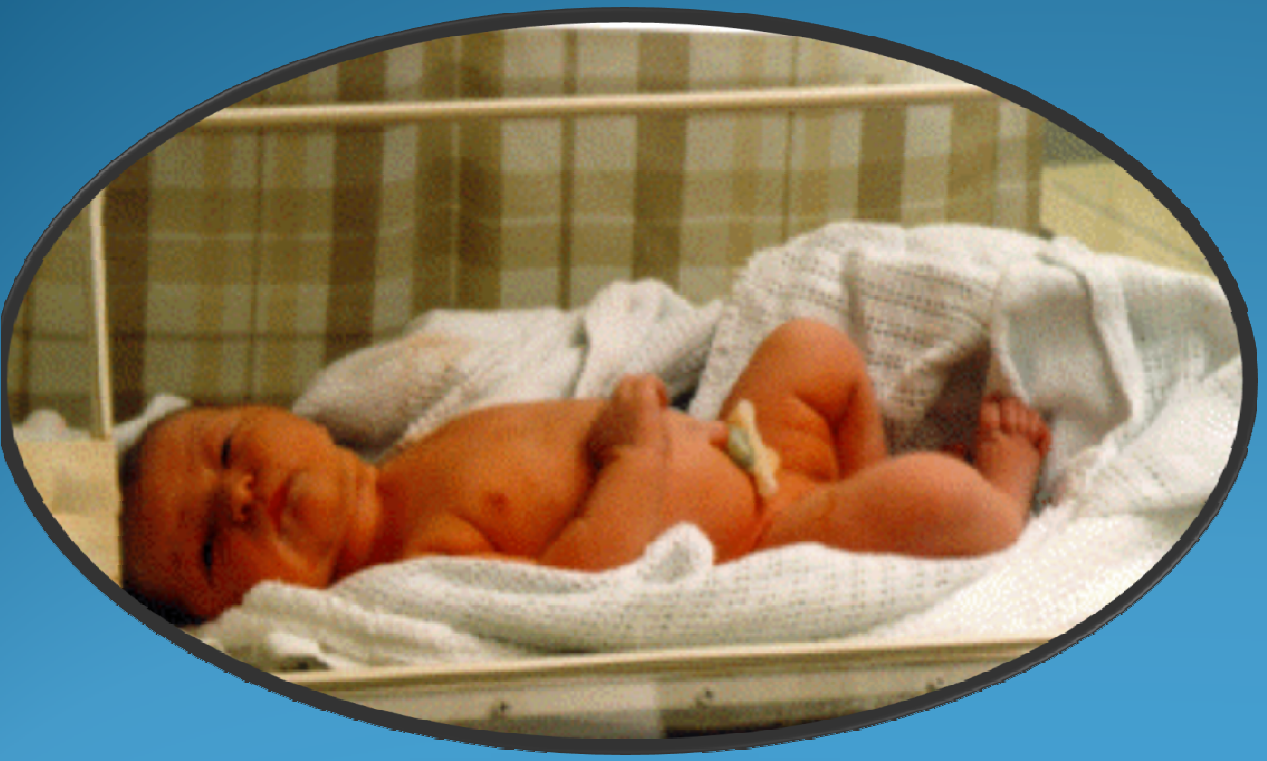
Neonatal jaundice

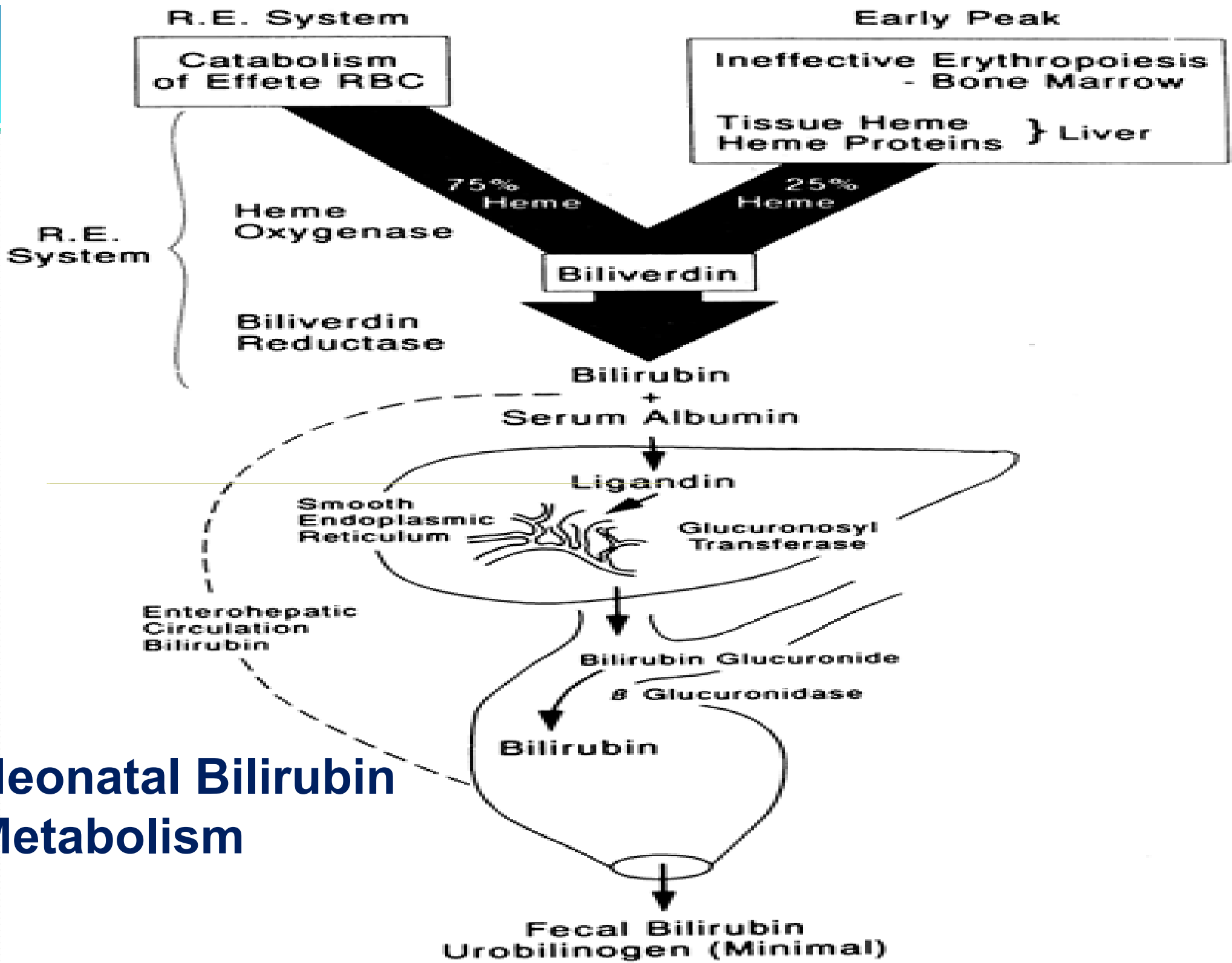


Dr. BINOD KUMAR SINGH

Neonatal Jaundice

- Visible form of bilirubinemia appears in
  - **Adult sclera at total serum bilirubin >2mg / dl**
  - **Newborn skin at total serum bilirubin >7 mg / dl**
- Occurs in **60% of term and 80% of preterm neonates**
