atresia, chronic diarrhea, α-1 antitrypsin deficiency, hepatitis)
  - Mortality rate 20%
Vitamin K Deficiency Bleeding

- Early:
  - Intracranial, GI bleeds, skin

- Classic:
  - Oozing from umbilicus, cephalohematoma, bleeding from circumcision site, ENT mucosal bleeding, skin bruising, bleeding from injection sites, GI, intrathoracic, intracranial bleeds

- Late:
  - Intracranial bleeds (>50%), GI, intrathoracic, skin; often preceded by minor bleed
Neonatal Vitamin K – A History

- Hemorrhagic Disease of the Newborn first described in 1894
- Relationship between hemorrhagic disease of the newborn and vitamin K deficiency described by Henrik Dam in 1940
- Study published in 1944 demonstrated that vitamin K immediately after birth prevents HDN
- Recommended as standard of care by the AAP since 1961
- 5 States have laws requiring vitamin K and neonates
  - OR, NY, IL, VA, MA

www.nobelprize.org
Controversy is not new...

- Cases of severe hemolytic anemia resulting in kernicterus in the 1950s, due to massive doses (up to 80mg/kg) of water-soluble form.

- Report in the 1970s suggested vitamin K was necessary only in “high-risk” neonates, led some centers to do “selective administration”
  - Led to re-appearance of VKDB → most returned to universal administration.

- Concern for increased cancer risk with parenteral form in 1990s (Golding et al)
  - Resulted in several countries switching to PO form.
  - Claims not substantiated in multiple subsequent publications (Ross et al, Fear et al).

- Case report of allergic reaction resulting in shock in 2014; first and only ever case with IM form (some reports with IV form).
Refusal of Vitamin K by Parents of Newborns: A Survey of the Better Outcomes Through Research for Newborns Network

Jaspreet Loyal, MD, MS, James A. Taylor, MD, Carrie A. Phillips, MD, PhD, Neera K. Goyal, MD, Nirmol Dhayapasuman, MD, Eugene D. Shapiro, MD, and Eve Colson, MD, MHPE
Department of Pediatrics, Yale University (Drs Loyal, Shapiro, and Colson), New Haven, Conn; Department of Pediatrics, University of Washington (Dr Taylor), Seattle; Department of Pediatrics, Oregon Health & Science University (Dr Phillips), Portland; Department of Pediatrics, Cincinnati Children’s Hospital Medical Center (Dr Goyal), Cincinnati, Ohio, and Academic Pediatric Association (Ms Dhayapasuman), McLean, Va

Parental Refusal of Vitamin K and Neonatal Preventive Services: A Need for Surveillance

Lauren H. Marciewicz1,2,2, Joshua Clayton1,3, Matthew Maenner1,4, Erika Odom2, Ekwutosi Okoroh2, Deborah Christensen1, Alyson Goodman1, Michael D. Warren5, Julie Taylor4, Angela Miller2, Timothy Jones3, John Dunn7, William Schaffner1,5, and Althea Grant2
1Centers for Disease Control and Prevention, Epidemic Intelligence Service, Atlanta, GA, USA
2Centers for Disease Control and Prevention, Division of Blood Disorders, National Center on Birth Defects and Developmental Disabilities, Atlanta, GA, USA
3Tennessee Department of Health, Nashville, TN, USA
4Centers for Disease Control and Prevention, Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Atlanta, GA, USA
5Vanderbilt University School of Medicine, Nashville, TN, USA

Reasons for Refusal of Newborn Vitamin K Prophylaxis: Implications for Management and Education

Harvey James Harrick, MD,1 Elizabeth Kaye Gabie, MD,1 Emily Huruska Freeman, MSN, CNP-P,C, Laurie Louise Dunn, MD,2 Sarah Pritchett Zimmerman, MD,3 Molly Moriarty Rusan, MD,4 Olivia Reed Limthavong, MD, MS,5 Mary Ellen Wright, MSN, APRN, CNMP, Leslie Ann Moss, M$k, CHES,7 Ashley Cockrell Skinner, PhD,8

