Neonatal Jaundice

Immature newborn brain is susceptible to toxicity from unconjugated bilirubin resulting in "Kernicterus" or "bilirubin brain damage".

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Jaundice is the visible manifestation of chemical bilirubinemia. In adults sclera appears jaundiced when serum bilirubin exceeds 2 mg/ dl. In neonates, evaluation of sclera is difficult because of physiological photophobia. Icterus, however, becomes apparent on the skin when serum bilirubin reaches more than 5 mg/ dl. Almost all neonates (60% Term and 80% Preterm) will have bilirubin greater than 5 mg/ dl in the first week of life and about 6% of term babies will have levels exceeding 15 mg/ dl.

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Bilirubin Physiology

1. *Source of production:* Bilirubin is derived from the breakdown of heme proteins which are present in hemoglobin, myoglobin and certain heme containing enzymes. Three fourths of the bilirubin comes from hemoglobin catabolism. One gram of hemoglobin results in the production of 34 mg of bilirubin. A normal term newborn produces about 6-10 mg/kg/ day of bilirubin.

2. *Metabolism*
   i. Bilirubin is bound to albumin for transport in the blood. This bound bilirubin does not enter the central nervous system and is nontoxic.
   ii. Upon reaching the liver, only bilirubin enters the liver cell and gets bound to ligandin which helps to transport it to the site of conjugation.
   iii. Conjugation occurs with glucuronic acid to produce mono- and diglucuronides which are water soluble.
   iv. The conjugated bilirubin is transported with the bile to the gut. In the sterile newborn gut, there is an enzyme called beta- glucuronidase which converts bilirubin glucuronide into unconjugated bilirubin which is reabsorbed into the

circulation. This is called enterohepatic circulation and is particularly important in babies who are infrequently fed from birth. With frequent feeding early colonization of gut occurs. These bacteria reduce bilirubin glucuronide into stercobilin which is excreted in stool, thus inhibiting the enterohepatic circulation.

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Assessment of jaundice

Clinical criteria: It is very widely used and utilizes the principle that clinical jaundice first becomes obvious in the face followed by a downward progression as it increases in intensity. Assessment of jaundice should be done in natural light. The finger is pressed on the baby's skin, preferably over a bony part, till it blanches. The underlying skin is noted for yellow color. Extent of jaundice thus detected gives a rough estimate of serum bilirubin. Clinical estimation of bilirubin by experienced person, though reliable, has to be confirmed by laboratory methods.

Clinical criteria to assess jaundice

Area of body	Range of bilirubin (mg/100 ml)
Face	4-8
Upper trunk	5-12
Lower trunk & thighs	8-16
Arms & lower legs	11-18
Palms & soles	>15

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Physiological jaundice

Immaturity in bilirubin metabolism at multiple steps results in the occurrence of hyperbilirubinemia in the first few days of life. These are:

- Increased bilirubin load on the hepatic cell
- Defective uptake from plasma into liver cell
- Defective conjugation
- Decreased excretion
- Increased entero-hepatic circulation

Characteristics of physiological jaundice

- First appears between 24-72 hours of age
- Maximum intensity seen on 4-5th day in term and 7th day in preterm neonates
- Does not exceed 15 mg/ dl
- Clinically undetectable after 14 days.
- No treatment is required but baby should be observed closely for signs of worsening jaundice.

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Pathological jaundice

Presence of any of the following signs denotes that the jaundice is pathological. Treatment is required in the form of phototherapy or exchange blood transfusion. One should investigate to find the cause of pathological jaundice.

- Clinical jaundice detected before 24 hours of age
- Rise in serum bilirubin by more than 5 mg/ dl/ day
- Serum bilirubin more than 15 mg/ dl
- Clinical jaundice persisting beyond 14 days of life
- Clay/white colored stool and/or dark urine staining the clothes yellow
- Direct bilirubin >2 mg/ dl at any time

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Causes of jaundice

Hyperbilirubinemia in the first week of life is usually of the indirect variety. Causes are usually classified based on the time of onset of jaundice. While referring a baby with jaundice make sure that either the mother is referred or mother's blood sample is sent.