- However, **significant jaundice** occurs in 6 % of term babies

Neonatal Bilirubin Metabolism

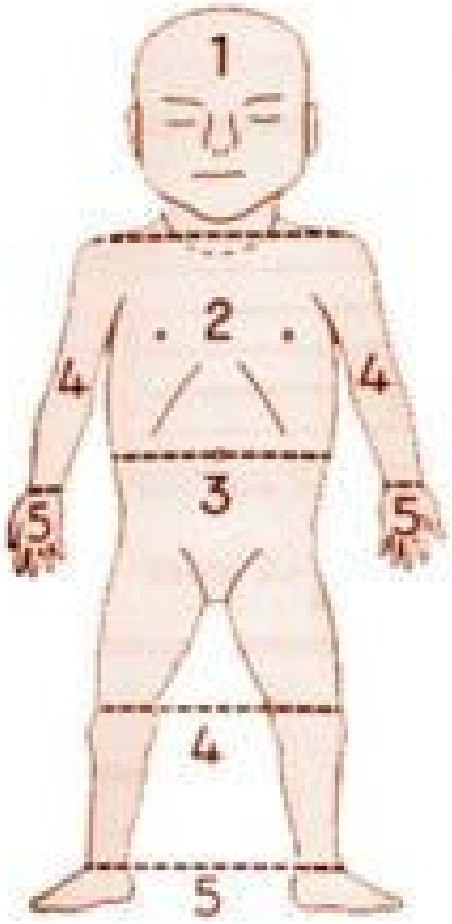


Clinical assessment of jaundice

Area of body	**Bilirubin levels mg/dl**
Face	4-8
Upper trunk	5-12
Lower trunk & thighs	8-16
Arms and lower legs	11-18
Palms & soles	> 15