Factors Associated With Refusal of Intramuscular Vitamin K in Normal Newborns

Jaspreet Loyal, MD, MS, James A. Taylor, MD, Carrie A. Phillips, MD, PhD, Neera K. Goyal, MD, Kelly E. Wood, MD, Carl Seashore, MD, Beth King, MPP, Eve Colson, MD, MHPE, Veronika Shabanova, PhD, Eugene D. Shapiro, MD, on behalf of the BORN investigators
Mostly white, over age 30, college graduates

Most also refused erythromycin and hepatitis B vaccine

Internet most common source of information (70%), followed by “medical providers” (33%)

Concerns:
- Synthetic or toxic ingredients (37%)
- Excessive dose (28%)
- Side effects (24%)
- Prefer “natural” sources (24%)
- Unnecessary (21%)

11% accepted IM prophylaxis when counseled about risks
Oral Vitamin K (Far) Superior to Vitamin K Shot for Newborns

by Sarah Pope MGA | Updated: Feb 04, 2019 | Affiliate links

It is heartening to see so many new parents starting to question the hospital standard of care for newborns. This trend is why many are now demanding (safe) oral vitamin K as an alternative to the routine and immediate jab of (toxic and synthetic) vitamin K within minutes of birth.
Consequences

Notes from the Field: Late Vitamin K Deficiency Bleeding in Infants Whose Parents Declined Vitamin K Prophylaxis – Tennessee, 2013

Vitamin K deficiency bleeding (VKB) is a coagulopathy that develops in infants who do not have sufficient vitamin K stores to support production of clotting factors. In adults, vitamin K is obtained from food and from vitamin K synthesized by gut bacteria; however, placental transfer in humans is limited, cord blood and infant liver reserve pools of vitamin K are substantially below adult levels (1,2). As a result, infants are predisposed to VKB, which is classified as early, classic, and late, according to when it presents. In the United States, administration of intramuscular vitamin K at birth to prevent all forms of VKB has been standard practice since first recommended by the American Academy of Pediatrics in 1953 (3). Without prophylaxis, evidence of early and classical VKB ranges from 0.5% to 1.7% of births; incidence of late VKB ranges from 4 to 7/10,000 infants (4,5). The relative risk for developing late VKB has been estimated at 10 times greater among infants who do not receive intramuscular vitamin K than in infants who do receive it (4).

During February-September 2013, four confirmed cases of late vitamin K deficiency bleeding were diagnosed at a children’s hospital in Nashville, Tennessee. The four infants had laboratory-confirmed coagulopathy, defined as an elevation of prothrombin time (PT) greater than or equal to four times the laboratory limit of normal, confirmed by vitamin K administration, and symptomatic bleeding. Three of the infants were born at major area hospitals, and one was born at home. The infants all had been healthy and developing normally until experiencing unexplained sudden bleeding at age 4 to 11 weeks. Three of the infants had diffuse intracranial hemorrhage, and the fourth had gastrointestinal bleeding. Additionally, a perinatal laboratory-confirmed coagulopathy was identified in the event of one of the patients. In each case, parents had declined intramuscular vitamin K administration at birth. The Tennessee Department of Health initiated a public health investigation of this cluster and requested assistance from CDC.

All four of the infants survived. The infant with gastrointestinal bleeding recovered fully. The three with intracranial hemorrhage are being followed by neurologists; one has an apparent gross motor deficit. although deficits have not yet been identified in the other infants, all are currently aged <1 year; and the neurodevelopmental impact of the two infants might become apparent in the context of further development. Preliminary inquiries of Tennessee hospital discharge data during 2007–2012 revealed no confirmed cases of late vitamin K deficiency bleeding, defined as an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code of either hemorrhagic disease of the newborn (776.0) or vitamin K deficiency (280.9), plus any codes for symptoms of bleedings, including intracranial or gastrointestinal hemorrhages, epistaxis, bruising, or hemorrhage. During this period, 406,742 live births occurred in Tennessee. To assess the proportion of newborns who did not receive vitamin K prophylaxis in 2013, records of a random sample of infants born during January–October 2013 at each of three Nashville area hospitals and at four major Tennessee regional birthing centers were reviewed, at the tertiary hospital with the highest proportion of neonates not administered vitamin K. 3.4% of 3,486 infants discharged from the neonatal nursery received no vitamin K injection. In contrast, 28.0% of 218 newborns at birthing centers did not receive vitamin K. Case finding efforts revealed no additional cases of late VKB in Tennessee in 2013.

