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Bilirubin encephalopathy

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Abstract
Neonatal jaundice is a yellowish discoloration of the white part of the eyes and skin in a newborn baby due to high bilirubin levels. Other symptoms may include excess sleepiness or poor feeding. Complications may include seizures, cerebral palsy, or kernicterus. In many cases there is no specific underlying disorder (physiologic). In other cases it results from red blood cell breakdown, liver disease, infection, hypothyroidism, or metabolic disorders (pathologic). A bilirubin level more than 34 µmol/l (2 mg/dL) may be visible. Concerns, in otherwise healthy babies, occur when levels are greater than 308 µmol/L (18 mg/dL), jaundice is noticed in the first day of life, there is a rapid rise in levels, jaundice lasts more than two weeks, or the baby appears unwell. In those with concerning findings further investigations to determine the underlying cause are recommended.
The need for treatment depends on bilirubin levels, the age of the child, and the underlying cause. Treatments may include more frequent feeding, phototherapy, or transfusions. In those who are born early more aggressive treatment tends to be required. Physiologic jaundice generally lasts less than seven days. The condition affecting over half of babies in the first week of life of babies that are born early about 80% are affected.

Keywords: Bilirubin levels, cerebral palsy, kernicterus, neonatal jaundice, seizures

Introduction
Normally, hyperbilirubinemia resolves on its own as the infant processes the bilirubin and excretes it. However, in some infants, it can become harmful and will need treatment. If not detected or left untreated and levels rise too high, some of the bilirubin may cross the blood brain barrier and settle into brain tissue where it can cause acute bilirubin encephalopathy (ABE). This encephalopathy, if not detected early and treated, can develop into kernicterus. Kernicterus is a potentially fatal disease and results in permanent injury to specific parts of the brain [1].
To help quantify the degree of ABE, the Bilirubin-Induced Neurological Dysfunction (BIND) score was developed. It describes three phases of worsening encephalopathy and the clinical signs in each phase:

Initial phase
- Lethargy, decrease in tone or activity.

Intermediate phase
- Moderate stupor, irritability and variable activity.
- Increased tone, some retrocollis/opisthotonus.
- Minimal feeding, high-pitched cry.

Advanced phase:
- Deep stupor to coma, hyper-tonicity.
- Retrocollis/opisthotonus.
- No feeding, shrill cry, seizures, death.

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Screening steps [4-5]**:** The content of this section is based on the Ontario Ministry of Health and Long-Term Care (MOHTLC) Quality-Based Procedure (QBP) titled Hyperbilirubinemia in Term and Late Pre-Term Infants (≥ 35 weeks) (2013).

The key objectives of the QBP for Hyperbilirubinemia are to:

- Ensure all newborns receive bilirubin screening between 24-72 hours of life (if not clinically indicated and performed earlier)
- Ensure infants receive systematic bilirubin monitoring as per the treatment graph and risk nomograms recommended by evidence-based guidelines
- Utilize health care resources responsibly through avoidance of unnecessary/excessive testing, timely discharge, appropriate outpatient follow-up and minimization of preventable readmission
- Reduce the incidence of severe hyperbilirubinemia and acute bilirubin encephalopathy [33].

