



# HYPERBILIRUBINEMIA IN THE NEWBORN

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# Learner Objectives



# Identification and Diagnosis of Neonatal Hyperbilirubinemia

Affects 60% full term neonates and 80% preterm neonates

# What is Hyperbilirubinemia

Hyperbilirubinemia occurs when there is too much bilirubin in the baby's blood.

Bilirubin is produced by the breakdown of red blood cells.

It can build up in the baby's blood, tissues, and fluids, causing yellowing of the skin, eyes, and other tissues (jaundice).

Mild jaundice usually resolves on its own within 1 or 2 weeks.

For breastfeeding jaundice, mothers should breastfeed the baby more often, and supplementing with donor breastmilk or formula may be necessary if the baby is not getting enough of the mother' breast milk



### Types of Bilirubin

 Indirect bilirubin (unconjugated)-initial form of bilirubin, produced from breakdown of red blood cells-not yet processed by the liver. It is bound to albumin to be transported through the bloodstream

 Direct bilirubin-(conjugated)-water-soluble bilirubin that has been processed by the liver and is bound to glucuronic acid allowing it to be excreted into the bile and then the intestines where it can be eliminated through the stools. It can be directly measured in the blood.





Hyperbilirubinemia testing Approximately 60% of full-term infants and 80% of preterm infants develop jaundice within several days of birth.

- Due to risks for neurotoxicity, all infants are required to have an objective bilirubin assessment within 48 hours of birth.
- Visual assessment can be challenging with differences in skin pigmentation.
  - Progressive yellowing of the skin and whites of the eyes.
  - Infant may demonstrate sleepiness, loss of appetite.
- Objective assessment is best for determination either by serum levels or transcutaneous bilirubin (TcB), and each method can result in different outcomes.

# Types of jaundice

# Pathologic

# Prolonged Physiologic

# **Breastfeeding-associated**

Physiologic



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# Physiologic jaundice: Normal bilirubin

Occurs when RBC breakdown exceeds capability of baby's liver to process.

- A healthy newborn's bilirubin levels rise and fall:
  - At birth: 1.5 mg/dL
  - Day 3-4: approximately 6.5 mg/dL
  - Day 10: approximately <1.5 mg/dL
- Levels gradually decline as excess hemoglobin breaks down and bacteria colonizes intestines.
- Normal to last longer in healthy, breastfed babies.

### Breastfeedingassociated jaundice

Caused by iatrogenic practices resulting in suboptimal intake allowing reabsorption of unconjugated bilirubin.

- Labor medications or events
- Infrequent or scheduled feedings
- Routine mother-infant separation
- Unnecessary formula supplementation
- Pacifier use
- Results from inadequate intake of breast milk calories causing inadequate output to eliminate unconjugated bilirubin especially in stool.



Prolonged physiologic jaundice Late-onset or breastmilk jaundice

- Appears later than physiologic newborn jaundice (day 4-7) when mature milk is more plentiful.
  - Seen in >2% of breastfed fullterm infants after day 7 of life.
- Bilirubin peaks by 2<sup>nd</sup> or 3<sup>rd</sup> week, may persist through 6-15 weeks of life.
- Baby does not appear affected (is lively, not sick).
- Usually self-limiting and benign.
  - Most cases not needing intervention, including breastfeeding interruption.
  - Increased feedings and exposure to sunlight can be sufficient.





Pathologic jaundice

- Occurs in 5-10% of newborns, requires intervention, can develop in first 24 hours of life, or anytime after birth.
- Visible when total serum bilirubin >5-7 mg/dL.
- Conjugated (direct) bilirubin >2 mg/dL or >20% of total level.
- Total serum bilirubin rate of rise >5 mg/dL per day.

Causes: blood incompatibility, congenital hemolytic anemia and drug-induced hemolytic anemia; family history of hemolytic disease, septicemia, biliary atresia, galactosemia, hypothyroidism, cystic fibrosis.

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Presence of any additional signs/symptoms can be indicative of potential underlying disease which also requires treatment .



## Bilirubin Nomogram



## Symptoms of jaundice

- Progressive yellowing of skin usually begins on the face/head and whites of eyes.
- Sleepiness.
- Lack/poor appetite.
- Testing is warranted to differentiate between normal and abnormal jaundice.





