Hypoglycemia and Jaundice in the Breastfeeding Newborn

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Faculty Disclosure Information

I have nothing to disclose, except that I am a firm believer that human milk is the optimal feeding for all human babies, with very few exceptions.

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Following this discussion on hypoglycemia you will be able to:

- To review the pathophysiology and definitions of hypoglycemia in the newborn.
- To discuss risk factors and screening guidelines for hypoglycemia in the newborn.
- To discuss strategies to avoid hypoglycemia in the breastfeeding infant.
- To discuss treatment of hypoglycemia in the breastfeeding infant.
**Glucose Homeostasis During Transition**

- Throughout gestation the fetus receives its entire supply of glucose (70% of its energy needs) from the maternal circulation
  - Facilitated diffusion via the placenta
  - Fetal plasma glucose levels 70% to 80% of maternal venous plasma levels
- Glucose utilization by the fetus is approximately 5 mg/kg per minute with amino acids and lactate as additional energy sources

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**Glucose Homeostasis**

- Principal energy substrates during life
  - glucose, amino acids, lactate
  - Glucose crosses placenta by facilitated diffusion
  - Fetal endocrine milieu dominated by insulin
    - does not cross placenta
    - fetal secretion influenced by both glucose and amino acids in fetal plasma
  - 3rd trimester glycogen storage in liver, heart, skeletal muscles
    - Hepatic glycogen increases from 3.4 mg/g at 8 wk to 50 mg/g at term
    - stores may be inadequate in preterm or prenatally stressed infants

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**What Changes at Birth?**

- At birth the infant must supply its glucose needs of approximately 5 to 8 mg/kg/minute (70% used by the brain) through
  - a balance of exogenous sources (human milk) and
  - endogenous glucose production through gluconeogenesis, glycogenolysis, and ketogenesis, provided adequate substrates are available
Within minutes of cutting the umbilical cord:

- 3-to 5-fold surge in glucagon and catecholamines, which initiate glycogen breakdown;
- high endogenous growth hormone and cortisol facilitate onset of gluconeogenesis within several hours;
- insulin secretion is blunted so serum concentrations of insulin fall;
- processes that ensure the availability of glucose and other fuels are collectively described as *counter-regulation* activated primarily by glucagon and adrenalin.

Metabolic Events at Birth

- Abrupt switch from state of net glucose uptake and glycogen synthesis to independent glucose production
- Maintenance of normoglycemia:
  - Adequate glycogen stores
  - Maturation of glycogenolytic and gluconeogenic pathways
  - Integrated endocrine response

Normoglycemia

Hypoglycemia
Regulation of Blood Glucose After Birth

- Utilization in tissues → endogenous production
- Insulin secreted in response to rises in blood glucose
- Counterregulatory hormones—glucagon and adrenaline
- Substrate concentration affects gluconeogenesis
  - Glucose—suppresses gluconeogenesis
  - Lactate, pyruvate, glucogenic amino acids—activate gluconeogenesis

Metabolic Substrates After Birth

- Blood glucose concentration falls in babies who are not fed
- Healthy term (AGA) babies mobilize alternative substrates (free fatty acids, ketone bodies)
- Breastfed babies have lower glucose, higher ketone bodies than formula fed
- 50% of energy in diet from fatty acids

Hypoglycemia

- The term refers to a low blood glucose concentration
- Neonatal hypoglycemia is not a medical condition
  - a feature of illness
  - a failure to adapt from the fetal state of continuous transplacental glucose consumption to the extrauterine pattern of intermittent nutrient supply
Hypoglycemia

- Transient hypoglycemia in the immediate newborn period is common and occurs in almost all mammalian species.
- In healthy term human infants, even if early enteral feeding is withheld, it is self-limited as glucose levels spontaneously rise within 2 to 3 hours.

The early self-limited period of hypoglycemia

- Not considered pathologic.
- Little practical value in measuring blood glucose concentrations of asymptomatic babies in the first 2 hours.
- Even when low blood glucose concentrations develop secondary to prolonged intervals (8 hours) between breast feedings, a marked ketogenic response provides glucose-sparing fuel to brain.
- Neonatal brain has an enhanced capability to use ketone bodies relative to infants (4-fold) and adults (40-fold).

Patterns of Metabolic Adaptation for Preterm and Term Infants in the First Neonatal Week

- 156 term, 62 preterm (<37 wks) healthy infants, demand fed
  - breastfed 71 term; 4 preterm (unclear for NG fed)
- Whole blood glucose, gluconeogenic precursors (pyruvate, alanine, lactate, glycerol), ketone bodies (hydroxybutyrate, acetoacetate), non-esterified fatty acid obtained, before feeds from birth to 6 days old.
- Results (Term):
  - 27-112 mg/dl range (12% infants <46 mg/dl)
  - lowest day 1; positive correlation of blood glucose and postnatal age
  - breastfed (27-95 mg/dl; mean 65 mg/dl)
  - formula fed (45-112 mg/dl; mean 72 mg/dl)

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Patterns of Metabolic Adaptation for Preterm and Term Infants in the First Neonatal Week

Results (Term) (cont.)
- Ketone body concentration significantly greater breastfed than formula through day 3
- Both demonstrated ketogenic response to low glucose concentrations
- Multiple regression analysis—only interval between feeds was correlated to blood glucose concentration

Results (Preterm)
- 27-217 mg/dl range, mean 76 mg/dl (27-112 mg/dl term)
- Significantly lower day 1 than subsequent days
- Low ketone body concentrations compared to term infants

Conclusions
- Vigorous ketone body production normal adaptation to extrauterine life in term babies; severely limited in preterm
- Major determinant of blood glu is interval between feeds
  - Prolonged intervals of up to 8 hours NOT associated with excessively low blood glucose concentrations
  - Breastfed infants demonstrate effective counter regulation
- “…Factors other than blood glucose are important in the neonatal period, and while guidelines are important for clinical management, rigid definitions are inadequate and should be avoided…”

Breastfed Infants: Glucose & Ketone Bodies

Breastfed term infants vs. formula-fed infants up to 1 week old have:
- Lower blood glucose and
- Higher ketone bodies

Infants who lose most weight postnatally have the highest ketone body conc.