Kramer's criteria

Schema for grading extent of jaundice



Grade	Extent of Jaundice
0	None
1	Face and neck only
2	Chest and back
3	Abdomen below umbilicus to knees
4	Arms and legs below knees
5	Hands and Feet

FETAL BILIRUBIN METABOLISM

Bilirubin detected in amniotic fluid at 12 weeks of gestation

Unconjugated bilirubin excreted across placenta

UDPGT activity at term ~1% of adult

UDPGT activity reaches adult levels by 6–14 weeks

Physiological jaundice

Characteristics

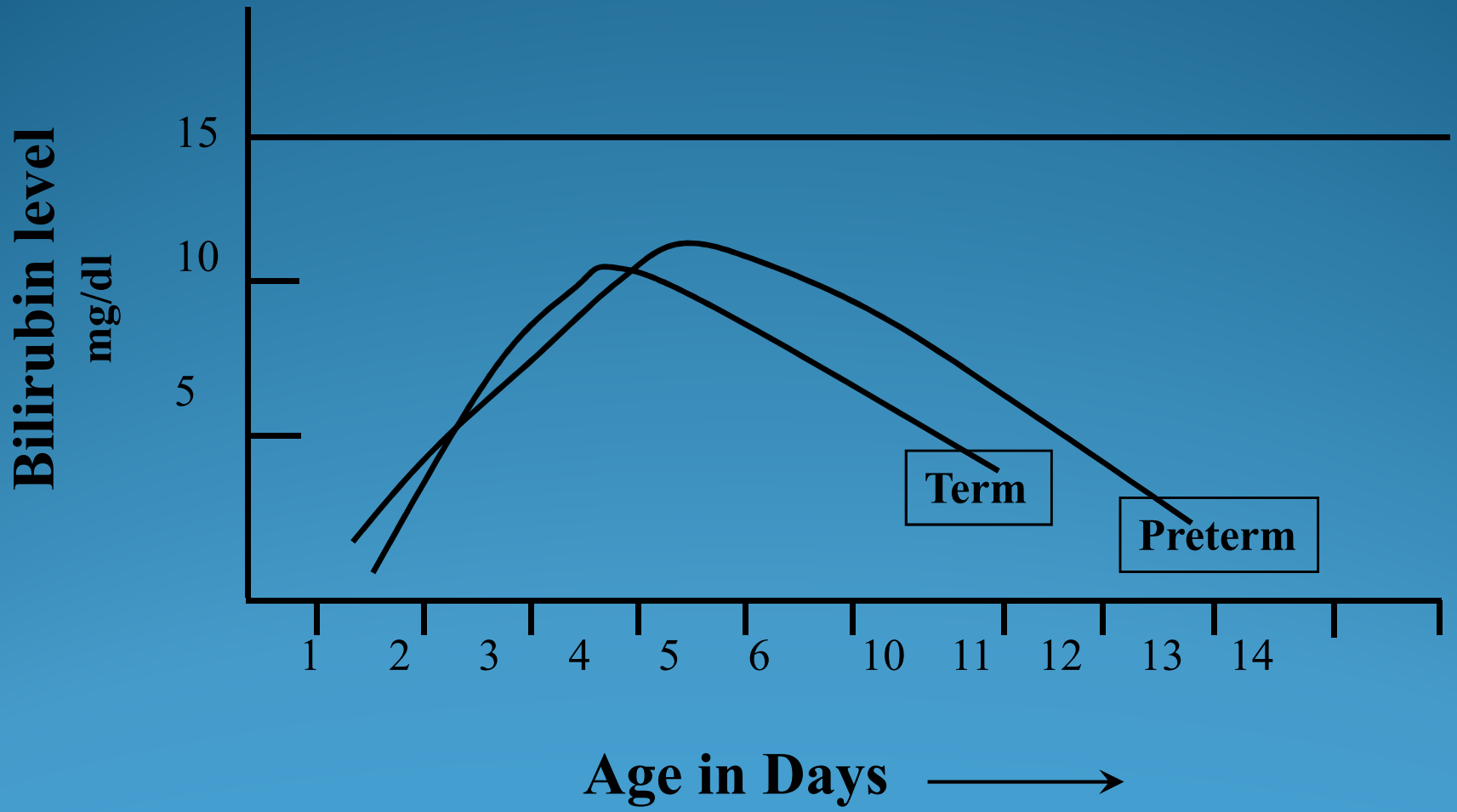
- Appears after 24 hours
- Maximum intensity by 4th-5th day in term & 7th day in preterm
- Serum level less than 15 mg /dl
- Clinically not detectable after 14 days
- Disappears without any treatment

