Management of Jaundice in the Breastfed Infant

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Objectives
- Understand the basic pathophysiology of neonatal jaundice
- Learn to identify common jaundice patterns and contributing factors
- Explain when referral to a care provider is indicated
- Be able to explain to families basic principles of jaundice treatment and course
- Be able to counsel families of jaundiced infants on maintenance and optimization of breastfeeding

Bilirubin

Where does the bilirubin come from?
- Normal full-term newborn has a Hct of 50% - 65%
- Because of the low O2 tension delivered to the fetus via the placenta, the fetus requires more hemoglobin to carry the oxygen
- After birth, these extra RBCs are broken down

Hemoglobin
### Pathophysiology Bilirubin Cycle

- **Bone Marrow**
  - RBCs 80%
- **Heme Catabolism**
- **Liver**
  - Unconjugated bilirubin – Albumin (Indirect bilirubin)
  - Excetration Conjugated bilirubin into Bile (Direct Bilirubin)
- **Enterohpatic circulation of urobilinogen**
- **Stercobilin in Feces**

### Risk Factors
- Blood type ABO or Rh incompatibility
- Drugs: diazepam (Valium), oxytocin (Pitocin)
- Ethnicity: Asian, Native American
- Maternal illness: gestational diabetes
- Birth trauma: cephalohematoma, instrumented delivery
- Excessive weight loss due to infrequent feedings
- Infections: TORCH
- Male gender
- Prematurity
- Previous sibling with hyperbilirubinemia

### Differential Diagnosis

- **Unconjugated** (Indirect)
  - Physiologic
  - Pathologic (ABO, sepsis)
- **Conjugated** (Direct)
  - Pathologic (Biliary atresia)

### Bilirubin Checks
- **Order:**
  - Total Bilirubin = Direct + Indirect
  - Direct Bilirubin
- **If you’re really worried:**
  - Consider a CBC
  - Consider a Coombs Test/DAT (Direct agglutination test)
  - CMP

### Why all the fuss?
- Bilirubin is a cell toxin
- Too much in the bloodstream will be deposited in various tissues of the body, including brain tissue, causing cell death
- Destroyed brain cells do no regenerate
- Too much brain damage = kernicterus

### Kernicterus
- Progressive lethargy
- Rigidity
- High-pitched cry
- Opisthotonos: rigid body w/ arched back
- Fever
- Seizures
- 50% mortality rate
Kernicterus

- Survivors
  - Choreoathetoid cerebral palsy
  - Asymmetric spasticity
  - Paresis of upward gaze
  - High frequency deafness
  - Mental retardation

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"TSB (total serum bilirubin) is, at best, a poor risk indicator for kernicterus and, at worst, an excuse for not intervening when intervention is necessary"

There’s a lot we don’t know

- When bilirubin is bound to albumin (indirect), it cannot cross the blood-brain barrier
- Lab and clinical data are consistently showing that direct bilirubin, not total serum bilirubin, is a better predictor of neurotoxicity
- Where do babies get albumin from?
  - Albumin comes from good nutrition and adequate intake of milk

**Root Causes of Identified Cases of Kernicterus**

- Early discharge (<48 hours) with no early follow-up (within 48 hours of discharge).
  - This problem is particularly important in near-term infants (35-37 weeks’ gestation).
  - DOL #5 home visit so important
  - Parental teaching so important
  - Failure to check the bilirubin level in an infant noted to be jaundiced in the first 24 hours.
  - Failure to recognize the presence of risk factors for hyperbilirubinemia.

**What is the typical jaundice scenario?**

- 95% of the time
- Normal physiologic jaundice

**Kramer’s Rule**

1. Face: 4-6 mg/dl
2. Chest, upper abd: 8-10 mg/dl
3. Lower abd, upper thighs: 12-14 mg/dl
4. Arms, lower legs: 15-18 mg/dl
5. Palms, soles: 15-20 mg/dl

Refer to a care provider for >/= zone 2

**Normal Physiologic Jaundice**

- 95% of the jaundice you will see
- Usually just face and chest
- Usually occurs in first week of life
- Begins on 2nd day, peaks on 3rd or 4th day, then disappears
  - For jaundice persisting beyond the 4th day of life, refer to a care provider