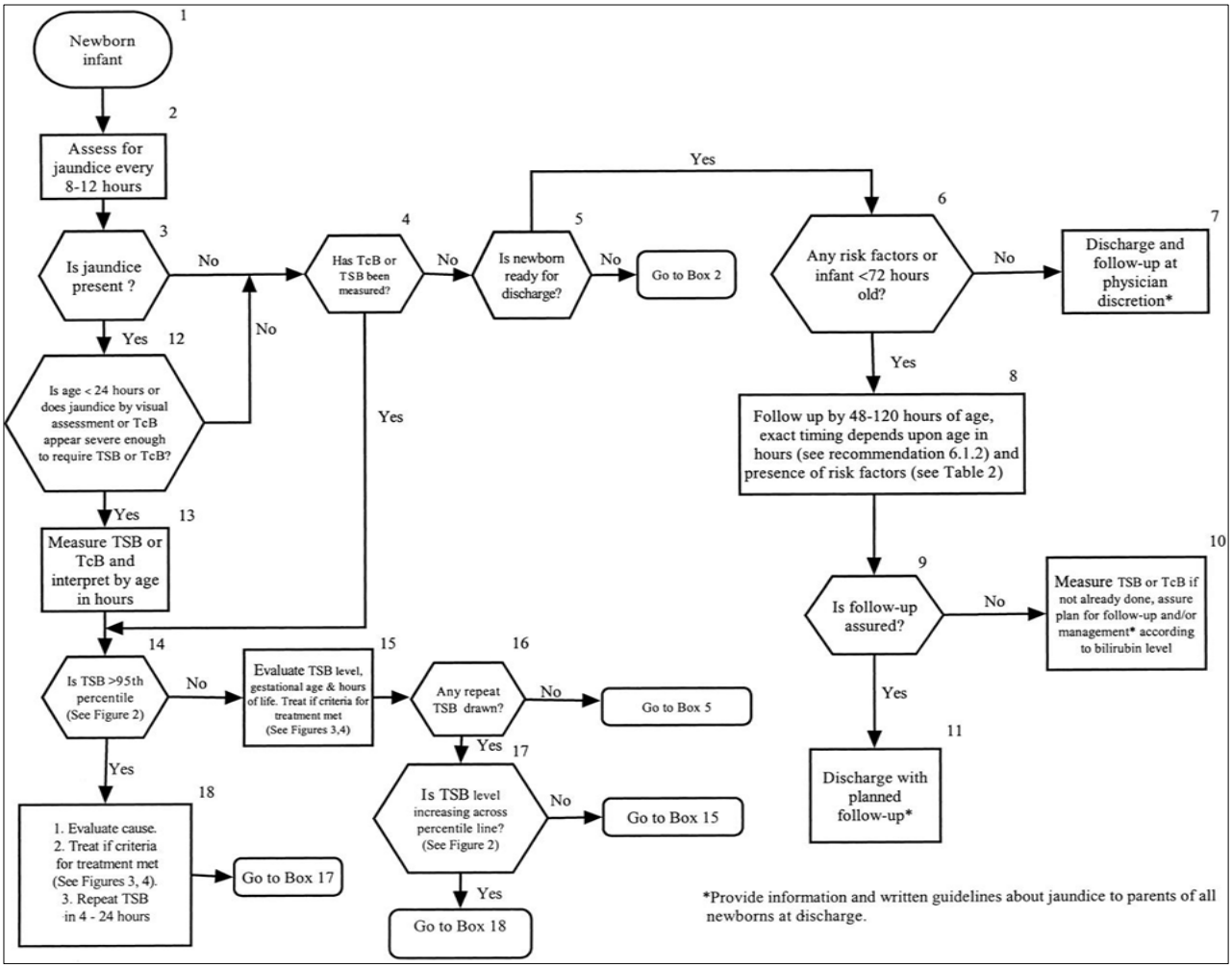

Fig 1: Diagnosis of Neonatal Jaundice [6]

Assessment of Jaundice [7-11]

Physical Assessment

- **Visual assessment**: Jaundice moves from head to toe, with the eyes affected last. Serum bilirubin (approx.)

= 85 micromols/L - When yellow tinge first becomes visible
= 150 micromols/L - Yellow tinge appears on trunk
= 200 micromols/L - Yellow tinge appears on legs
= 250 micromols/L - Eyes (sclera) are affected

- Although visual assessment alone cannot determine the degree of jaundice, a general Assessment of the extent of jaundice can be done under bright light. It is important to:
- Blanch skin to determine underlying colour.
- Press over a bony prominence for best results (nose, forehead).
- Check sclera.

Level of activity: Increasing levels of unconjugated bilirubin in the brain can lead to decreased levels of Consciousness or alertness. Infants may become lethargic and less responsive [39].

- **Level of hydration**: [12-14]
- Monitor intake and output.
- Adequate hydration is necessary to help maintain enough fluid to help with the absorption and excretion of conjugated bilirubin once it passes through the liver.
- **Stools:**
- Monitor frequency, type and colour of stools (meconium versus transitional).
- Unconjugated bilirubin can accumulate in stool and thus has the potential to be Reabsorbed [38].
- Conjugated bilirubin can also become unconjugated in the gut and become reabsorbed into the blood stream.

Laboratory Assessment

- Obtain serum bilirubin levels as per algorithm

- Serum albumin - to help determine how much albumin is available for binding
- CBC and differential – can help determine level of red blood cell destruction, haemolytic anemia, sepsis or polycythemia [42]
- Direct Antiglobulin Test (DAT) - to look for presence of maternal antibodies in infant's serum.
- G6PD (glucose-6-phosphate dehydrogenase) – helps maintain RBC wall integrity; a deficiency indicates enzyme deficiency and a possible metabolic reason for jaundice.