Which suggests:
- Provision of alternate fuels constitutes normal adaptive response to transiently low nutrient intake during the establishment of breastfeeding.
- Breastfed infants may tolerate lower plasma glucose levels without significant clinical manifestations or sequelae.
Breast fed vs. non-breast fed infant

- Difference in metabolic responses
  - Exclusively breast fed babies have lower glucose values than those fed infant formula.
  - Able to tolerate lower glucose levels without symptoms
  - Able to mount a higher ketogenic response
  - Presence of milk (especially breast milk) in gut has not only implications as glucose source but also acts as an agent in increasing activity of glucose producing hormones and enzymes
  - Plasma and gut amino acids and peptides have a more normal pattern after breast feeding compared to formula feeding

- If accept that optimally breastfed infant’s lower blood glucose is the physiologic norm, and breastfed infants tolerate lower plasma glucose levels without significant clinical manifestations or sequelae
  - Assume adaptive metabolic response systems are functioning normally

- One case series of hypoglycemia in “healthy, breastfed term newborns” (Moore 1999)
  - all were feeding poorly at discharge
  - revealed no urinary ketones in any of the three symptomatic infants
  - suggesting a defective ketogenic response to fasting
What is a NORMAL glucose?

- It depends!
- No Consensus re Definition of Hypoglycemia/ Normoglycemia
- Values different in whole blood, plasma, serum
  - Glu concentration in plasma or serum 10-15% higher than in whole blood
- Varying study methodologies (age of infant, feeding regimens, time from last feeding)

Normal Pattern of Glucose Levels


Plasma glucose levels in term infants who are appropriate size for gestation & exclusively breast fed

Diwaker KK, Sasidhar MV. Arch Dis Child Fetal Neonatal Ed 2002; 87:F46-F48
**So What is Hypoglycemia?**

- Much disagreement! (Can't define normal glucose 😐)
  - Whole blood glucose level <30 mg/dl in term infant, <20 mg/dl in preterm infants (Cornblath and Reisner 1965)
    - dominated its management for many years.
  - Serum glucose <40-45 mg/dl after 1st 24 hours (Srinivasan 1986; Heck 1987)
  - Neurological dysfunction at blood glucose <46 mg/dl (Koh 1988, Lucas 1988)
  - First 24 hrs, <30 mg/dl term infant, <22 mg/dl in preterm or LBW <2.5 kg (AAP 1992)
  - Quantitative plasma glucose <40 mg/dl (AAP 1998)

**Definition of Hypoglycemia**

- Remains controversial in the newborn infant because of a lack of significant correlation between plasma glucose concentration, clinical symptoms, and long-term sequelae.
- Expert panel convened by NIH in 2008 concluded *there has been no substantial evidence-based progress in defining what constitutes clinically important neonatal hypoglycemia, particularly regarding how it relates to brain injury* (Hay et al, J Pediatr. 2009;153(5):612-617)

**Why Do We Care? CNS Effects**

- Animal and postmortem studies of infants indicate severe and prolonged hypoglycemia is associated with neuroanatomical patterns of brain damage different from distribution of hypoxic/ischemic damage.
- Neonate has adaptive responses to hypoglycemia, which may be protective to cerebral metabolism
  - increase in cerebral blood flow
  - use of alternative metabolic substrates
    - ketone bodies
    - lactate

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Hypoglycemia - Occipital injury

Figure 1. A, ADC map revealed extensive areas of restricted diffusion within the occipital cortex and white matter, the corpus callosum, and optic radiations. B, early T2w axial image on day 4. An abnormal signal from the occipital white matter was demonstrated. C, late T2w axial image on day 17. Generalized occipital lobe atrophy was demonstrated on follow-up.

Occipital brain injury associated with neonatal hypoglycemia can result in long-term disability, epilepsy, and visual impairment.

Peter M. Filan, Terrie E. Inder, Fergus J. Cameron, Michael J. Kean, Rod W. Hunt
Neonatal hypoglycemia and occipital cerebral injury

Figure 2. A, ADC map; B, early T2w axial image on day 6; and C, late T2w axial image on day 44 from case 4.

Hypoglycemia - Occipital injury

Bilateral occipital lesions


Why is the brain vulnerable?

Glucose need for brain metabolism

Table 1. Average Equation of Percentile for Total Cerebrospinal Fluid pH, Glucose, and pH, and pCO2 in Normal Neonates and Infants

<table>
<thead>
<tr>
<th>Substance</th>
<th>Sleep</th>
<th>Day</th>
<th>Maxima Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>99.7%</td>
<td>94.3%</td>
<td>98.2%</td>
</tr>
<tr>
<td>pH (total CO2)</td>
<td>0.3</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>pH (basal CO2)</td>
<td>0.2</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Lactate</td>
<td>0.6</td>
<td>0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Data from de Beer et al. reference 1, and from reference 5, should be corrected for reference 6, and then for reference 7.

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Definition of Hypoglycemia

- Blood glucose test results vary enormously
  - source of blood sample, the assay method, whether whole blood, plasma or serum
- Plasma or serum glucose concentrations are 10-15% higher than in whole blood
- Breastfed, formula-fed and mixed-fed infants follow the same pattern of glucose values
  - initial fall in glucose over the first 2 hours
  - followed by a gradual rise in glucose over the next 96 hours, whether fed or not
- Breastfed infants have slightly lower glucose and higher ketone bodies than artificially-fed infants

Normal Pattern of Glucose Levels


Incidence of Hypoglycemia

- Varies with definition chosen, population studied, and feeding initiation and frequency
- Many authors have suggested numeric definitions of hypoglycemia, usually between 30-50 mg/dL (1.7 – 2.8 mmol/L) and varying by postnatal age
- No scientific justification for the value of <47 mg/dL that has been adopted by some clinicians
- Literature cites anywhere from 0-20% of newborns—what does this mean?
- More likely seen in preemies or with "risk factors"
"Significant hypoglycemia is not and can never be defined by a single number that can be applied universally to every individual patient. Rather, it is characterized by a value(s) that is unique to each individual and varies with both their state of physiologic maturity and the influence of pathology." Cornblath

What is significant hypoglycemia?