Parents of the four infants with VKB were asked why they declined vitamin K prophylaxis for their neonates. Reasons included concern about an increased risk for leukemia when vitamin K is administered, an impression that the injection was unnecessary, and a desire to minimize the newborn’s exposure to “toxins.”
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Diagnosis</th>
<th>Gender</th>
<th>Birth History</th>
<th>Feeding</th>
<th>Presenting Signs</th>
<th>Bleeding Location</th>
<th>Head CT Findings</th>
<th>Additional Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 mo</td>
<td>Male</td>
<td>Born at home and no vitamin K or circumcision</td>
<td>Exclusively breastfed</td>
<td>Enuresis, bruising, somnolence, and poor feeding</td>
<td>Intracranial</td>
<td>Multiple subdural hematomas and midline shift</td>
<td>Neurosurgical evacuation of hematoma</td>
<td>Neurologically intact 3 months post-ICH and undergoing workup for hepatobiliary disease</td>
</tr>
<tr>
<td>2</td>
<td>8 wk</td>
<td>Female</td>
<td>Born in hospital and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Vomiting, fever, and lethargy</td>
<td>Intracranial</td>
<td>Left frontoparietal and bilateral frontal subarachnoid hemorrhages</td>
<td>Anticonvulsant for recurrent seizures</td>
<td>Mild neurological delays 5 months post-ICH and PSOM score 0.5 (mild)</td>
</tr>
<tr>
<td>3</td>
<td>3 mo</td>
<td>Female</td>
<td>Born at home and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Bloody stools</td>
<td>Gastrointestinal</td>
<td>Not done</td>
<td>None</td>
<td>No long-term effects to date</td>
</tr>
<tr>
<td>4</td>
<td>6 wk</td>
<td>Male</td>
<td>Born in hospital and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Fussiness, somnolence, and poor feeding</td>
<td>Intracranial</td>
<td>Parenchymal hemorrhage filling the entire left hemisphere and effacement of left lateral ventricle and midline shift</td>
<td>Neurosurgical evacuation of hematoma and anticonvulsant for recurrent seizures</td>
<td>Right hemiparesis and cognitive delays at 3 mo post-ICH and PSOM score 2.5 (poor, severe deficits)</td>
</tr>
<tr>
<td>5</td>
<td>7 wk (twin)</td>
<td>Male</td>
<td>Born in hospital and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Fussiness, enuresis, pallor, and poor feeding</td>
<td>Intracranial</td>
<td>Multiple acute subdural, subarachnoid, and parenchymal hemorrhages</td>
<td>Erythrocyte transfusions × 3 and anticonvulsant for recurrent seizures</td>
<td>Moderate neurological delays, 4 mo post-ICH and PSOM score 1.5 (moderate deficits)</td>
</tr>
<tr>
<td>6</td>
<td>7 wk (twin)</td>
<td>Male</td>
<td>Born in hospital and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Asymptomatic twin</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>No long-term effects to date</td>
</tr>
<tr>
<td>7</td>
<td>12 wk</td>
<td>Female</td>
<td>Born in birthing center and no vitamin K</td>
<td>Exclusively breastfed</td>
<td>Vomiting and acholic stools</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Excess choledochal cyst</td>
</tr>
</tbody>
</table>

Abbreviations:
CT = Computed tomography
ICH = Intracranial hemorrhage
PSOM = Pediatric stroke outcome measurement
Is oral better than nothing?