Note: Baby should, however, be watched for worsening jaundice

Why does physiological jaundice develop?

- **PHYSIOLOGIC MECHANISMS OF NEONATAL JAUNDICE**
- **Increased bilirubin load on liver cell**
- Increased erythrocyte volume
- Decreased erythrocyte survival
- Increased early labeled bilirubin
- Increased enterohepatic circulation of bilirubin
- **Decreased hepatic uptake of bilirubin from plasma**
- Decreased ligandin
- **Decreased bilirubin conjugation**
- Decreased uridine diphosphoglucuronosyl transferase activity
- **Defective bilirubin excretion**
- Excretion impaired but not rate limiting

Course of physiological jaundice



Pathological jaundice

- Appears within 24 hours of age
- Increase of bilirubin > 5 mg / dl / day or increasing by more than 0.2 mg/dL per hour
- Serum bilirubin > 15 mg / dl
- Jaundice persisting after 14 days
- Stool clay / white colored and urine staining clothes yellow
- Direct bilirubin> 2 mg / dl

Causes of jaundice

Appearing within 24 hours of age

- Hemolytic disease of NB : Rh, ABO
- Intrauterine Infections: TORCH,syphilis , malaria, bacterial
- Deficiency of red cell enzymes: G6PD,pyruvate kinase
- Hereditary spherocytosis
- Lucey-Driscoll Syndrome
- Crigler_Najjar syndrome

Causes of jaundice

Appearing between 24-72 hours of life

- Physiological jaundice

After 72 hours of age

- Sepsis
- Neonatal hepatitis
- Extra-hepatic biliary atresia
- Breast milk jaundice
- Metabolic disorders