1. *Appearing within* 24 *hours of age*
   Hemolytic disease of newborn: Rh, ABO and minor group incompatibility
   Infections: intrauterine viral, bacterial; malaria
   G-6PD deficiency

2. *Appearing between* 24-72 *hours of life*
   Physiological

Sepsis neonatorum

Polycythemia

Concealed hemorrhages: cephalhematoma, subarachnoid bleed, IVH.

Increased enterohepatic circulation

3. ***Appearing after 72 hours***

Sepsis neonatorum'

Neonatal hepatitis

Extra hepatic biliary atresia

Breast milk jaundice

Metabolic disorders

Remember that

- The age of appearance may overlap and the above mentioned grouping is only a general classification.
- Infection must be ruled out in jaundice appearing any time after third day of life.
- Even after extensive investigations, cause remains uncertain in over one third of cases.
- Neonatal jaundice may be multifactorial in origin.

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Risk factors of jaundice

A simple pneumonic for risk factors is JAUNDICE

J - Jaundice within first 24 hrs of life

A - A sibling who was jaundiced as neonate

U - Unrecognized hemolysis

N – Non-optimal sucking/nursing

D - Deficiency of G6PD

I - infection

C – Cephalhematoma /bruising

E - East Asian/North Indian

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Common causes in India

- Physiological
- Blood group incompatibility
- Intrauterine and postnatal infections
- G-6PD deficiency
- Bruising and cephalhematoma
- Breast milk jaundice

Breast milk jaundice: This condition may persist as a prolonged physiological jaundice or it may appear for-the first time after the first week. It is common in solely breast fed babies and the intensity is maximum between 10-14 days of life. The bilirubin levels are never high enough to require exchange though phototherapy may occasionally be necessary. If bilirubin is less than 15 mg/ dl at 3 weeks one need not worry. But if bilirubin is > 15 mg/dl at 3 weeks, cessation of breast milk for 48 hours will decrease bilirubin levels dramatically and breast milk can be resumed without any risk of recurrence of jaundice. However, more frequent breast feeds without cessation results in improvement in many.

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Approach to a jaundiced baby

The following four questions need to be answered

What is the birth weight?

What is the gestation?

What is the postnatal age in hours?

Is the jaundice physiological or pathological?

If the jaundice is physiological and baby is well only observation is necessary.

In deeply jaundiced newborn one must also evaluate for presence or absence of bilirubin toxicity (kernicterus). Kernicterus is identified by lethargy and poor feeding, poor or absent Moro's reflex, opisthotonus or convulsions.

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Workup for pathological jaundice

1. *Review maternal and perinatal history*

   Family history of jaundice, liver disease

   Previous sibling with jaundice for blood group incompatibility

   Maternal illness during pregnancy

Previous history of malaria

Traumatic delivery, delayed cord clamping, oxytocin use

Birth asphyxia, delayed feeding, delay in meconium passage

Breast feeding

2. *Physical examination*

Prematurity

Small for gestation: polycythemia, hepato-splenomegaly, cataract, rash.

Extravascular bleed: cephalhematoma

Pallor: hemolysis, blood loss

Petechiae: sepsis, TORCH infections

Hepatosplenomegaly: Rh-isoimmunization, sepsis, TORCH infections

3. *Laboratory tests* (must in all*)

Serum bilirubin total and direct*

Blood group and Rh for mother and baby*

Direct Coomb's test on infant

Hematocrit*

Peripheral smear for RBC morphology, evidence of hemolysis and, reticulocyte count

Sepsis screen

Liver and thyroid function tests in cases with prolonged jaundice

TORCH titres

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Management

Management of jaundice is directed towards reducing the level of bilirubin and preventing CNS toxicity.

1. Prevention of hyperbilirubinemia
   i. Early and frequent feeding
   ii. Adequate hydration
2. Reduction of bilirubin: This is achieved by phototherapy or/and exchange transfusion.

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Phototherapy

This involves exposure of the naked baby to blue, cool white or green light of wave length 450-460 nm. The light waves convert the bilirubin to water soluble nontoxic forms which are then easily excreted. Every attempt should be made to find out the cause of jaundice. The advantages of phototherapy are that it is noninvasive, effective, inexpensive and easy to use. Clinical assessment of bilirubin level should not be relied upon in an infant under phototherapy. Frequent feeding every 2 hrly and change of posture should be promoted in an infant receiving phototherapy. Eye shades should be fixed.External genitalia may be covered as long as the infant is receiving phototherapy. Additional oral intake of plain water or glucose water is neither recommended nor necessary.