**Normal Physiologic Jaundice**

- Occurs in both formula and breastfed infants at equal rates
- Caused by:
  - Increased amount of bilirubin produced
  - Immature liver

Normal Physiologic Jaundice

- $\text{Bili} > 15$
- Dehydration is going to make it worse
  - Problems with breastfeeding
  - Delayed lactogenesis II
  - Infrequent formula feeding
- Refer to a care provider if you see a baby who is dehydrated

Dehydration

Normal Physiologic Jaundice

- Reabsorption of extravascular blood
  - Severe caput or cephalohematoma can make it worse
- Once milk is in and the baby is making the yellow seedy poops (at least 4 in 24 hrs), you're usually in the clear

Normal Physiologic Jaundice

- May serve an evolutionary purpose

Prevent Exaggeration

- “Breast non-feeding Jaundice”
  - Prevent a delay in lactogenesis II
    - BF initiated within 1 hour of birth
    - Rooming-in, Lying-in
    - Feed according to baby's cues (10/24 hrs)
  - When these three things are done, formula fed and breastfed infants have equal incidence of exaggerated physiologic jaundice (Gartner and Herschel 2001)

In other words . . .

The old term “breastmilk jaundice” is actually hospital-caused jaundice

Or

Non-baby friendly jaundice
What is the ONLY reason to ever interrupt breastfeeding in the jaundiced baby?

Galactosemia

Other Causes

Gastrointestinal Problems
- Increased enterohepatic circulation secondary due to intestinal obstruction
  - Cystic fibrosis
  - Hirschsprung disease
  - Ileal atresia
  - Pyloric stenosis
  - Other causes of intestinal obstruction

Gastrointestinal Problems
- Bilirubin metabolism problems
  - Crigler-Najjar syndrome
  - Gilbert syndrome
  - Hypothyroidism
  - Hypoxia
  - Lucey-Driscoll syndrome

Hematological Problems
- ABO incompatibility
- Rh incompatibility
- Clotting disorders
- Autoimmune disease
- Hemoglobinopathies
- Microangiopathies
- Red cell enzyme defects - Glucose-6-phosphate deficiency, pyruvate kinase deficiency
- Red cell membrane defects - spherocytosis, elliptocytosis
**Miscellaneous**
- Acidosis
- **Dehydration**
  - Hypoalbuminemia
  - Infant of a diabetic mother
  - Medication
  - Sepsis
  - Swallowed maternal blood

**G6PD**
- Widespread and frequently unrecognized
- Mediterranean and in the Middle East, Arabian peninsula, Southeast Asia, and Africa.
- Occurs in 11% to 13% of African Americans, and kernicterus has occurred in some of these infants
- G6PD level should be checked in any jaundice infant requiring lights with an ethnic risk

**Gilbert’s Syndrome**
- Also known as constitutional hepatic dysfunction and familial non-hemolytic jaundice.
- Inherited gene mutation
- 5% of the population
- Reduced activity of the enzyme glucuronyltransferase, which conjugates bilirubin

**Isoimmune Hemolytic Disease**
- Maternal antibodies attack RBCs in the newborn
- Leads to hemolysis
- Causes jaundice and anemia
- Mom blood type O & baby blood type A, B or AB
- Rh or Kell antibody
- Positive direct coombs test in baby

**Biliary Atresia**
- Biliary atresia: abnormal bile ducts inside or outside the liver
- Bile ducts
  - remove waste from the liver
  - carry salts that help the small intestine digest fat
- Bile flow from the liver to the gallbladder is blocked.
- Leads to liver damage and cirrhosis of the liver
Prevention

- Educated pregnant women on the importance of:
  - Early initiation of breastfeeding
    - In the first hour after birth
  - Skin-to-skin
  - How to establish a milk supply
  - Rooming-in

Prevention

- Exclusive breastfeeding should be encouraged
- Feeding anything prior to the onset of breastfeeding:
  - delays the establishment of good breastfeeding practices by the infant
  - delays establishment of adequate milk production
  - increases the risk of starvation and exaggerated physiologic jaundice.