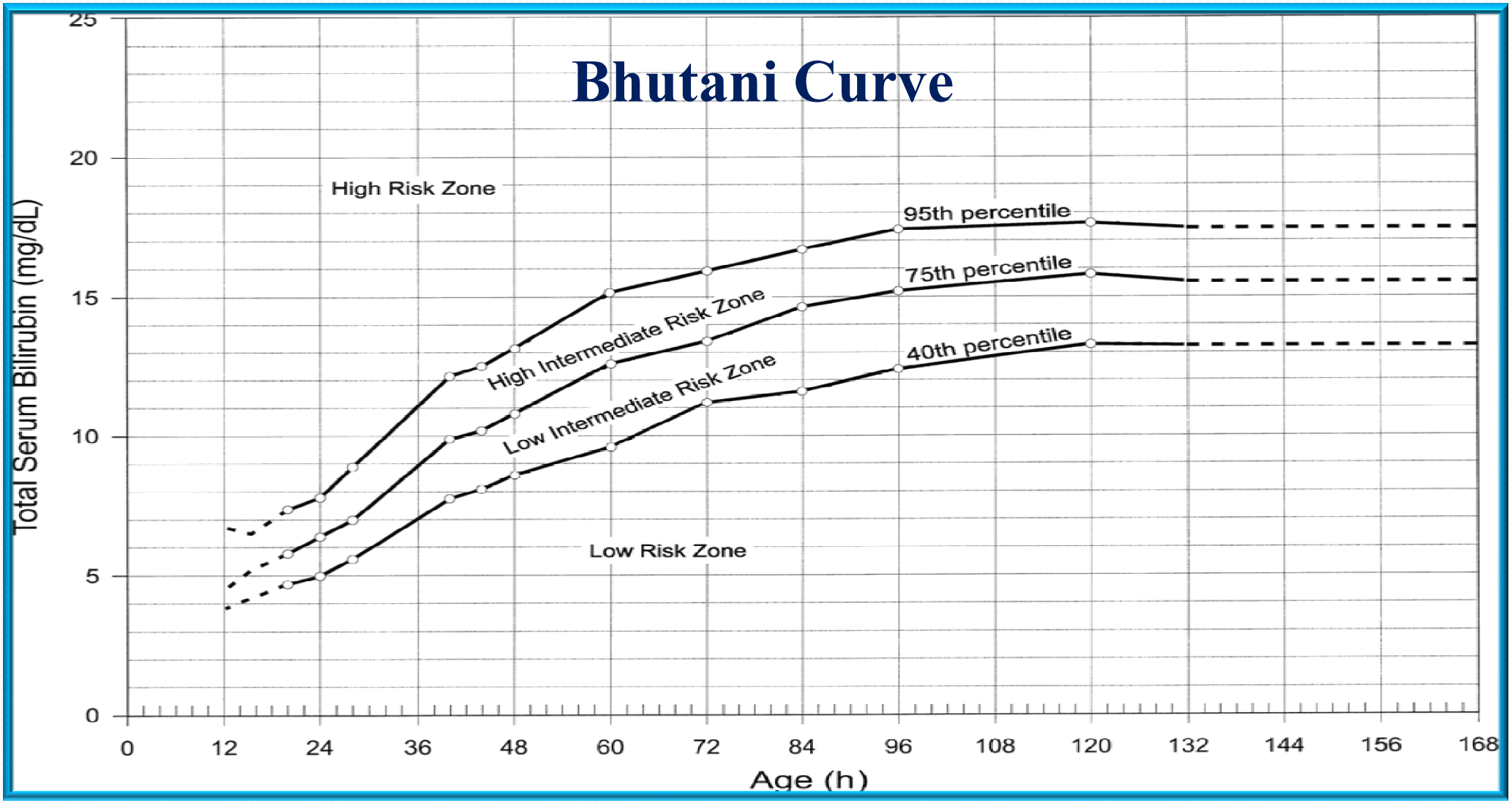
Common causes in India

- Physiological
- Blood group incompatibility
- G_6PD deficiency
- Bruising and cephalhaematoma
- Intrauterine and postnatal infections
- Breast milk jaundice

Risk factors for Severe hyperbilirubinemia

Predischarge TSB or TcB measurement in high-risk or high-intermediate zone
Lower gestational age
Exclusive breastfeeding, especially if it is not going well and infant has excessive weight loss
Jaundice in the first 24 hours of age
Isoimmune or other hemolytic disease
Previous sibling with jaundice
Cephalohematoma or significant bruising
East Asian race

Assessing the Risk of Jaundice by Numbers



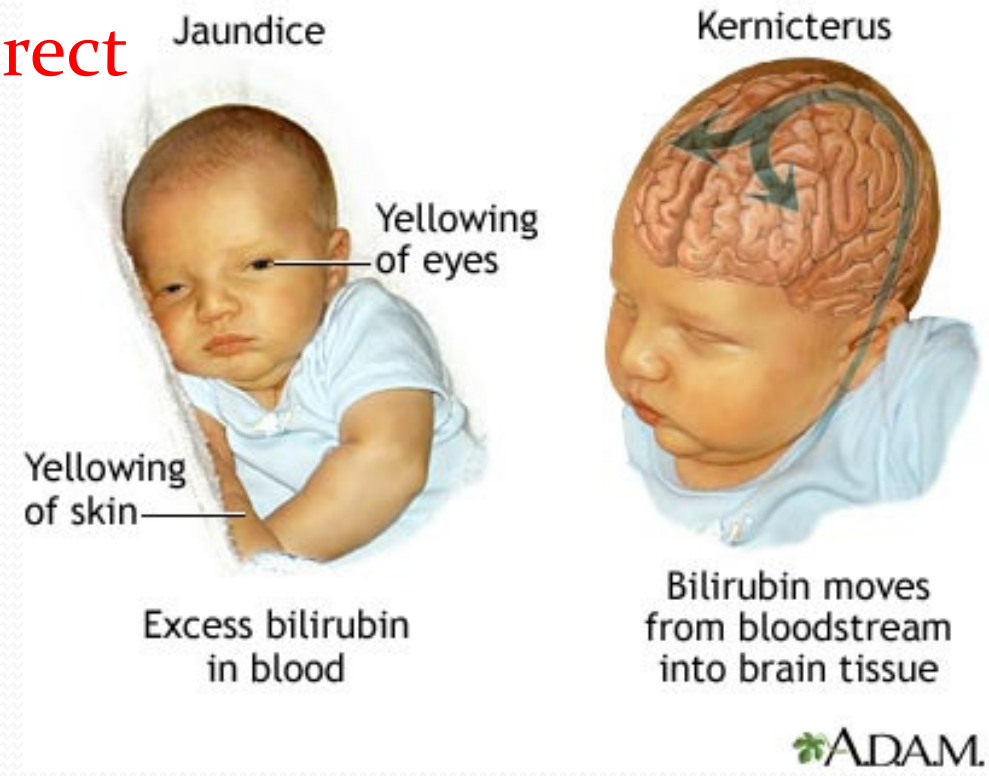
The general symptom of neonatal jaundice