<table>
<thead>
<tr>
<th>Country</th>
<th>Years</th>
<th>Medication</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1993-1994</td>
<td>Oral Vitamin K on days 1, 3-5, and 21-29 IM Vitamin K once at birth</td>
<td>2.5 per 100,000 IM Vitamin K once at birth 0 per 100,000</td>
</tr>
<tr>
<td></td>
<td>1994-1995</td>
<td>Oral Vitamin K once at birth</td>
<td>4.4 per 100,000 IM Vitamin K once at birth 0.64 per 100,000</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1988-1990</td>
<td>Oral Vitamin K1 once at birth</td>
<td>4.4 per 100,000 IM Vitamin K1 once at birth 0.64 per 100,000</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1992-1994</td>
<td>Oral Vitamin K once at birth and 25 µg daily from weeks 1-13 in breastfed babies</td>
<td>11.1 per 100,000 IM Vitamin K1 once at birth 0.64 per 100,000</td>
</tr>
<tr>
<td>Sweden</td>
<td>1987-1989</td>
<td>Oral Vitamin K1 once at birth</td>
<td>6 per 100,000 IM Vitamin K1 once at birth 0 per 100,000</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1995</td>
<td>2 mg mixed preparation of oral Vitamin K on days 1 and 4</td>
<td>4.7 per 100,000 IM Vitamin K1 once at birth 0 per 100,000</td>
</tr>
<tr>
<td>Germany</td>
<td>1988-1989</td>
<td>Oral Vitamin K1 once at birth</td>
<td>7.2 per 100,000 IM Vitamin K1 once at birth 0.3 per 100,000</td>
</tr>
<tr>
<td>Germany</td>
<td>1993-1994</td>
<td>Oral Vitamin K1 once at birth and 28-22 in well babies: ‘unwell’ babies had IM or SQ instead of oral on day 1</td>
<td>2.7 per 100,000 IM Vitamin K1 once at birth 0.3 per 100,000</td>
</tr>
<tr>
<td>Japan</td>
<td>1981-1983</td>
<td>None</td>
<td>10.5 per 100,000 IM or oral K1 once at birth 4.2-7.8 per 100,000</td>
</tr>
<tr>
<td></td>
<td>1988-1990</td>
<td>1 to 3 doses of oral MK-4 on days 1, 7, and 28</td>
<td>2.8 per 100,000 IM or oral K1 once at birth 4.2-7.8 per 100,000</td>
</tr>
<tr>
<td>Thailand</td>
<td>1981-1984</td>
<td>None</td>
<td>72 per 100,000 IM or oral K1 once at birth 4.2-7.8 per 100,000</td>
</tr>
</tbody>
</table>

IM = Intramuscular [Vitamin K shot]. MN4 is a type of Vitamin K2 that is not available in most countries.

Data from the UK, Sweden, Switzerland (1986-1988), Germany (1988-1989), Japan, and Thailand were compiled in one paper by Shearer, 2009; Data from Australia, the Netherlands, Germany (1993-1994), and Switzerland (1995) compiled in one paper by Cornelli et al. (1997).
Table 5
Incidence rates of late VKDB in different countries with agreed case definition after exposure to different oral regimens of phylloquinone.