Therapeutic Options: Phototherapy

Phototherapy (PTx) remains the mainstay of treating hyperbilirubinemia in neonates. PTx is highly effective and carries an excellent safety track record of over 50 years. It acts by converting insoluble bilirubin (unconjugated) into soluble isomers that can be excreted in urine and feces. Many review articles have provided detailed discussion on phototherapy related issues. The bilirubin molecule isomerizes to harmless forms under blue-green light (460 to 490 nm); and the light sources having high irradiance in this particular wavelength range are more effective than the others [42].

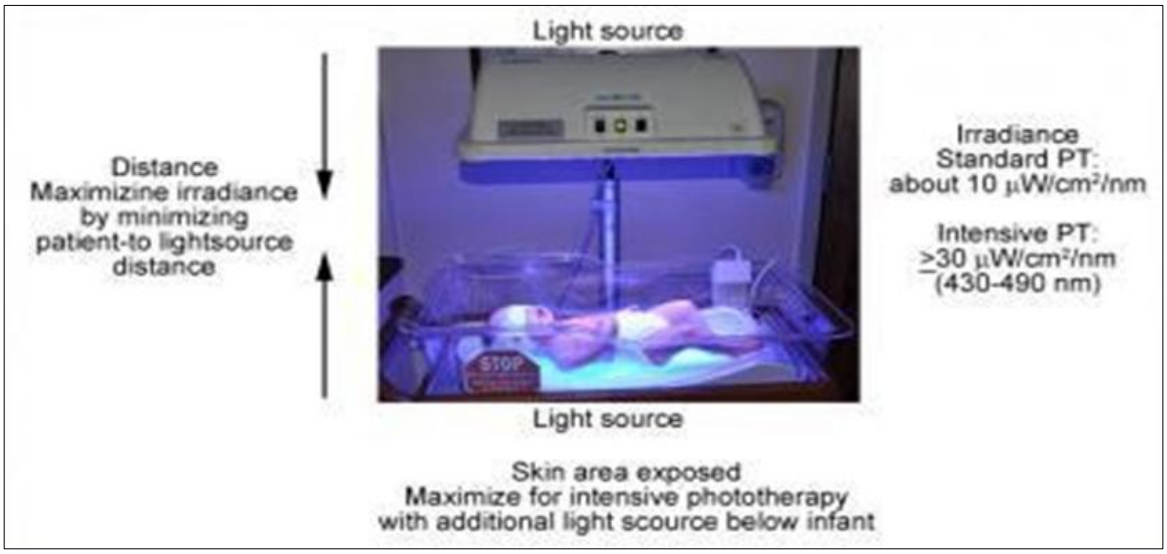

Fig 2: Phototherapy

Types of phototherapy lights [15-16]

The phototherapy units available in the market have a variety of light sources that include florescent lamps of different colors (cool white, blue, green, blue-green or turquoise) and shapes (straight or U-shaped commonly referred as compact florescent lamps ie CFL), halogen bulbs, high intensity light emitting diodes (LED) and fibro-optic light sources. With the easy availability and low cost in India, CFL phototherapy is being most commonly used device. Often, CFL devices have four blue and two white (for examination purpose) CFLs but this combination can be replaced with 6 blue CFLs in order to increase the irradiance output. In last couple of years, blue LED is making inroads in neonatal practice and has been found to at least equally effective. LED has advantage of long life (up to 50,000 hrs) and is capable of delivering higher irradiance than CFL lamps. Fiber-optic units can be used to provide undersurface phototherapy in conjugation with overhead CFL/LED unit to enhance the efficacy of PTx but as a standalone source, fiber-optic unit is lesser effective than CFL/LED unit. It is important that a plastic cover or shield be placed before phototherapy lamps to avoid accidental injury to the baby in case a lamp breaks.

Maximizing the efficacy of phototherapy [17]

The irradiance of PTx lights should be periodically measured, and a minimum level of 30 μW/cm2 /nm in the wavelength range of 460 to 490 nm must be ensured. As the irradiance varies at different points on the footprint of a unit, it should be measured at several points. The lamps should be changed if the lamps are flickering or ends are blackened, if irradiance falls below the specified level or as per the recommendation of manufacturers. Expose maximal surface area of the baby [34, 42]. Avoid blocking the lights by any equipment (say radiant warmer), a large diaper or eye patch, a cap or hat, tape, dressing or electrode etc. ensure good hydration and nutrition of the baby. Make sure that light falls on the baby perpendicularly if the baby is in incubator. Minimize interruption of Ptx during feeding sessions or procedures.