- Yellow skin
- Yellow eyes(sclera)
- Sleepiness
- Poor feeding in infants
- Brown urine
- Fever
- High-pitch cry
- Vomiting

Kernicterus

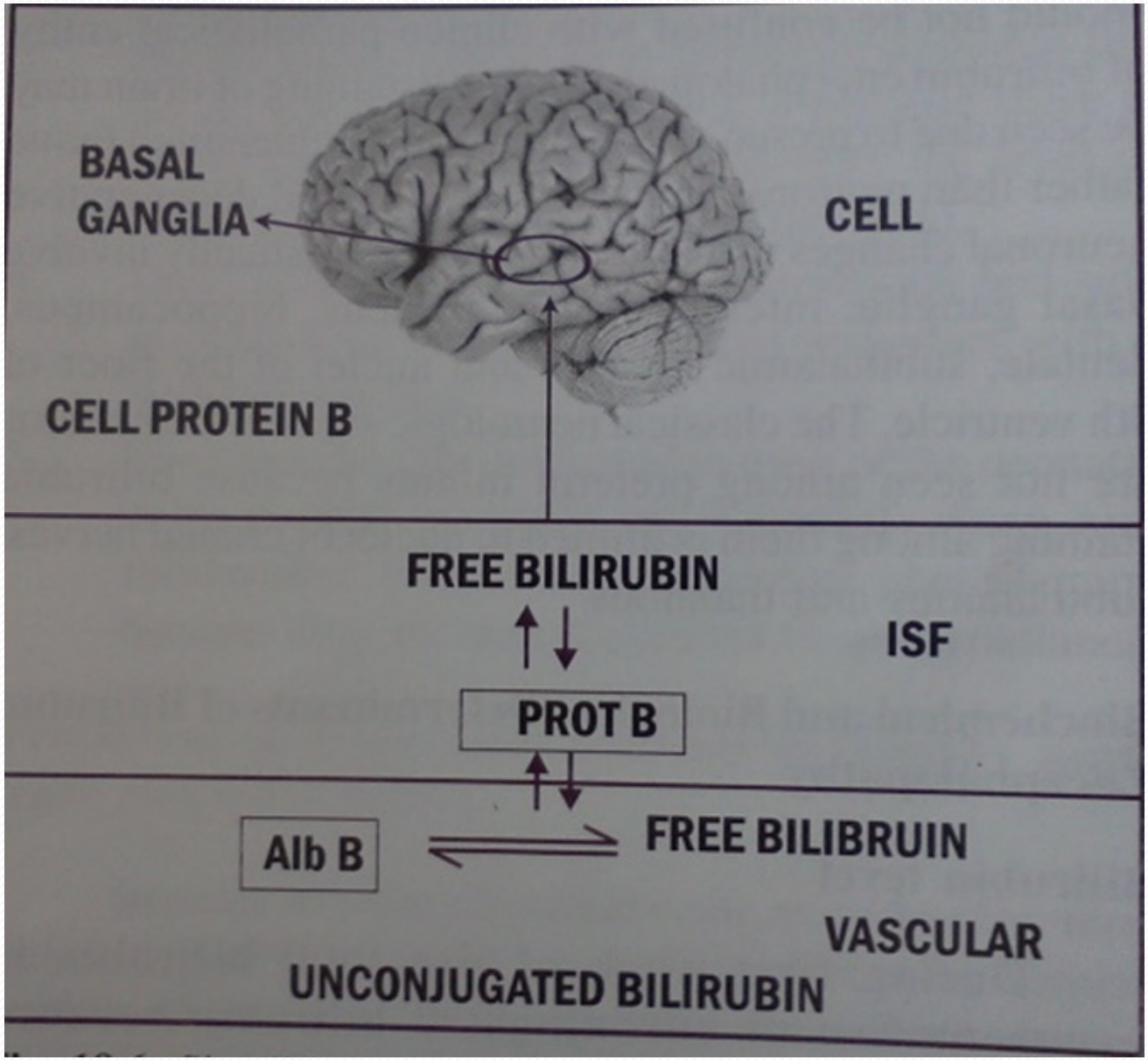
- Kernicterus denotes chronic and permanent sequelae of bilirubin toxicity.