Yellowing advances downward from the head through the body.



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# **Risk Factors for Hyperbilirubinemia**

- Hepatitis, galactosemia, biliary atresia or sepsis cause an abnormality of excretion or reabsorption of bilirubin.
- Bruising and ingested maternal blood requires conjugation of additional RBCs.
- Blood incompatibility, lack of enzymes or antibodies against the baby's own RBCs can create a rapid rise in bilirubin level.
- Jaundice within first 24 hrs of life
- Prematurity
- Maternal diabetes
- Asian, Native American, Hispanic, Eskimo ancestry
- Sibling with neonatal jaundice, phototherapy or exchange transfusion
- Delayed meconium passage
- Poor BF, wt loss >10%

#### Lower Gestational Age

Preterm infants are metabolically immature and at higher risk for BIND at lower bilirubin levels than their term counterparts.

Early use of phototherapy helps decrease BIND and minimize the need for exchange transfusion

## Jaundice in First 24 Hours of Life

Hemolysis:

Hemolytic Disease of the Newborn: Rh, ABO and Minot Group Incompatibility

Infections: Intrauterine Viral, Bacterial, Malarial, G-6PD Deficiency Predischarge Bilirubin Near Threshold at Discharge Bilirubin levels can increase after discharge, especially if the discharge is at 24 hours of age.

If feeding is not going well this increases the risk

If there was a cephalohematoma the resulting jaundice level may not increase until after 24 hours Phototherapy Before Discharge

 Rebound Effect



Parent or Sibling Needing Phototherapy or Exchange Transfusion

 Higher Risk for Newborn to have Hyperbilirubinemia



Family History of Inherited Red Blood Cell Disorder Pyruvate kinase deficiency

Crigler–Najjar syndrome

**Gilbert Syndrome** 

Exclusive Breastfeeding With Suboptimal Intake Poor Breastfeeding, Weight Loss>10%

Suboptimal intake decreases stooling and increases reabsorption of indirect bilirubin into the bloodstream.

Daily weights, assessment of urine and stool output and assessment of breastfeeding should include number of feeds and latch adequacy. Additionally, swallowing sounds and breast filling.

#### Down Syndrome

Neonates with Down syndrome have a substantial risk of early hyperbilirubinemia. The American Academy of Pediatrics currently advises obtaining an early screening complete blood count from neonates with Down syndrome.

Assessing their TSB is also advisable.

Macrosomic Infant of a Diabetic Mother Hypoxemia in utero due to maternal and fetal hyperglycemia with hyperinsulinism in the fetus

Increase in the metabolic rate and oxygen consumption because of these two factors as the body attempts to metabolize the excess sugar substrate

Due to hypoxemia in utero the fetus produces more erythropoietin to produce more RBC to transport oxygen Glucose-6-Phosphate-Dehydrogenate Deficiency (G6PD Deficiency) • Glucose-6phosphate dehydrogenase (G6PD) deficiency, an X-linked recessive enzymopathy that decreases protection against oxidative stress, is now recognized as one of the most important causes of hazardous hyperbilirubinemi a leading to kernicterus in the United States and across the globe.



AAP Guidelines 2022 • The guidelines provide clinical guidance on the prevention and treatment of hyperbilirubinemia in newborns greater than 35 weeks of gestational age.



From: Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

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#### Pediatrics. 2022;150(3). doi:10.1542/peds.2022-058859



Figure Legend:

Approach to identify newborns with maternal anti-erythrocyte antibodies and to guide early management.<sup>15</sup>

**AAP Guidelines** 2022 Based on a comprehensive review of evidence, 25 total recommendations are provided in 5 key categories

Prevention of hyperbilirubinemia

Assessment and monitoring for hyperbilirubinemia

Treatment of hyperbilirubinemia

Post-discharge follow-up

Hospital policies and procedures

Treatment Modes for Hyperbilirubinemia Risks vs Benefits

# Hyperbilirubinemia treatment

Phototherapy

- A special fluorescent light that is effective in breaking down bilirubin without the process of conjugation.
- Similar in exposure to natural sunlight.
  - Commonly recommended intervention (indirectly) as an at-home treatment for babies who may be susceptible for increasing bilirubin level post discharge.
- Initiation of phototherapy follows an AAP algorithm for hyperbilirubinemia management.