<table>
<thead>
<tr>
<th>Country and reference</th>
<th>Oral dose regimen</th>
<th>Observation period</th>
<th>Birth population</th>
<th>Estimated no. receiving regimen</th>
<th>Incidence rate per 105 infants&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Incidence rate per 10&lt;sup&gt;5&lt;/sup&gt; infants receiving regimen&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Netherlands&lt;sup&gt;33&lt;/sup&gt;</td>
<td>1 mg at birth; 25 µg/d for 13 weeks&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10/02 to 12/94</td>
<td>439,000</td>
<td>0.5 (0.1–1.6)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.1 (0.0–0.7)</td>
<td></td>
</tr>
<tr>
<td>Germany&lt;sup&gt;33&lt;/sup&gt;</td>
<td>3 × 1 mg (days 1, 4–10 and 28–42)</td>
<td>04/93 to 12/94</td>
<td>1,400,000</td>
<td>1.9 (1.3–2.8)</td>
<td>1.3 (0.8–2.0)</td>
<td></td>
</tr>
<tr>
<td>Germany&lt;sup&gt;33&lt;/sup&gt;</td>
<td>3 × 2 mg (days 1, 4–10 and 28–42)</td>
<td>01/95 to 12/98</td>
<td>3,200,000</td>
<td>0.7 (0.6–1.5)</td>
<td>0.4 (0.2–0.7)</td>
<td></td>
</tr>
<tr>
<td>Germany (Crem)&lt;sup&gt;32&lt;/sup&gt;</td>
<td>3 × 2 mg (days 1, 4–10 and 28–42)</td>
<td>01/97 to 12/00</td>
<td>1,320,926</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany (MM)&lt;sup&gt;32&lt;/sup&gt;</td>
<td>3 × 2 mg (days 1, 4–10 and 28–42)</td>
<td>01/97 to 12/00</td>
<td>1,817,769</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia&lt;sup&gt;36&lt;/sup&gt;</td>
<td>3 × 1 mg (days 1, 3–5 and 21–28)</td>
<td>01/93 to 03/94</td>
<td>325,000</td>
<td>2.5 (1.1–4.8)</td>
<td>1.5 (0.5–3.6)</td>
<td></td>
</tr>
<tr>
<td>Denmark&lt;sup&gt;53&lt;/sup&gt;</td>
<td>1 mg (once at birth)</td>
<td>04/90 to 11/92</td>
<td>134,500</td>
<td>4.5 (1.6–10.3)</td>
<td>4.3 (1.6–10.3)</td>
<td></td>
</tr>
<tr>
<td>Denmark&lt;sup&gt;56&lt;/sup&gt;</td>
<td>2 mg at birth; 1 mg weekly for 3 months&lt;sup&gt;e&lt;/sup&gt;</td>
<td>11/92 to 06/00</td>
<td>507,850</td>
<td>0 (0–0.9)</td>
<td>0 (0–0.9)</td>
<td></td>
</tr>
<tr>
<td>Switzerland&lt;sup&gt;35&lt;/sup&gt;</td>
<td>2 × 2 mg (days 1 and 4)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>01/95 to 12/95</td>
<td>83,000</td>
<td>4.7 (1.3–11.9)</td>
<td>1.2 (0–6.5)</td>
<td></td>
</tr>
</tbody>
</table>

95% confidence intervals are shown in parentheses. Crem, Konakion Cremophor and MM, Konakion MM preparations.

<sup>a</sup>Case definition of late VKDB includes secondary cases in which a condition predisposing to VK malabsorption (e.g. cholestasis) had been identified after the bleeding had occurred but excludes cases in which a predisposing condition had been diagnosed before the bleeding.

<sup>b</sup>Estimated incidence rate for infants who received complete regimen.

<sup>c</sup>In the Netherlands only breast-fed infants received regimen.

<sup>d</sup>Data modified from original publication<sup>30</sup> to exclude cases with a predisposing condition diagnosed before the bleeding.

<sup>e</sup>In Denmark from 1992 to 2000 only Konakion Cremophor was used.

<sup>f</sup>In Switzerland in 1995 Konakion MM was available and widely used in addition to Konakion Cremophor.
What about oral?

<table>
<thead>
<tr>
<th>Recommended oral vitamin K prophylaxis</th>
<th>Oral vitamin K dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>3 × 1 mg*</td>
</tr>
<tr>
<td></td>
<td>3 × 2 mg</td>
</tr>
<tr>
<td>Birth population</td>
<td>1,400,000</td>
</tr>
<tr>
<td>Number of cases</td>
<td>27</td>
</tr>
<tr>
<td>Idiopathic cases</td>
<td>8</td>
</tr>
<tr>
<td>Secondary cases</td>
<td>19</td>
</tr>
<tr>
<td>Incidence/100,000 live births based on all cases</td>
<td>1.93 (1.27–2.80)</td>
</tr>
<tr>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis failures (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Complete prophylaxis</td>
<td>1.29 (0.76–2.03)</td>
</tr>
<tr>
<td>Complete and incomplete prophylaxis</td>
<td>1.64 (1.04–2.47)</td>
</tr>
</tbody>
</table>

von Kries et al, Cornelissen et al
Best oral options?