Management of Jaundice

- AAP 2004
- Bhutani Curve

Changes in Serum Bilirubin Levels in the Neonate

- Haemolytic
- Obstructive
- Decreased enzyme activity

- Serum Bilirubin (µmol/L)
- Days after birth

Bhutani Curve

- High Risk Zone
- Low Risk Zone
- High Risk Zone
- Low Risk Zone

Postnatal Age (Hours)

- Serum Bilirubin (µmol/L)
Management of Jaundice

- Optimize breastfeeding
  - Assess latch and position
  - Educate on early feeding cues
  - Assess stool and urine output
  - Assess frequency of feeds
  - Watch a feeding
  - AC/PC weights

- Identify at risk dyads
  - Pay especially close attention to late-preterm babies
    - 34 weeks, and 36 weeks and 6 days
    - "Imposters"
    - Greater risk of feeding difficulties
    - Less mature liver
    - Lower threshold to start supplementation

- Supplementation with expressed breastmilk, banked human milk, or formula (in that order of preference) should be limited to infants with at least one of the following:
  - A clear indication of inadequate intake: weight loss in excess of 10% after attempts to correct breastfeeding problem.
  - Failure in milk production or transfer adjusted for duration of breastfeeding and documented by pre-and post feeding weights after attempts to increase milk production and milk transfer.

- Supplementation with expressed breastmilk, banked human milk, or formula (in that order of preference) should be limited to infants with at least one of the following:
  - Evidence of dehydration defined by:
    - Significant alterations in serum electrolytes, especially hyponatremia, and/or
    - clinical evidence of significant dehydration (poor skin turgor, sunken fontanelle, dry mouth, etc.).
Management of Jaundice

- If a supplement is needed

- If you are working with a provider who interrupts breastfeeding
  - Make sure you provide education to the mother on maintaining her supply
  - Low-supply with breastfeeding resumes may cause bilirubin levels to rise again
  - Encouragement to continue breastfeeding is of the greatest importance

Management of Jaundice

- Phototherapy
  - Bilirubin blanket
  - Overhead lights
  - Home vs hospital
  - Interruption for durations of up to 30 minutes to permit breastfeeding without eye patches does not alter the effectiveness of the treatment.


Management of Jaundice

- Exchange transfusion
  - Second-line treatment
  - IVIG in infants with Rh or ABO isoimmunization can significantly reduce the need for exchange transfusions.

Tips for Mothers

- Nurse your baby as much as possible, ideally at least 8-12 times daily (breastmilk helps eliminate bilirubin since it helps them have more frequent stools)
- Know your baby’s feeding cues, so you don’t miss an opportunity for a feeding
- Make sure your baby has a proper latch and gets a full feeding at each nursing session
- Do not supplement with anything without talking to your care provider or lactation consultant first
Tips for Mothers

- Watch for signs of dehydration
  - Dry mouth,
  - No tears,
  - Red brick-dust urine
  - Inadequate stools
- Remember that nothing about your breastmilk is bad for baby
- Trust your Mommy instinct, but if things worsen don’t hesitate to speak to a lactation consultant and your doctor

Case Study

Prenatal History

- 27yo single mother
- Unintended, but welcome pregnancy
- G2P1 w/ dates by 1st trimester US
- Quad screen was abnormal, but amniocentesis was normal
- A + blood type
- GBS negative

Prenatal History

- Mother chronically depressed
- Also caring for 3yo daughter
- Works as CNA
- No help from baby’s father
- Grandmother of baby supportive
- Regular prenatal care
- Plans to breastfed, because sister did
- Caucasian mother, African-Am. father

Birth History

- NSVD at 36 wks
- 7.5 hr labor without augmentation
- Apgars 9 and 9
- Birth weight 5lbs 10oz (2550g)
- Healthy baby

Postpartum

- Baby removed from mom right after birth per her preference for routine cares
- Nursing gives formula b/c baby is “small”
- Nursing comments mom is sleeping a lot and leaving baby in bassinette
- PPD #1 Good latch and suck observed
Discharged Home

- Day of life 2
- Friday afternoon
- Good pees and poops from baby
- Rounding MD notes normal exam
- Nursing notes mention slight jaundice
- Bili was not checked
- Discharge weight 5 lbs 7 oz
  - <5% loss from birth weight

Visit to WIC Office Tuesday

Mother states that son "Looks kind of red." Born at 36 weeks. Eating, pooping, peeing well. Eating every couple hours. She just noticed redness today. Seems like it is all over. No fever. Did not notice any yellow eyes. No behavioral changes.