- No one level or duration of low glucose can be defined as definitely pathologic
- Risk to infant depends on a number of factors:
  - Gestational age
  - Birth weight
  - Age after birth
  - Other co-morbidities
- A pragmatic approach is needed

ABM Protocols

ABM Clinical Protocol #1: Guidelines for Glucose Monitoring and Treatment of Hypoglycemia in Breastfed Neonates

Revision June, 2006

Nancy Wight, Kathleen A. Marinelli and the Academy of Breastfeeding Medicine: Protocol Committee

A central goal of the Academy of Breastfeeding Medicine is the development of clinical protocols for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not define an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.
So how do we operationalize low glucose?

- A meta-analysis (studies published 1986-1994) of low plasma glucose thresholds in full-term normal newborns who were mostly mixed fed (formula and breastfeeding) or formula-fed
- Present recommended low thresholds for plasma glucose based on hours after birth
- Authors specifically noted that *given the lower plasma glucose levels in normal breastfed infants, the low thresholds for exclusively breastfed infants might even be lower*

**Table 1. Recommended Low Thresholds: Plasma Glucose Level.**

<table>
<thead>
<tr>
<th>Hour after birth</th>
<th>≤5th Percentile PGL (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 (nadir)</td>
<td>28 (1.6 mmol/L)</td>
</tr>
<tr>
<td>3-47</td>
<td>40 (2.2 mmol/L)</td>
</tr>
<tr>
<td>48-72</td>
<td>48 (2.7 mmol/L)</td>
</tr>
</tbody>
</table>


ABM Clinical Protocol 1; http://www.bfmed.org/Resources/Protocols.aspx

- Clear that the routine monitoring of blood glucose in healthy term infants
  - not only unnecessary
  - is potentially harmful to establishment of healthy mother-infant relationship and successful breastfeeding patterns
- This recommendation supported by the World Health Organization, the AAP, the NIH and the National Childbirth Trust of the United Kingdom
  - all conclude that early and exclusive breastfeeding is safe to meet the nutritional needs of healthy term infants
  - healthy, full-term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding
Testing Methods

- Bedside glucose reagent test strips inexpensive and practical, but not reliable
  - especially at low glucose concentrations
  - may be utilized for screening, but laboratory levels sent STAT must confirm results before dx of hypoglycemia made, especially in asymptomatic infants
- Other bedside rapid measurement methods such as reflectance colorimetry and electrode methods may be more accurate
- Continuous subcutaneous glucose monitoring, as is used in diabetics, used experimentally in neonates with good correlation with laboratory glucose values, but not recommended for screening

Risk Factors for Hypoglycemia

- At risk neonates:
  - excess utilization of glucose, which includes the hyperinsulinemic states
  - inadequate production or substrate delivery
- Neonates at increased risk for developing neonatal hypoglycemia should be routinely monitored for blood glucose levels irrespective of the mode of feeding

Table 2: At Risk Infants for Whom Routine Monitoring of Blood Glucose is Indicated

- Small for gestational age (SGA), < 10th percentile for weight
- Large for gestational age (LGA), >90th percentile for weight
- Discordant twin, weight 10% < larger twin
- Infant of diabetic mother, especially if poorly controlled
- Low birth weight (<2500g)
- Perinatal stress, severe acidosis or hypoxia-ischemia
- Cold stress
- Polyhydramnios (venous Hct > 70%)
- Hyponatremia
- Erythroblastosis fetalis
- Beckwith-Wiedemann Syndrome
- Microphallus or midline defect
- Suspected infection
- Respiratory distress
- Known or suspected infant errors of metabolism or endocrine disorders
- Maternal drug treatment (e.g. tetraethylbase, propranolol, oral hypoglycemics)
- Infants displaying symptoms associated with hypoglycemia (see Table 3)

*In unscreened populations where LGA may represent undiagnosed and untreated maternal factors...
Risk Factors for Hypoglycemia

- Prematurity
  - reduced energy reserves (fat, glycogen)
  - increased insulin:glucose ratio
  - decreased ketogenesis
  - immature gluconeogenic pathways
  - more sensitive to effects of hypoglycemia

Risk Factors for Hypoglycemia

- Small for gestational age
  - heterogeneous group
  - most concern: <3rd percentile; asymmetric IUGR; ? abnormal end diastolic flow velocities (Hawdon 1972)
  - high brain:body mass ratio (increased glucose consumption)
  - reduced fat stores
  - delayed maturation of gluconeogenesis (Haymond 1974, Hawdon 1993)
  - hyperinsulinism

Risk Factors for Hypoglycemia

- Stress hypoglycemia
  - Sepsis, perinatal asphyxia, cold stress
  - catecholamine response to stress central to counterregulation
  - circulatory failure leads to reduced mobilization of substrate from periphery, accumulation of lactate, exhaustion of liver glycogen, reduced capacity for gluconeogenesis
Risk Factors for Hypoglycemia

- Transient hyperinsulinism
  - Most common in infants of diabetic mothers
- Erythroblastosis fetalis
- Excessive glucose infusions in labor
- Maternal administration of β-sympathomimetics
- Beckwith-Wiedemann Syndrome

Pathogenesis of Hypoglycemia in Neonates: Main Causes

- Decreased substrate availability (low stores)
- Increased energy use (long labor, cold stress, resp. distress, etc.)
- Hyperinsulinism
  - IDM
  - Beckwith-Wiedemann
  - Islet cell hyperplasia; tocolytic drugs, etc.
- Other causes: erythroblastosis, ExTx, sepsis, CHD, metabolic disorders, etc.

Non-specific symptoms

<table>
<thead>
<tr>
<th>Table 3: Clinical Manifestations of Possible Hypoglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instability, tremors, jitteriness, exagerrated Moro reflex, high-pitched cry, seizures or myoclonic jerks, lethargy, listlessness, limpness, hypotonia, coma, cyanosis, apnea or irregular breathing, tachypnea, hyperthermia, temperature instability, vasoconstrictor instability, poor suck or refusal to feed</td>
</tr>
</tbody>
</table>

Jitteriness and tachypnea statistically significant at predicting low blood glucose.
Symptomatic vs. Asymptomatic

- Neurodevelopmental sequelae
  - Direct causation or association
  - Alternate brain fuels
- Infants who develop symptomatic hypoglycemia were probably hypoglycemic but asymptomatic at an earlier stage