#### Phototherapy

Although considered relatively safe, phototherapy does have side effects, and some NICUs tend to overuse phototherapy.

Phototherapy employs the use of light sources, usually LED's (light-emitting diodes), emitting light in the blue and green spectra [2]. These wavelengths of light convert bilirubin to less toxic water-soluble photo isomers that can be safely excreted in the bile and urine [5]. Factors that influence the efficacy of phototherapy are the spectrum of light, the irradiance, and the surface area of skin exposed at any one time [6].

# Hyperbilirubinemia treatment

#### Bili Bed



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#### Bili Blanket



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#### Short-term Side Effects of Phototherapy

Interference with maternal-infant interaction

Imbalance of thermal environment water loss

Electrolyte disturbance

Bronze baby syndrome

Circadian rhythm disorder.
Possible Long-Term Effects of Phototherapy Immune or inflammatory childhood allergies

Neurological disorders and hearing loss

ADHD and ASD

Patent ductus arteriosus

## Hyperbilirubinemia treatment

Distance Maximizine irradiance by minimizing patient-to lightsource distance



Light source

Skin area exposed Maximize for intensive phototherapy with additional light scource below infant

Irradiance Standard PT: about 10 µW/cm²/nm

> Intensive PT: >30 μW/cm²/nm (430-490 nm)

#### 18 17,5 16,5 5 14,5 14 13,5 13,5 12,5 11,5 11,5 11 10 9,5 36 48 60 72 84 20 Hour of life GA 32-34 sett GA 30-31 sett -GA 35-37 sett

Phototherapy By Gestational Age and Bilirubin Levels

#### Phototherapy threshold graph for different GA



## Exchange transfusion

Treatment of last resort for bilirubin levels that poorly respond to phototherapy or rise to dangerously high levels.

- Estimated 5% of complications.
- Occurs in 3-4 per 1,000 infants.
- Requires admission to NICU.

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# Treatment for physiologic jaundice

### None is required

- As long as bilirubin levels remain within adequate levels for age (Low or Low Intermediate).
- Thorough and concise breastfeeding assessment is essential to ensure adequate milk transfer.



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- Focus on those babies identified with risk factors.
  - Educate family of risk for hyperbilirubinema and on signs of adequate vs inadequate milk transfer.
  - Support continued feeding of breast milk by educating on collection techniques for supplementation if needed.
  - Monitor infant's bilirubin levels, feedings, diapering, and weight.

Breastfeedingassociated jaundice Treatment of this preventable type of jaundice is remedied by improved breastfeeding practices.

- Implementation of supportive breastfeeding policies based on WHO Ten Steps to Successful Breastfeeding, including:
  - Trained staff to support breastfeeding mothers and babies.
  - Increase frequency and quality of breastfeeding.
  - Rooming-in with frequent skin-toskin contact.
  - Unlimited access to mother's breast with effective sucking.
  - Compression of breast during breastfeeding.
  - Supplementation of hand expressed breast milk via spoon or syringe.



## Lactation support

Since breastfeeding-associated jaundice is preventable, assist the improvement process along with other professionals.

- Partner with nursing to assess breastfeeding at patient's bedside.
  - Helps both of you understand what you each see.
  - Involves mother/family in understanding everyone's concerns.
  - Fosters collaborative POC including the mother/family.
  - Fully supports continuity of care.
- Collaborate with medical staff.
  - Physicians that distrust breastfeeding or lack knowledge of lactation are quick to blame breastfeeding for jaundice.
  - Demonstrate your competence by discussing your assessment and present a plan of care that meets their goals.

Treatment for prolonged physiologic jaundice Likely to receive request from mother or physician for breastfeeding assessment.

- Prior to hospital discharge provide mother lactation resources in her community for problems or concerns.
  - Review anticipatory guidance on early concerns and on breastfeeding goals.
- Conduct thorough breastfeeding assessment including condition of mother's breasts.
  - Document assessment, interventions, evaluation and POC.
- Communicate encounter to referring physician.