WIC Office Visit

- Day of life 6
- Mom’s milk is in
- Weight 5lbs 6oz (5% loss)
- Mom seems a little overwhelmed
- Endorses breastfeeding every 2-3 hrs, but sleeping through the night

WIC Office Visit

- Mild scleral icterus and jaundice to abdomen noted
- Alert with normal tone
- Urine has been clear to light yellow
- Very worried b/c brother of mom died in infancy due to a “liver problem and had jaundice”

What would you advise?

1. Go to ER right away
2. Call to MD’s office
3. Phone call to check in again in am
4. Hey, don’t worry, red is in!

Results

- STAT Total Bili is 24 mg/dl (H)
  - Direct Bili is also 0.4 mg/dl (H)
- Reminder:
  - Indirect = unconjugated
    - Has not yet passed through the liver
    - Bound in the blood to albumin
  - Direct = conjugated
    - Bound in the liver to glucuronic acid
**What would expect for treatment?**

1. Home bili blanket with close follow-up
2. Admission back to hospital for lights
3. Re-check in 2 days
4. Re-draw the bili. This must be an error.

**What do you want to know?**

- Bili level and age in hours at draw
- Where on the curve
- Percent weight loss
- How is feeding going?
- Hydration status
- Any known risk factors?
- Is baby alert and vigorous?
- Your exam

**Admit to Hospital**

- On admission
  - Indirect bili 16.4 mg/dl (H)
  - Direct 0.5 mg/dl
  - Potassium a little elevated
  - Lytes otherwise normal
  - CBC w/diff normal
  - Newborn screen normal

- Placed under bili lights in NICU
- Next am bili 13.5 mg/dl
- Noon re-check bili 13.0 mg/dl
- W/u negative for cause
- Pt discharged 6pm with home bili blanket on DOL #7
- F/u next day with MD

**Bhutani Curve**

**Day of life 8**

- Weight 5 lbs 11oz (1 oz over birth wt)
- Afebrile
- Normal exam
- Some persistent jaundice
- Bili re-check 14.2 mg/dl
- Told to discontinue bili blanket
- Re-check in 24 hrs
How do we figure out when to stop or start the lights?

**Day of life 9**
- Bili re-check 12.8 mg/dl
- Good pees and poops
- Acting normal
- Bili blanket stopped
- Plan to re-check in 24 hrs

**Day of Life 10**
- Indirect Bili 14.9 mg/dl
- Good pees and poops
- Acting normal
- Re-check in 24 hrs

**Day of life 11**
- Full WCC with MD
- Mild jaundice noted
- Otherwise normal exam
- Good weight gain
- Bili re-check 13.8 mg/dl
- Re-check in 2 days

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**Johnson Nomogram**

- Day of life 9
  - Bili re-check 12.8 mg/dl
  - Good pees and poops
  - Acting normal
  - Bili blanket stopped
  - Plan to re-check in 24 hrs

- Day of life 10
  - Indirect Bili 14.9 mg/dl
  - Good pees and poops
  - Acting normal
  - Re-check in 24 hrs

- Day of life 11
  - Full WCC with MD
  - Mild jaundice noted
  - Otherwise normal exam
  - Good weight gain
  - Bili re-check 13.8 mg/dl
  - Re-check in 2 days
Days of Life 16-18
- Clinic Bili check DOL 16: 14.5 mg/dl
  - Slightly up from last check
  - Results called to mom who is very frustrated and fearful
- Mom visits a couple of different ERs and urgent cares with concerns about baby looking jaundice
  - Bili’s all around 13 to 14

Day of Life 19
- Clinic visit
- Mom worried about worsening jaundice
- Large weight gain
- Afebrile
- Normal behavior
- Exclusively breastfed
- Total bili 18 mg/dl
- Direct bili 0

Johnson Nomogram

What is the diagnosis?
- G6PD (glucose-6-phosphate dehydrogenase) deficiency
- Gilbert’s Syndrome
- Isoimmune hemolytic disease
- Biliary atresia
- Hypothyroidism
- Intestinal obstruction
- Exaggerated physiologic jaundice secondary to
  - Sepsis
  - Dehydration
  - Gestation < 38 weeks

Answer
Prolonged unconjugated hyperbilirubinemia
- His indirect is elevated = unconjugated
- Prolonged jaundice is defined as
  - >14 days in term infants
  - >21 days in preterm infants

Let’s think back through our differential again . . .
Differential Diagnosis
Unconjugated Hyperbilirubinemia

What is the reason for his Unconjugated Hyperbilirubinemia?
1. His uncle’s mystery liver disease
2. Gilbert’s Syndrome
3. Some sinister component in breastmilk
4. Dehydration
5. Physiologic jaundice
6. G6PD
7. Hemolytic disease
8. Biliary atresia

MD wasn’t sure . . .

jaundiced uncle thing?