Adverse neurodevelopmental outcome of moderate neonatal hypoglycemia

- Retrospective data - nutrition study
- Post hoc regression analysis
- Bayley motor and developmental scales as dependent variables
- Hypoglycemia: < 2.6 mmol/L (< 46 mg/dL)
- Hypoglycemia for at least 5 days associated with 3.5 X risk of impairment


Symptomatic Hypoglycemia in Otherwise Healthy, Breastfed Term Newborns

- 3 cases that presented at home with seizures or apnea, day 3
  - Admitted between 1993-1997; all 3 male
  - Geographic area with 65,000 annual births (0.005%)
  - Full-term with no recognized perinatal risk factors for hypoglycemia
  - 2 of 3 primips; all normal pregnancy and SVD
  - All three feeding poorly at and after discharge
- Outcomes: 2 normal; 1 delayed in special school
- All 3: No urinary ketones defective ketogenic response

Moore AM, Perlman M. Pediatrics 1999; 103:837-839
Hypoglycemia and the neonatal brain

“Evidence from studies of humans and other animals suggests that cortical damage and long-term sequelae occur after prolonged hypoglycemia sufficiently severe to cause neurologic signs.”

Prevention of Hypoglycemia

- Antenatal
  - good control of maternal diabetes
- Intrapartum
  - avoid excessive maternal glucose infusion
- Early Postpartum
  - dried immediately to reduce evaporative heat loss which increases energy demands
  - skin-to-skin contact as soon as possible to maintain core temperature and facilitate suckling and milk production
  - early enteral feeds should have the highest priority in healthy infants, whether term or preterm (Williams 1997)

Feeding

- “Most effective method of preventing hypoglycemia is feeding with milk as soon as possible after delivery” (Williams 1997)
- Breastmilk preferred over formula
  - promotes ketogenesis
  - formula has insulinogenic effect (Lucas 1991)
- No justification for prelacteal glucose water feeds
  - glucose water lower energy density than milk
  - no evidence that aspiration of colostrum any more harmful than that of glucose or water
- Infants who cannot feed should be started on an appropriate IV glucose infusion
To Prevent/Minimize Hypoglycemia

- Assess Hx, PE for risk factors for hypoglycemia
- Very selective glucose screening
- Mother and infant continuously together
  - Skin to skin
- Early and frequent breastfeeding - within 30-60 minutes of birth

Hypoglycemia: Clinical Management General Principles

- Account for the overall metabolic and physiologic status of the infant;
- Not necessary to disrupt the mother-infant relationship and breastfeeding;
- Immediate intervention needed for infants with clinical signs/ symptoms because severe, prolonged, symptomatic hypoglycemia may result in neurologic injury;

Hypoglycemia: Clinical Management General Principles

- Monitor infants at highest risk;
- Confirm plasma glucose is low;
- Demonstrate that symptoms resolve after restoring plasma glucose to normal;
- Observe and document all these events
Healthy Term Infants

- Early and exclusive breastfeeding meets nutritional and metabolic needs of healthy, term newborn infants
- Healthy term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding
- Routine supplementation of healthy, term infants with water, glucose water or formula unnecessary and may interfere with establishing normal breastfeeding and normal metabolic compensatory mechanisms
- Initiate breastfeeding within 30-60 minutes of life and continue on demand
  - Early breastfeeding not precluded because the infant meets criteria for glucose monitoring

Healthy Term Infants

- Initiation and establishment of breastfeeding is facilitated by skin-to-skin contact of mother and infant
  - Maintains normal infant body temperature and reduces energy expenditure (enabling maintenance of normal blood glucose) while stimulating suckling and milk production
  - Feedings should be frequent
  - 10-12 times per 24 hrs first few days after birth
- Routine monitoring of blood glucose in asymptomatic, term newborns is unnecessary and may be harmful

AAP Committee on Fetus and Newborn

“...no study has shown that treatment of a transiently low blood glucose level offers a better short-term or long-term outcome than the outcome resulting with no treatment.... Furthermore, there is no evidence that asymptomatic hypoglycemic infants will benefit from treatment.”

Pediatrics 1993; 92(3): 474-476
At-risk or symptomatic infants

- Screen for hypoglycemia; frequency and duration related to specific risk factors of individual infant
- Suggest monitoring begin within 30-60 minutes for infants with suspected hyperinsulinemia, no later than 2 hours for infants in other risk categories
- Monitoring should continue until acceptable, pre-prandial levels consistently obtained
- Reasonable (although arbitrary) goal to maintain plasma glucose conc 40-50 mg/dl (2.2 to 2.8 mmol/L)
- Bedside glucose screening tests must be confirmed by formal laboratory testing
- Treatment should begin immediately in symptomatic infants

Selective Screening for Hypoglycemia

- SGA (<10th %tile)
- Discordant (smaller) twin
- LGA (>90th %tile, in certain populations)
- IDM
- LBW (<2500 gm)
- Post-asphyxia
- Erythroblastosis fetalis
- Polycythemia/hyperviscosity
- Cold stress/hypothermia
- Presence of microphallus or midline defect
- Beckwith-Wiedemann Syndrome or other endocrine or inborn errors of metabolism
- Other stressors, such as RDS, sepsis, etc.

Management of Documented Hypoglycemia:
Asymptomatic Infant

- Continue breastfeeding (approx every 1-2 hours) or feed 1-5 ml/kg of expressed human milk or substitute nutrition
- Recheck blood glu conc before subsequent feedings until value is acceptable and stable
- Avoid forced feedings
- If glu remains low despite feedings, begin IV glu
- Breastfeeding may continue during IV glu
- Carefully document response to treatment
Symptomatic Infant or with plasma glu levels < 20-25 mg/dL (< 1.1-1.4 mmol/L)

- Initiate IV 10% glucose solution with mini-bolus
- Do not rely on oral or intragastric feeding to correct extreme or symptomatic hypoglycemia
- Glu conc in symptomatic infants should be maintained > 45 mg/dL (> 2.5 mmol/L)
- Adjust IV rate by blood glu concentration
- Encourage frequent breastfeeding
- Monitor gluc conc before feedings as IV is weaned until values stabilize off intravenous fluids
- Carefully document response to treatment