## Pathologic jaundice

Incidence of dangerous bilirubin levels is associated with disjointed care during first week post birth.

In-patient care to reduce incidence should include:

- Total serum bilirubin level to guide treatment plan.
- Phototherapy and support for breastfeeding effectiveness.

Discharge instructions should include:

- Physician follow-up by age 3-5 days of life, or within 48-72 hours post DC.
- Parent education of condition and role that breastfeeding and breast milk have in the treatment.
- Prevent mother-baby separation by allowing mother to stay with baby in-hospital or arrange for home treatment with home health nurse visits.

## Lactation support

# Assist the infant's expelling of unconjugated bilirubin by:

- Thorough assessment of breastfeeding especially focused on milk transfer.
  - Implement supplementation for inadequate milk transfer via alternative feeding method.
  - Educate on benefits for baby and mother with use of mother's own milk.



- Educate and assist mother/family on expression and collection techniques.
- Devise a POC for supplementation collaboratively with mother and family.
- Follow up each shift (if possible) or daily.
- If needing to supplement after discharge, devise a POC for home including outpatient follow-up visit.



## Why Is Hyperbilirubinemia Concerning?

 Severe hyperbilirubinemia can cause kernicterus, a type of brain damage that leads to movement problems (cerebral palsy) and hearing loss. Informed guidance on hyperbilirubinemia management, including preventive treatment thresholds, is critical to safely minimize neurodevelopmental risk.



## Kernicterus

#### Acute Bilirubin encephalopathy: extremely high bilirubin level resulting in chronic, long-term sequalae associated with brain damage.

• Prematurity, asphyxia, starvation, and hemolytic disease disrupt the blood-brain barrier, allowing bilirubin to pass and attach to nerve cells.



## Acute bilirubin encephalopathy (ABE)

Bilirubin level that results in ABE varies with the gestational age and postnatal age of the infant.

 Additional factors: birth weight, co-morbidities and the availability of albuminbinding sites.

## Bilirubin Encephalopathy

Bilirubin encephalopathy (BE) is caused by very high levels of bilirubin. Bilirubin is a yellow pigment that is created as the body gets rid of old red blood cells. High levels of bilirubin in the body can cause the skin to look yellow (jaundice).

If the level of bilirubin is very high or a baby is very ill, the substance will move out of the blood and collect in the brain tissue if it is not bound to albumin (protein) in the blood. This can lead to problems such as brain damage and hearing loss. The term "kernicterus" refers to the yellow staining caused by bilirubin. This is seen in parts of the brain on autopsy.

## Symptoms of Bilirubin Encepalopathy

• The symptoms depend on the stage of BE. Not all babies with kernicterus on autopsy have had definite symptoms.

## Early Stage

#### Extreme jaundice

#### Absent startle reflex

#### Poor feeding or sucking

Extreme sleepiness (lethargy) and low muscle tone (hypotonia)

## Middle Stage

#### High-pitched cry

Irritability

May have arched back with neck hyperextended backwards, high muscle tone (hypertonia)

Poor feeding

## Late-Stage BIND

#### Stupor or coma

No feeding

Shrill cry

Muscle rigidity, markedly arched back with neck hyperextended backwards

Seizures

## Treatment

Treatment depends on how old the baby is (in hours) and whether the baby has any risk factors (such as prematurity). It may include:

Light therapy (phototherapy)

Exchange transfusions (removing the child's blood and replacing it with fresh donor blood or plasma)

## Outlook (Prognosis)

BE is a serious condition. Many infants with late-stage nervous system complications die.

Complications may include:

Permanent brain damage

Hearing loss

Death

## Kernicterus

Kernicterus is a permanent disabling neurologic condition characterized by some or all of the following:



# Educating the Family on Hyperbilirubinemia



### Observation of Baby For Jaundice-What To Look For

- Yellowing of your baby's skin and the whites of his or her eyes. This often starts on a baby's face and moves down his or her body.
- Pressing gently on the skin with your finger will help to see if the skin is yellow if your baby is darker skinned.