Administering phototherapy [18]

Make sure that ambient room temperature is optimum (250 to 280) to prevent hypothermia or hyperthermia in the baby. Remove all clothes of the baby except the diaper. Cover the baby's eyes with patches, ensuring that the patches do not block the baby's nostrils. Place the naked baby under the lights in a cot or bassinet if weight is more than 2 kg or in an incubator or radiant warmer if the baby is small (›2kg). Keep the distance between baby and light 30 to 45 cm (or as per manufacturer recommendation). Ensure optimum breastfeeding. Baby can be taken out for breastfeeding sessions and the eye patch can be removed for better mother-infant interaction. However, minimize interruption to enhance effectiveness of phototherapy. There is no need to supplement or replace breast milk with any other types of feed or fluid (e.g. breast-milk substitute, water, sugar water, etc.)

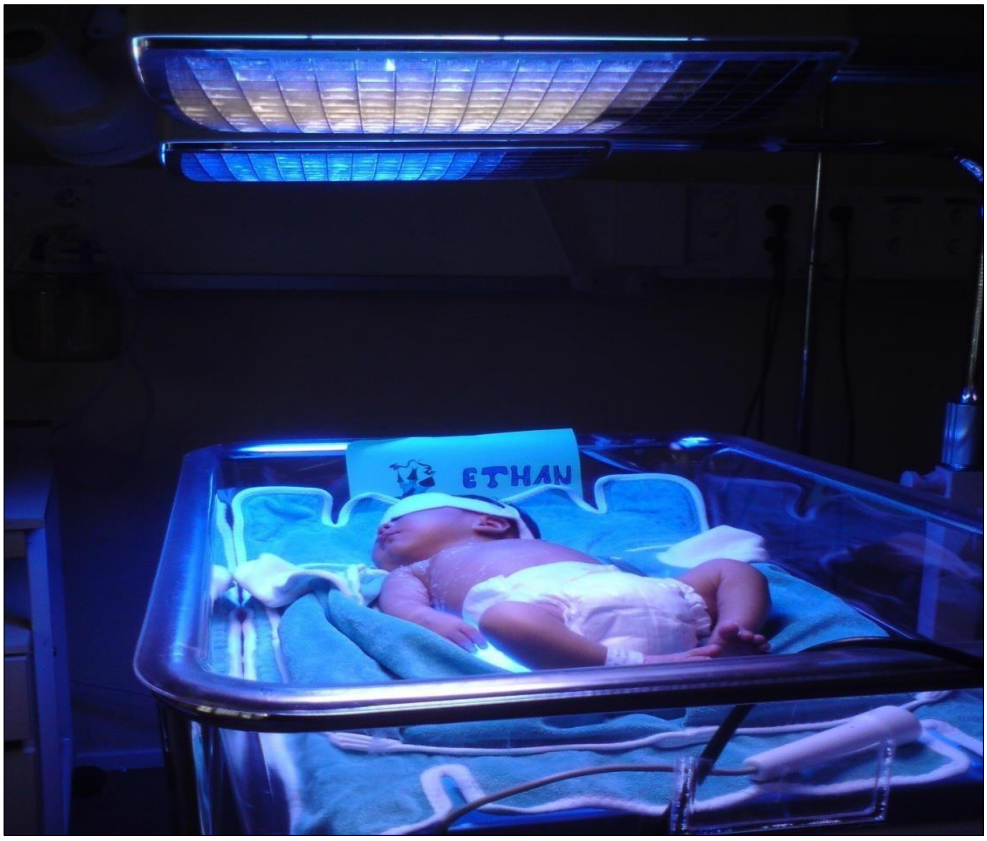

Fig 3: Phototherapy administration

Monitoring & stopping phototherapy [19]

Monitor temperature of the baby every 2 to 4 hr. Measure TSB level every 12 to 24 hours. Discontinue PTx once two TSB values 12 hr apart fall below current age specific cut offs. The infant should be monitored clinically for rebound bilirubin rise within 24 hours after stopping phototherapy for babies with hemolytic disorders.

Role of sunlight

Exposing the baby to sunlight does not help in treatment of jaundice and is associated with risk of sunburn and therefore should be avoided.

Conclusion

Bilirubin concentration is a highly sensitive parameter in detection of cases of neonatal jaundice. Recommendation for the duration of photo therapy can be decided based on the results of visual assessment and total serum bilirubin concentration. The phototherapy is the main treatment method of neonatal jaundice. It is an effective treatment method normally drugs is not ordinarily used.

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