Supporting the Mother

- Normal, healthy baby developing hypoglycemia may jeopardize breastfeeding
- Reassure mother nothing wrong with her milk, supplementation usually temporary
- Have mother hand-express or pump milk; feed to her infant
  - help overcome feelings of maternal inadequacy
  - help establish a full milk supply
  - stimulate breasts expression with appropriate frequency (8 times/24 hours) until baby latching and suckling well to protect milk supply
- Keep infant at breast or return infant to the breast as soon as possible
- Skin-to-skin care easily done
  - may lessen the trauma of intervention
  - also provide physiologic thermoregulation, metabolic homeostasis

Breastfeeding Plans

- Term infants
  - to breast within an 30-60 min of delivery; demand feeds thereafter (at least 10-12 breastfeedings/24 hours)
- Healthy preterm infants (32-36 weeks)
  - offer breast as soon as possible after birth; then Q 3 hours/on demand
  - supplemental feedings by NG or cup/bottle to support breastfeeding behaviors
  - expressed mom’s milk; donor milk; formula until mom’s milk available
  - 80-100 cc/kg/d sufficient to maintain blood glucose
  - decrease supplements as infant improves at breast
  - Baby Weigh Scale helpful in determining intake at breast
Breastfeeding Plans

- Healthy preterm infants <32 weeks
  - initiate gavage feeds of expressed mom’s milk/donor milk/formula at 60-80 cc/kg/d
  - smaller infants, initiate TPN, and advance on gavage human milk per protocol
- SGA infants
  - initiate enteral feeds of human milk, and/or TPN, early
  - feed Q 3 hours

Breastfeeding Plans

- Infants of diabetic mothers
  - hypoglycemia most likely occur first 24 hours of life
  - breastfeed as soon as possible after birth, and thereafter on demand, but frequently
  - antenatal colostrum expression (Chapman 2013, Forster 2011, Salam 2012, Cox 2006)
  - if pre-feed blood glucose at 3 hours of age normal, unlikely to require supplements
  - if plasma glucose <47mg/dl at this age, institute supplementary feeds (MOM>PDHM>formula)
  - most studies of neurodevelopmental outcome among IDM’s similar to that of controls if hypoglycemia appropriately treated

Summary

- Clear routine monitoring of blood glucose in healthy term infants not only unnecessary, but potentially harmful to establishment of healthy mother-infant relationship and successful breastfeeding patterns
- This recommendation has been supported by the World Health Organization, the AAP, the NIH, ABM, and the National Childbirth Trust of the United Kingdom
  - All conclude early and exclusive breastfeeding is safe to meet the nutritional needs of healthy term infants
  - Healthy, full-term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding
Following this discussion on jaundice you will be able to:

- Define jaundice and differentiate the types associated with breastfeeding.
- Review the physiology of bilirubin.
- Understand the relationship of jaundice and breastfeeding.
- Know how to successfully support breastfeeding in the jaundiced baby, and why it is so important to do so.

**What is Jaundice?**

- Neonatal jaundice
  - serum bilirubin sufficiently elevated to cause at least minimally visible yellowing of skin, ocular sclerae, or both
  - most infants this correlates with serum bilirubin level >5mg/dl

**Jaundice**

- Physiologic hyperbilirubinemia of the newborn
- Associated with breastfeeding:
  - “Breast (non)feeding Jaundice”
    - “Early-Onset Jaundice”
    - Starvation jaundice of the newborn
  - “Breast Milk Jaundice”
    - “Late-Onset Human Milk Jaundice”
    - Prolongation of physiologic jaundice
- Pathologic jaundice
Physiology of Neonatal Jaundice

- Relatively low oxygen tension in utero
- Fetus adapts by making more RBC's
- After delivery into relatively oxygen rich environment, infant ↓ need for so many RBC's
  - Excess fetal cells have shortened half-life
  - Released Hgb broken down to heme in the reticuloendothelial system (RES)
  - Cells in the RES oxidize heme to biliverdin
- Biliverdin is water soluble
- Rapidly degraded to bilirubin
- One gram of Hgb produces 34 mg of bilirubin

Biliverdin

- Nontoxic, water-soluble green pigment
  - In primitive animals, amphibia, birds and reptiles is major end-product of heme degradation
  - Why in mammals is water-soluble, non-toxic biliverdin converted to water-insoluble, potentially toxic bilirubin?

Biliverdin Theories

- Fetus has significant heme degradation
  - Biliverdin cannot cross placenta to maternal circulation;
    - Large, polar molecule
  - Bilirubin crosses placenta,
  - Maternal liver disposes of it
- Bilirubin is effective and potent antioxidant
  - Could physiologic jaundice provide an important antioxidant for prevention of oxygen free radical injury during the newborn period, when other antioxidants are not synthesized as readily?
Bilirubin Transport and Metabolism

- Bilirubin released from the RES into circulation
  - Bound to albumin for transport
  - Some bilirubin is unbound or “free”
  - With increasing amounts of bilirubin, the amount of free bilirubin also increases as binding sites are used up

Transfer to the hepatocyte occurs

- Uptake-release from albumin, crosses cell membrane, enters cytoplasm and bound to ligandin
- Conjugation-enzyme glucuronyl transferase places 1-2 molecules of glucuronic acid on each molecule of bilirubin.
  - Water soluble conjugated bilirubin—“direct bilirubin”
  - Less efficient in newborn
- Excretion into bile

Enterohepatic Circulation of Bilirubin

- Bilirubin glucuronide readily hydrolyzed to unconjugated bilirubin
  - Spontaneous and by intestinal mucosal enzyme β-glucuronidase
- In newborn, hydrolysis accelerated by:
  - 10X greater conc. of β-glucuronidase than in adult
  - alkaline pH proximal small intestine facilitates nonenzymatic hydrolysis
  - monoglucuronide form
  - absence of clostridial bowel bacteria to convert bill to soluble reduction products—stercobilin
- Unconjugated bilirubin absorbed
  - 6X increase in reabsorption that may last 9 weeks
  - Enterohepatic recirculation
So, What Causes Physiologic Jaundice?