## **Newborn Behavioral Observations**



## Seizures

## Feeding Adequacy

Newborns should be taking 8-12 feedings per 24 hours

By approximately day 3 the breasts should start filling and during a feeding swallowing can be heard

Weight loss should not exceed 10% and should stop as the milk comes in with weight gain to birthweight by the end of the second week or earlier

Urine and stool output are assessed

## Stool and Urine Output

Day 1-at least one wet diaper and one meconium stool

Days 2 and 3-at least 2 wet diapers and two stools (meconium to greenish brown) each day

Days 4-7-usually around 5-5 wet diapers and 5-10 stools (transitions to liquidy yellow and often seedy) After Discharge Pediatric Visit If the baby should be seen within 24-48 hours is that feasible?

Will the parent(s) be able to get to the appointment?

Are there ways to facilitate the visit

## Communication For Optimal Outcomes

An intense tone may either frighten new parents Tone or cause them to shut down Avoid language that will frighten the parents Use language that the parents will understand Language both considering primary language and education level Avoid technical terms and long definitions that focus on physiology; Keep it Give facts in brief, short segments; Simple Stop frequently to clarify whether information is understood Provide a copy of information given Provide

When To Contact Healthcare Provider Infant's skin or the whites of the eyes are becoming yellow or increasingly yellow.

Baby is lethargic or not eating at least 8 times in 24 hours

Baby has less than expected wet or dirty diapers for his/her days of life

\*\*\*Baby has seizures-call 911

Home Phototherapy Versus Readmission

- Gestational age ≥38 weeks
- ≥48 hours old
- Clinically well with adequate feeding
- No known hyperbilirubinemia neurotoxicity risk factors
- No previous phototherapy
- TSB concentration no more than 1 mg/dL above the phototherapy treatment threshold
- An LED-based phototherapy device will be available in the home without delay
- TSB can be measured daily



# Late Preterm Jaundice Legal Issues With Hyperbilirubinemia

## Late Preterm Baby With Jaundice



# History

Mother G6P3

Baby born at 35 weeks gestation

Weight: 4lbs 6oz

APGAR scores: 10; 10

Nursing fairly-well during first day

Sleepy

Maintaining temperature

## Infant at 24 Hours

Baby began to have evident jaundice above the umbilicus

Blood test revealed bilirubin level of 18gm/dl

## Physician "Recommendation"

- Transfer baby to NICU
- Double Bili Lights
- Supplement breastfeeding with formula


# Parent's Decision

Parents requested physician to discharge baby home with parents

Mother requested OB to discharge her home

Parents requested home phototherapy with a daily home visit for blood testing

Why is this a good/bad idea?

# Home Trajectory

- Mother and Baby were discharged home
- Phototherapy equipment was delivered to the home with a homecare visit to explain the treatment plan
- Mother nursed the baby every two hours around the clock and maintained phototherapy at all other times
- A homecare RN visited every 24 hours for three days
- At 48 hours post birth the bilirubin level was 16
- At 72 hours post birth the bilirubin level was 10
- At 96 hours post birth the bilirubin level was 6

## Outcomes

Jaundice cleared with no adverse effects

Exclusive breastfeeding was maintained



#### Late Preterm Black Baby With Jaundice



Mother G1P0; Black

Baby born at 35 weeks gestation

Weight: 5lbs 8oz

APGAR scores: 9; 10

Nursing poorly during first day with formula supplements given

Sleepy

Maintaining temperature

## History

Baby had no visual evidence of jaundice

## Infant at 24 Hours

Blood test revealed bilirubin level of <mark>10gm/dl</mark>

#### Physician "Recommendation"

- Discharge Baby to home with mother at 24 hours (Friday)
- Return to Pediatrician within 48 hours
- Supplement breastfeeding with formula

## What is the risk?



## Outcome

On Sunday baby began having visible seizures

Baby was transferred by ambulance to a hospital with a NICU

Baby's bilirubin was 31

Baby was placed under double phototherapy

Baby's jaundice resolved within 7 days

Seizures and severe developmental delays occurred due to kernicterus

### Lawsuit

A lawsuit was filed against the physician and hospital with a ruling of negligence and a large financial sum awarded to the parents

Baby had permanent brain damage

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