- The Netherlands
  - 1mg orally after birth, then 25 mcg daily day 8 to 13 weeks
  - Mimics formula feeding
  - Efficacy initially appeared similar to parenteral (0 cases in 2 years)
  - Failures ultimately seen in babies with cholestasis; other cases related to missed doses
  - Recently increased to 150 mcg daily → still failed to prevent VKDB in biliary disease (Witt et al)

- Denmark
  - 2mg orally after birth, then 1mg weekly for 3 months
  - Rates of VKDB same as IM (0 cases in 7.5 years)
  - Prevented even in babies with cholestasis
  - Abandoned in 2000 due oral product coming off the market
    - Now give 2g IM
Best oral options?

- Germany
  - 2mg PO x 3 doses (birth, day 4-10, day 28-42)
  - Data based on larger population size than Dutch/Danish experiences
  - Rates of VKDB still higher than IM
Lessons from the Europeans?

- Multiple dose regimens do better at preventing late VKDB than a single oral dose at birth, but not as well as IM.

- English hospital in 1990s (Croucher et al):
  - Dose #1 given in hospital, dose #2 provided to mother for the community midwife to give at 1 week, general practitioners were instructed to give dose #3 in office at 6 weeks.
  - >10% of babies didn’t get the 2nd dose
  - >60% didn’t get the third
Is oral vitamin K an option in US?

- Regurgitation
- Unpredictable absorption
- Missed doses/lack of structured home nursing in many areas
- Likely won’t work in babies with cholestasis/malabsorption
- No proven or approved oral formulation available in the US
Oral options in the US?

FDA Approved:
- Phytonadione 5mg tablet
- IM formulation 1mg/0.5ml
Should we offer PO vitamin K?

- Is oral better than nothing?
- Should we give dosing advice?
- Which formulation to use?
- 1/3 of nursery sites surveyed have an oral protocol (Loyal et al 2017)

Are Pediatricians Complicit in Vitamin K Deficiency Bleeding?

Melissa Weddle, MD, MPH, Allison Empey, MD, Eric Grossen, MD, MPH, Aaron Green, Joy Green, Carrie A. Phillips, MD, PhD

PEDIATRICS Volume 136, number 4, October 2015
Evidence on: The Vitamin K Shot in Newborns

Vitamin K is a substance that our body needs to form clots and stop bleeding. We get vitamin K from the food we eat. Some vitamin K is also made by the good bacteria that live in our intestines. Babies are born with very small amounts of vitamin K stored in their bodies, which can lead to serious bleeding problems if not supplemented.

What is Vitamin K Deficiency Bleeding?

Free Materials

FAQs

Real Stories

Articles

Links to Other Resources

Podcasts
Other issues...

- Maternal supplementation – does raise levels in the breast milk, but no studies have been done on babies who have not received vitamin K as well → no data on prevention of bleeding

- Do you circumcise? What about after an oral dose?

- Lingual frenotomy?

- Do you have them sign a refusal form?
Other Controversies for Another Day...

- Other refused newborn interventions/alternative practices
- Screening for congenital CMV
- Timing of circumcision
- Ankyloglossia - to clip or not to clip?
- THC positive moms?
- Universal maternal drug screening?
- Intubation for meconium?
- Car seat testing
Thank You!
References

- Benitz, WE and COMMITTEE ON FETUS AND THE NEWBORN. Hospital Stay for Healthy Term Newborn Infants. *Pediatrics*. 2015; 135;948.
- Centers for Disease Control and Prevention. Prevention of Perinatal Group B Streptococcus Disease. MMWR 2010;59(No. RR-10):[1-31].
- Croucher C, Azzopardi D. Compliance with recommendations for giving vitamin K to newborn infants, *BMJ*. 1994; 308(6933);894-895.
References

- D McMillan, Canadian Paediatric Society, Fetus and Newborn Committee; Routine administration of vitamin K to newborns, Paediatrics & Child Health, Volume 2, Issue 6, 1 November 1997, Pages 429–431
- Puopolo KM, Benitz WE, Zaoutis TE, AAP COMMITTEE ON FETUS AND NEWBORN, AAP COMMITTEE ON INFECTIOUS DISEASES. Management of Neonates Born at >35 0/7 Weeks’ Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Pediatrics. 2018;142(6):e20182894