- Increased RBC breakdown
- Decreased hepatic uptake
- Relative deficiency of hepatic glucuronyl transferase
- Increased enterohepatic circulation

Sum of these physiologic alterations

- Elevated unconjugated serum bilirubin
- Visible jaundice in more than half of all newborns in first week of life
- Regardless of feeding method

Epidemiology of Physiologic Jaundice

- Virtually all babies have physiologic jaundice
  - 40% healthy newborns have a TB 5mg/dL at 24 hr and 7mg/dL at 36 hr (Bhutani 1999)
  - Taught bili rises to 5-6mg/dl by 3rd day, falls to 2-3mg/dl by 7 days, 1mg/dl by 2 weeks (Kivlahan 1984)
- Asian and Native American infants rise more rapidly (8-12mg/dl on day 4-5), and fall slower
- Exaggerated in premature infants
- Method of feeding: breastfeeding vs. formula

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Pathological Jaundice

- Rapid or early rise of bilirubin may signal a pathological condition
  - Higher than 5 mg/dl 1st 24 hours
  - Rising faster than 0.5 mg/dl/hr
- Three possible categories:
  - Overproduction of bilirubin
    - hemolysis, resorption of hemorrhage, ↑ enterohepatic uptake
  - Decreased rate of conjugation
    - Glucuronyl transferase deficiency
  - Abnormalities of excretion or reabsorption
    - hepatitis, biliary atresia

What’s the Big Deal?

- Bilirubin is a cell toxin
- High free unconjugated bilirubin can be deposited in tissues, including the brain
- Bilirubin encephalopathy and kernicterus describe clinical and pathological findings associated with bilirubin deposition in the brain
  - 2% >20mg/dl; 0.15% >25mg/dl; 0.01 >30mg/dl (1995-56 birth cohort 50,000 CA; Newman 1999)
  - >90% infants with kernicterus; bili >25mg/dl (Ip et al 2004)
    - 10% mortality
    - 70% long-term morbidity
Hyperbilirubinemia and Breastfeeding

- “Starvation jaundice” of the newborn
  - Early-onset breast "non-feeding" jaundice (Gartner 1997)
- Late-onset human milk jaundice
  - (prolonged human milk-associated physiologic jaundice)

Many studies report risk of hyperbilirubinemia 1.8-7 times higher in breastfed infants
- Meta-analysis of 25 studies (Schneider 1986):
  - 13% breastfed babies with peak bilirubin ≥12 mg/dl
  - 4% formula-fed babies with peak bilirubin ≥12 mg/dl
- Large cohort, bilirubin days 2 and 3 (Hassal 1986):
  - 9% breastfed infants with bilirubin > 12.9 mg/dl
  - 2.2% formula-fed infants with bilirubin > 12.9 mg/dl
  - Mean maximum bilirubin higher in breastfed than formula-fed babies

Feeding, Jaundice, and the First 5 Days of Life

- How to reconcile differences in bilirubin between optimally breastfed/formula-fed infants and those with breastfeeding jaundice?
- Inadequate intake of milk and calories
  - Starvation jaundice
    - Initiation of feeds, frequency, water supplements, weight loss
    - 10–18% of exclusively breastfed U.S. newborns lose more than 10% of birth weight (Dewey 2003, Manganero 2001, Nommsen-Rivers 2009)
  - Increased enterohepatic circulation
    - Delayed passage of meconium
    - Decreased frequency of stooling
Type of Feeding

- Serum bilirubin same at 3 days of life in breast and formula fed infants. No cause for hyperbilirubinemia found in 56% (Maisels 1983)
- Breast and formula fed infants controlled for time of initiation of feeds and frequency of feeds: no significant differences in bilirubin (Dahms 1973)
- Breast and formula fed infants in first 96 hours of life did not differ in bilir or degree of weight loss.
  - Weight loss correlated with increased serum bilin independent of feeding method (Frisberg 1989)

Frequency of Feedings

- Critical role of frequency of nursing as a factor in neonatal jaundice:
  - DeCarvalho 1982: with increased frequency of nursing during each of the first 3 days of life (from 6 up to 12 times a day) there is a proportionate lowering of serum bilirubin measured day 3 of life
  - Kuhr 1982: correlate reduced human milk intake and water supplementation of breastfeeding with increased serum bilirubin

Frequency of Feedings

- Yamauchi 1990: frequency of breastfeeding and volume of milk ingested in first 2 days in Japanese infants rooming-in. On day 6, transcutaneous bilin inversely correlated with frequency of nursing in first 24 hours:
  - ≤ 4 times - 26% elevated
  - 7-8 times - 12% elevated
  - ≥ 9 times - 0% elevated
- Suggests that sufficient frequency of nursing (> 9 or more times) during the first day of life may be critical to establishing successful breastfeeding and preventing breastfeeding jaundice
Water Supplementation

- Water and glucose water supplementation are correlated with higher serum bilirubin levels than those in unsupplemented infants (De Carvalho 1981, Adams 1985, Nicoll 1982, Kuhr 1982)

- Etiology?
  - Caloric deprivation: no association with increased bilirubin synthesis, decreased bilirubin conjugation; or decreased hepatic uptake
  - Water (or formula) supplementation diminishes the frequency of nursing, inhibiting the establishment of mature lactation

Stooling Patterns

- There are 450mg of bilirubin in the meconium of the average newborn which accumulates during fetal life
  - Passing this meconium critical to decreasing the bilirubin load from enterohepatic circulation
  - De Carvalho 1985: formula-fed infants excreted 40% more stool and 52% more stool bilirubin in first 3 days than breastfed infants
  - Serum bilirubin 6.8 mg/dl bottle-fed; 9.5 mg/dl breastfed
  - Among breastfed infants serum bili concentrations inversely correlated with stool weight, but not stool bilirubin

- Stool bilirubin excretion higher in infants with serum bili < 5mg/dl than in those with serum bili > 10mg/dl (Fashena 1948)
- Increased stooling frequency on days 2-3 in infants with lower serum bili regardless of mode of feeding (Tudehope 1991)
- % of jaundiced breastfed newborns doubled if first passage of meconium occurred > 8 hours after birth (Corchia 1993)
- First yellow stool appears 1 day earlier in formula-fed infants than breastfed (Salariya 1993)
Breast(non)feeding Jaundice

Etiology? (Early-Onset/Starvation)

- Exaggeration of the first phase of physiologic jaundice of the newborn in the breastfed infant;
- The result of un-physiologic management of breastfeeding;
- Expressed largely through insufficient frequency of breastfeeding;
- Associated with decreased stool volume and stool bilirubin excretion;
- Leads to increased enterohepatic reabsorption of bilirubin.