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Technique

i. Six to eight daylight tubes or four blue tubes are mounted on a stand and all electrical outlets are well grounded. Inexpensive commercial phototherapy units are freely available. Tubes are changed after every 1000 hours or 3 months of use. One may use 150 watt halogen bulb (life 1000 hours) for providing effective phototherapy. Blue CFL lamps may also be used which should be changed every 3000h.
ii. Check flux with help of fluxmeter. Ideal 6-8 $\mu w/cm^2/nm$.
iii. A Plexiglas shield should be used to cover the tube lights, if the unit is locally made.
iv. Baby is placed naked 45 cm away from the tube lights in a crib or incubator. If using closer, monitor temperature of the baby.
v. Eyes are covered with eye-patches to prevent damage to the retina by the bright lights; gonads should also be covered.
vi. Phototherapy is switched on.
vii. Baby is turned every two hours or after each feed.
viii. Temperature is monitored every two to four hours.
ix. Weight is taken at least once a day.
x. More frequent breastfeeding or 10-20% extra fluid is provided.
xi. Urine frequency is monitored daily.
xii. Serum bilirubin is monitored at least every 12 hours.
xiii. Phototherapy is discontinued if two serum bilirubin values are < 10 mg/dl.

xiv. Rebound bilirubin is measured 6-8 hours after stopping phototherapy.

Remember

Baby will appear bleached when under phototherapy and hence clinical assessment of jaundice is not reliable. Serum bilirubin must be monitored.

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Side effects of phototherapy

Increased insensible water loss: Provide more frequent and for longer duration extra breast feeding.

Loose green stools: weigh often and compensate with breast milk.

Skin rashes: Harmless, no need to discontinue phototherapy;

Bronze baby syndrome: occurs if baby has conjugated hyperbilirubinemia. If so, discontinue phototherapy;

Hypo or hyperthermia: monitor temperature frequently.

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Exchange transfusion

It is still the most effective and reliable method to reduce serum bilirubin.

Anticipation and early referral to a higher centre is indicated.

Choice of blood for exchange blood transfusion

(i) In ABO incompatibility: Use O cells of same Rh type, ideal is to have O cells suspended in AB plasma.

(ii) In Rh isoimmunization: In emergency use O-ve blood. Ideal is O -ve cells suspended in AB plasma. One may use baby blood group but Rh –ve blood also.

(iii) Other conditions: Baby's blood group.

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Maisel's chart

It is used for taking decision regarding treatment in cases of pathological jaundice. In presence of any of the following, treat as in next higher bilirubin category.

- Perinatal asphyxia
- Respiratory distress
- Metabolic acidosis

- Hypothermia
- Low serum protein
- Birth weight <1500 g
- Signs of clinical or CNS deterioration

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Prolonged indirect jaundice

Following conditions may lead to prolonged indirect jaundice:

- Crigler Najjar Syndrome
- Breast milk jaundice
- Hypothyroidism
- Pyloric stenosis
- Ongoing hemolysis, malaria

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Conjugated hyperbilirubinemia

This is rare in the newborn period and is defined as a direct bilirubin level of $\geq$ 2 mg/dl. It is important to document cause as it is never physiological.

***Approach**:* The following five questions need to be answered

Is the baby symmetric SGA?

Is the stool white or clay colored?

Is the urine high colored?

Are liver and spleen enlarged?

Is the baby on total parenteral nutrition?

Remember

Never discharge a baby with conjugated hyperbilirubinemia without attempting to find the cause.

Rule out or establish the diagnosis of extra hepatic biliary atresia within eight weeks of life when it is still surgically correctable.

These babies are preferably managed in a Level II neonatal unit.

Exclude metabolic conditions especially galactosemia.

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Causes of conjugated hyperbilirubinemia

1. Idiopathic neonatal hepatitis
2. Infections -Hepatitis B, TORCH, Sepsis
3. Malformations -Biliary atresia (extra and intrahepatic), choledochal cyst, bile duct stenosis.
4. Metabolic disorder -Galactosemia
   Hereditary Fructose intolerance
   Alpha-l antitrypsin deficiency
   Tyrosinemia
   Glycogen storage disease type IV
   Hypothyroidism
5. Total parenteral nutrition