Kernicterus is caused by damage to the brain centers of infants caused by increased levels of unconjugated-indirect bilirubin which is free (not bound to albumin).



- UCB is lipophilic and crosses the Blood-Brain Barrier
  - Only free UCB crosses, albumin-bound does not.
  - BBB of infants is more permeable than adults, and acidosis causes it to be even more permeable.
- UCB has an affinity for the basal ganglia, hippocampus, cranial nerve nuclei
- UCB interrupts metabolism in glial cells and causes apoptosis of neurons
  - Age of the cell is inversely proportional to susceptibility

Pathophysiology of Kernicterus



MAJOR CLINICAL FEATURES OF ACUTE BILIRUBIN ENCEPHALOPATHY

Initial phase

Hypotonia, lethargy, high-pitched cry, and poor suck.

Intermediate phase

Hypertonia of extensor muscles (with opisthotonus, rigidity, oculogyric crisis, and retrocollis), irritability, fever, and seizures.

Many infants die in this phase. All infants who survive this phase develop ***chronic bilirubin encephalopathy (clinical diagnosis of kernicterus).***

Advanced phase

Pronounced opisthotonus (although hypotonia replaces hypertonia after approximately 1 week of age), shrill cry, apnea, seizures, coma, and death.

Chronic bilirubin encephalopathy (kernicterus)

- Athetosis
- Complete or partial sensorineural deafness (auditory neuropathy)
- limitation of up-ward gaze
- Dental dysplasia
- Intellectual deficits.