(Gartner 1994)

Late-Onset Human Milk Jaundice

- Characterized by prolonged hyperbilirubinemia in otherwise healthy breastfed infants
  - Bilirubin rises 4th to 7th day when physiologic jaundice is resolving
  - Peak occurs ~2 weeks, may level off for several weeks at 15-20 mg/dl, resolving over next 4-16 weeks
- Once felt to be abnormal affecting <4% of breastfed infants
- 1/3 breastfed infants 2-3 weeks old visibly jaundiced with levels >5mg/dl; another 1/3 levels 1.5-5 mg/dl (Alonso 1991)
- Now recognized as normal extension of physiologic jaundice

Late-Onset Human Milk Jaundice

- Persistent unconjugated hyperbilirubinemia
  - Otherwise healthy infant
  - Normal weight gain
  - Normal stool and urine output
  - Otherwise normal physical exam
  - No signs or symptoms of underlying pathology
  - TSB generally does not exceed 12 mg/dl unless other factors present
  - Benign; resolves without treatment
Late-Onset Human Milk Jaundice

Etiology

- Results from enhanced enterohepatic resorption of unconjugated bilirubin due to an as yet unidentified factor in the majority of mature milk
  - Recent study correlated higher levels unconjugated total bilirubin with higher levels epidermal growth factor in serum affected infants and their mothers’ milk (Kumral 2009)
  - EGF thought to enhance absorption in neonatal intestine
  - 2/3 of transitional and mature human milk samples enhance the intestinal absorption of unconjugated bilirubin in rats, presumably because of an unidentified substance in human milk (Gartner 1966, 1983)
- Overtime, bilirubin declines to normal adult values even while breastfeeding continues

Late-Onset Human Milk Jaundice

Related Factors

- High serum bilirubin in the first week of life implies a large total body bilirubin pool
  - hemolysis, hematomas, insufficient early nursing
- Ingestion of “milk factor” promotes recycling of this large pool and prolonged jaundice
- Efforts to reduce the early bilirubin pool will mitigate against higher levels of human milk jaundice later

Table 1 “Not enough breastfeeding” jaundice versus breast milk jaundice

<table>
<thead>
<tr>
<th>Not enough breastfeeding jaundice</th>
<th>Breast milk jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>First week of life</td>
</tr>
<tr>
<td></td>
<td>Late in first second week of life</td>
</tr>
<tr>
<td>Feeding</td>
<td>Feeding poorly</td>
</tr>
<tr>
<td></td>
<td>Feeding well</td>
</tr>
<tr>
<td>Weight</td>
<td>Excessive weight loss or poor weight gain</td>
</tr>
<tr>
<td></td>
<td>Normal weight gain</td>
</tr>
<tr>
<td>Urine</td>
<td>Infrequent urine output</td>
</tr>
<tr>
<td></td>
<td>Frequent urine output</td>
</tr>
<tr>
<td>Stool</td>
<td>Infrequent meconium or transitional stools</td>
</tr>
<tr>
<td></td>
<td>Frequent yellow stools</td>
</tr>
<tr>
<td>Level of concern</td>
<td>A potentially serious problem</td>
</tr>
<tr>
<td></td>
<td>A benign condition</td>
</tr>
<tr>
<td>Treatment</td>
<td>Phototherapy if indicated</td>
</tr>
<tr>
<td></td>
<td>Dependent on other factors</td>
</tr>
<tr>
<td>Resolution</td>
<td>With improved breast milk intake and bilirubin excretion in stools</td>
</tr>
<tr>
<td></td>
<td>Spontaneous, within first 12 weeks of life</td>
</tr>
<tr>
<td>Breastfeeding management</td>
<td>Provide lactation support</td>
</tr>
<tr>
<td></td>
<td>Continue breast feeding</td>
</tr>
<tr>
<td></td>
<td>Trial of breastfeeding interruption not recommended for diagnosis</td>
</tr>
</tbody>
</table>

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Prevention of potentially toxic serum bilirubin concentrations

- Early initiation in immediate postpartum
- Skin-to-skin and rooming-in
- Encourage exclusive breastfeeding
- Optimize breastfeeding management from the beginning
- Teach early feeding cues
- Identify at-risk mothers and babies

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ABM Clinical Protocol #22 Guidelines for the Management of Jaundice
www.bfmed.org

Prevention of potentially toxic serum bilirubin concentrations

- Put to breast frequently
- No supplements with water or formula
- Lactation consultation as needed and early to optimize latch and milk transfer
- Careful monitoring of urine and stool; daily weights
- If evidence of insufficient intake, mothers may need to express milk to increase supply

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TABLE 1: Important Risk Factors for Severe Hyperbilirubinemia

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm birth</td>
</tr>
<tr>
<td>Birth weight ≤ 1500 g</td>
</tr>
<tr>
<td>Neonatal infection</td>
</tr>
<tr>
<td>Jaundice within the first 24 h</td>
</tr>
<tr>
<td>Neisseria gonorrhoea infection</td>
</tr>
<tr>
<td>Group B β-hemolytic streptococcal infection</td>
</tr>
<tr>
<td>Vaccination</td>
</tr>
<tr>
<td>Phototherapy</td>
</tr>
<tr>
<td>Use of statins</td>
</tr>
<tr>
<td>Intensive care</td>
</tr>
</tbody>
</table>

TABLE 2: Hyperbilirubinemia Neurotoxicity Risk Factors

<table>
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<th>Risk Factor</th>
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<td>Statins</td>
</tr>
<tr>
<td>Intensive care</td>
</tr>
</tbody>
</table>

TABLE 3: Other Risk Factors for Severe Hyperbilirubinemia to be Considered with the Gestational Age and the Pediatric TBI or TBI lead time (Figure 3)

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<td>Intensive care</td>
</tr>
</tbody>
</table>
At-risk Mothers and Babies

- Maternal
  - Diabetes; Rh-sensitization; separation
- Infant
  - Prematurity; late-preterm; ABO disease; G6PD deficiency; bruising; sleepy baby; separation
  - May need to consider medically indicated supplementation
    - Expressed MOM>donor milk>commercial milk substitute