What Was Done. . .

- Pediatrician suggested to mom a 24 hr “trial” off breastmilk
- If dramatic bili drop occurs -> dx “breastmilk” jaundice -> baby must stop breastfeeding
- Recommended Peds GI consult

Breastfeeding Interrupted

- Mom not able to pump due to stress
- Baby gets formula for 43 hrs
- Mom’s supply drops
- Bill re-check = 17.4 mg/dl (down from 18 mg/dl)
- Baby vomits formula and develops respiratory congestion & constipation
  - Seen in ER
  - Brief respiratory illness clears after 4-5 days

Day of Life 21

- Mom still wants to nurse. Worried about supply. Seeks out Dr. Mallory for lactation consult.
- Dr. Mallory steps in at this point and tells mom to put baby back to breast.
- Sent to St. Mary’s for Labs:
  - CBC
  - Hepatic function panel
    - AST, ALT, albumin, GGT, alk phos
  - G6PD level
  - Coombs test
  - All normal
- Indirect Bili is now 17.2 mg/dl (17.4 mg/dl)
Mom and pediatrician are still scared about the dead uncle . . .

Peds GI Consult for Prolonged Jaundice
- Peds GI call this "breastmilk jaundice"
- Stop breastfeeding and re-check bili every 2-3 days

Mom has stopped breastfeeding
- Day of Life 24
  - Indirect Bill 8.9
- Day of Life 39
  - Indirect Bill 6.4

Consequences
- Day of life 45
  - Hospitalized with RSV
  - Breastfed infants have fewer RSV infections, and when they do get sick with RSV, they have less severe cases and fewer hospitalizations.

What could have been done better?

- Baby taken away from mother right after birth
- Mother without adequate postpartum help
- Sufficient breastfeeding counseling and expectations
- Bili should have been drawn prior to hospital discharge
- Evidence supports universal screening (Johnson and Bhutani 1998)

What could have been done better?

- Friday discharge baby should have been seen in follow-up Saturday or Sunday
- Home visits!!!!!
- Babies should have a weight check within 1-2 days after hospital discharge to prevent exaggerated jaundice (AAP Subcommittee on Neonatal Hyperbilirubinemia 2001)
- Especially given risk factor of 36 week gestation

How should this baby have been managed?

- In infants with prolonged unconjugated hyperbilirubinemia
  - If no evidence of sinister cause:
  - If bili 12-17 mg/dl, support breastfeeding
    - Feed 10-12/24 hrs
    - Evaluate latch
    - Monitor poops and pees
    - Continue to monitor bilirubin levels every 12-24 hrs
  - If bili 17-25 mg/dl
    - Initiate phototherapy until <17 mg/dl
  - Once level <15 mg/dl, stop checking

Take Home Messages

- Let mom and baby initiate feeding and bonding before all of your routines
- Check bili in any baby with jaundice and <24 hrs old
- Follow-up the breastfed infant on day 3 to make sure milk is in and stools are transitioning
- Have parents monitor urines and stools
- Check weight and skin tone
- Observe latch

Take Home Messages

- Give mom breastfeeding education and expectations prenatally
- Night feeds are needed
- Encourage postpartum support plan
- Don't blame the breastmilk
  - No benefit to “trial off breastmilk”
  - No role for supplementation unless low supply, dehydrated baby etc.

Take Home Messages

- Use your Bhutani curve to know when the level needs to be re-checked
- Use lights when intervention needed according to the Johnson curve
  - MD involved at this point
  - Ensure adequate hydration and breastfeeding
  - Get a lactation specialist involved if any problems out of your comfort zone
Take Home Messages

- If you've ruled our sinister causes, prolonged unconjugated hyperbilirubinemia will resolve on its own
  - Probably Gilbert’s
  - Give it time and follow closely until bili <15

The End