Manual (Hand)-expression

- Keep in mind that you are applying pressure in back of the pools of milk that lie beneath the areola.
- Your milk will take a minute or so before it begins dripping
- Release and repeat in a rhythmic action.
  - Milk will start to drip and then may squirt out in a spray
- To get as much milk as possible, rotate your fingers around the breast to empty all the breast segments.
### Important Risk Factors for Severe Hyperbilirubinemia

- Pre-discharge TSB or TcB measurement in the high- or intermediate-risk zone
- Lower gestational age
- Exclusive breastfeeding, particularly if not going well and excessive wt loss
- Jaundice observed in first 24 hours
- Isoimmune or other hemolytic disease
- Previous sibling with jaundice
- Cephalohematoma or significant bruising
- East Asian race

### Evaluation of Hyperbilirubinemia

- Evaluate if infant shows clinical jaundice in first 24 hours of life, or develops moderate jaundice thereafter
- History—previous neonatal jaundice, inherited hemolytic disease, feeding, stooling
- Physical exam—well or ill-appearing, bruising, cephalohematomas
- Labs—
  - maternal: ABO and Rh screening
  - baby: bilirubin, type and Coombs, HCT, reticulocyte count, morphology
  - Other tests: thyroid screen, G6PD, hepatic glucuronyl transferase, RBC membrane

### Does Kernicterus Occur in Healthy Hyperbilirubinemic Breastfed Infants?

- 1979-1991: 6/22 infants with clinical kernicterus whose cases were reviewed for medical malpractice
  - 37-39 weeks gestation
  - all breastfed
  - no other etiology of hyperbilirubinemia
  - maximum weight loss 14.4 ± 8.4%
  - peak serum bilirubin 43.3 ± 3.9 mg/dl (39.0-49.7)
  - age at peak bilirubin 6.5 ± 2.1 days (4-10)
- Although rare, classic kernicterus can occur in apparently healthy term breastfed infants with “no other cause” for hyperbilirubinemia

(Maisels and Newman 1995)
Treatment Options for Jaundiced Breastfed Infants

- Continue breastfeeding
- Continue breastfeeding; administer phototherapy
- Supplement breastfeeding with formula; with or without phototherapy
- Interrupt breastfeeding temporarily; substitute formula
- Supplement breastfeeding temporarily; substitute formula; administer phototherapy
- All require close monitoring!!!

AAP discourages the interruption of breastfeeding in healthy term newborns and encourages continued and frequent breastfeeding...Supplementing with water or dextrose does not lower the bilirubin level...AAP Practice Parameter 2004

Management of Breast Milk Jaundice

- Interruption of breastfeeding to make the dx is not advised
  - However brief may jeopardize infant’s ability to return to exclusive breastfeeding
  - Unnecessarily harmful to the infant and traumatic to parents
  - May be falsely reassuring and obscure a potentially serious etiology
  - No Rx if clinically well and TSB remains below recommendations for phototherapy
Management of Breast Milk Jaundice

- If TSB > 12 mg/dl, further investigation for other etiology should occur
- If negative and TSB > 20 mg/dl, phototherapy recommended
  - Admit to hospital with mother rooming in to breastfeed
  - At this level some consider interruption in breastfeeding, but not required
  - Interruptions for 30 minutes for breastfeeding does not diminish effectiveness

Supplementation of Breastfeeding

- Cow’s milk based formula has been shown to inhibit bilirubin absorption
  - Small amounts are sometimes used
- If need to supplement with formula, strongly consider use of protein-hydralysate
  - More effective in lowering bilirubin
  - Less likely to induce allergy
  - Tastes bad!
  - Seen as medicine
  - Expensive
  - …so less likely to give up breastfeeding!
A Controlled, Randomized, Double Blind Trial of Prophylaxis Against Jaundice Among Breastfed Newborns (Gourley et al. 2005)

- N = 64 all breastfed
- Results: EHC and L-aspartic acid used as βGU inhibitor fecal bilirubin excretion
- 4 groups (given β-glucuronidase inhibitor)
  - Control (no inhibitor)
  - L-aspartic acid
  - Enzymatically hydrolyzed casein (EHC)
  - Whey casein

Hydrolyzed Formula and beta-glucuronidase

- BGU deconjugates bilirubin
  - Unconjugated bilirubin more easily absorbed
  - Enterohepatic circulation of bilirubin ↑
- Hydrolyzed Casein Formula
  - Contains BGU inhibitors
- Standard Formula
  - Contains negligible amounts of BGU
- Human Milk
  - Contains considerable amounts BGU
Supplements
Regardless of supplement chosen, if used:
- Cup or supplemental nursing device
- If bottles breastfeeding supportive
- If temporary interrupt breastfeeding MUST maintain/improve mom’s supply
- Encouragement to continue/resume breastfeeding is of utmost importance
  - Great fear that breastfeeding caused the problems

Treatment for the Jaundiced Breastfeeding Infant
- Encourage frequent breastfeeding
  - Assess success at breast and provide appropriate support
- Do not have to interrupt breastfeeding!
  - Data does not support this as necessary standard treatment
  - Interfere with maintenance of mother’s milk supply
  - Risk of engorgement and mastitis
  - Correlated with shorter duration of breastfeeding, which may be related to message mother gets that her milk may harm her baby
- If breastfeeding is interrupted, mother must be supported to maintain lactation
  - Re-initiate breastfeeding as soon as possible

Treatment for the Jaundiced Breastfeeding Infant
- If need supplementation, consider use of SNS with expressed human milk or formula
  - Do not use water or glucose water
- May require phototherapy
  - Bill-blanket at home may be more conducive to promoting and sustaining breastfeeding
- IV fluids only if dehydrated
  - May inhibit thirst drive for oral fluids, thus raising bilirubin
- Infants who are ill, preterm, have hemolytic disease, or manifest neurological signs consistent with bilirubin encephalopathy must be evaluated for etiology and further treatment
Prevention of potentially toxic serum bilirubin levels

- Early initiation
- Exclusive breastfeeding
  - Supplementation only if inadequate milk intake after attempt to “fix” breastfeeding
  - Documented failure milk production/transfer
    - Milk weights
    - Significant dehydration
    - MOM>Donor milk>formula

Optimize breastfeeding management from beginning
- Education on early feeding cues
- Identify at-risk moms and babies
  - Mom—diabetes, RH sensitization
  - Baby—ABO incompatible; premature (esp. late preterm); bruising

Thank you!!
kathleen.marinelli@cox.net