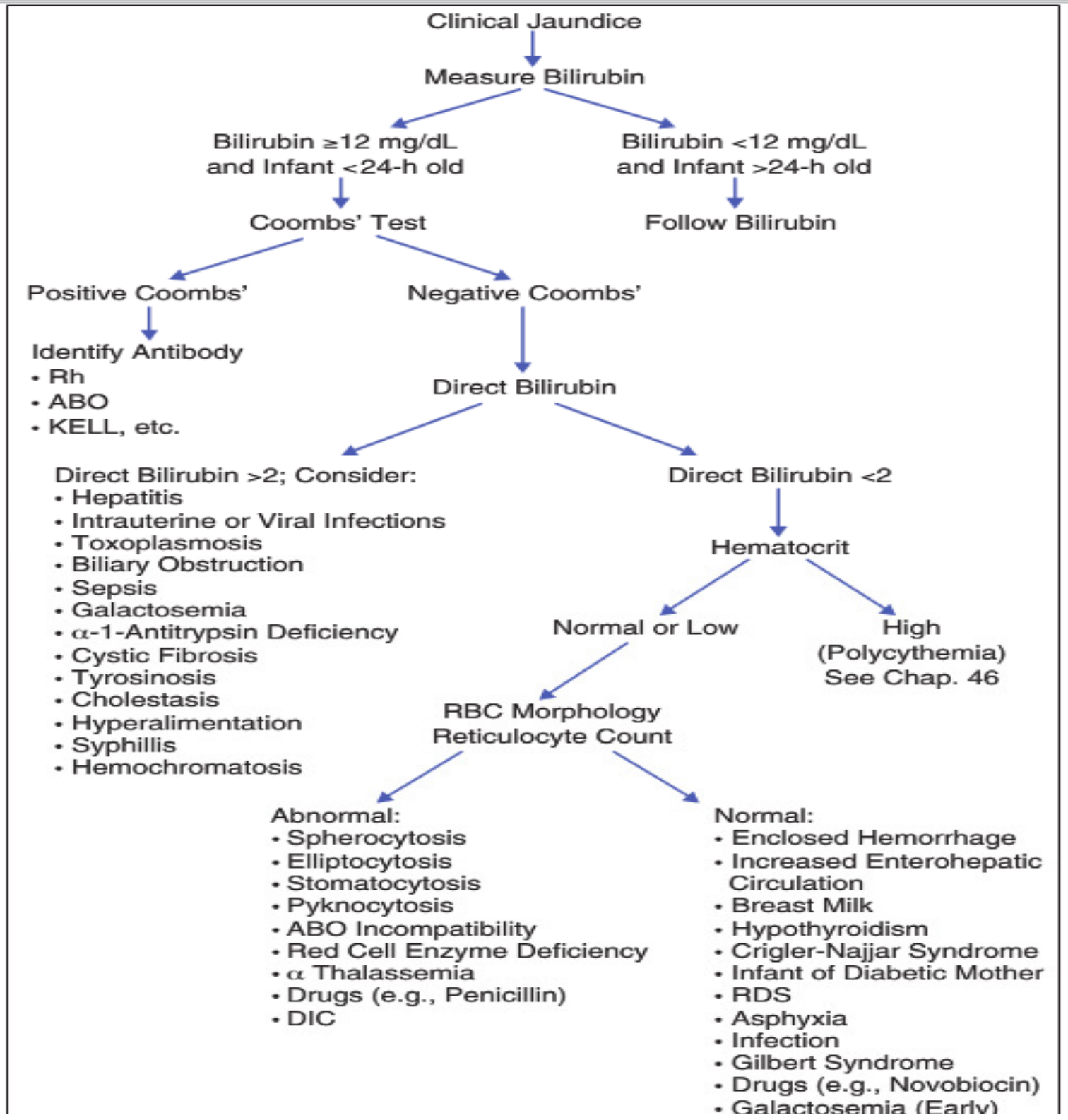
Approach to jaundiced baby

- Ascertain birth weight, gestation and postnatal age
- Assess clinical condition (well or ill)
- Decide whether jaundice is physiological or pathological
- Look for evidence of kernicterus* in deeply jaundiced NB

**Lethargy and poor feeding, poor or absent Moro's, opisthotonus or convulsions*

Workup

- Maternal & perinatal history
- Physical examination
- Laboratory tests (must in all)*
  - Total & direct bilirubin*
  - Blood group and Rh for mother and baby*
  - Hematocrit, retic count and peripheral smear*
  - Sepsis screen
  - Liver and thyroid function
  - TORCH titers, liver scan when conjugated hyperbilirubinemia


Clinical Jaundice
Measure Bilirubin
Bilirubin ≥12 mg/dL and Infant <24-h old
Bilirubin <12 mg/dL and Infant >24-h old
Coombs' Test
Follow Bilirubin
Positive Coombs'
Negative Coombs'
Identify Antibody
• Rh
• ABO
• KELL, etc.
Direct Bilirubin
Direct Bilirubin >2; Consider:
• Hepatitis
• Intrauterine or Viral Infections
• Toxoplasmosis
• Biliary Obstruction
• Sepsis
• Galactosemia
• α-1-Antitrypsin Deficiency
• Cystic Fibrosis
• Tyrosinosis
• Cholestasis
• Hyperalimentation
• Syphillis
• Hemochromatosis
Direct Bilirubin <2
Hematocrit
Normal or Low
High (Polycythemia) See Chap. 46
RBC Morphology
Reticulocyte Count
Abnormal:
• Spherocytosis
• Elliptocytosis
• Stomatocytosis
• Pyknocytosis
• ABO Incompatibility
• Red Cell Enzyme Deficiency
• α Thalassemia
• Drugs (e.g., Penicillin)
• DIC
Normal:
• Enclosed Hemorrhage
• Increased Enterohepatic Circulation
• Breast Milk
• Hypothyroidism
• Crigler-Najjar Syndrome
• Infant of Diabetic Mother
• RDS
• Asphyxia
• Infection
• Gilbert Syndrome
• Drugs (e.g., Novobiocin)
• Galactosemia (Early)

Management

- Rationale: reduce level of serum bilirubin and prevent bilirubin toxicity
- Prevention of hyperbilirubinemia: early feeds, adequate hydration
- Reduction of bilirubin levels: phototherapy, exchange transfusion, drugs

Treatment Modalities to Reduce Serum Bilirubin Concentration

Hydration
Phototherapy
Exchange transfusion
Drugs to increase conjugation
Inhibition of reabsorption (binding in the gut)
Inhibition of bilirubin production

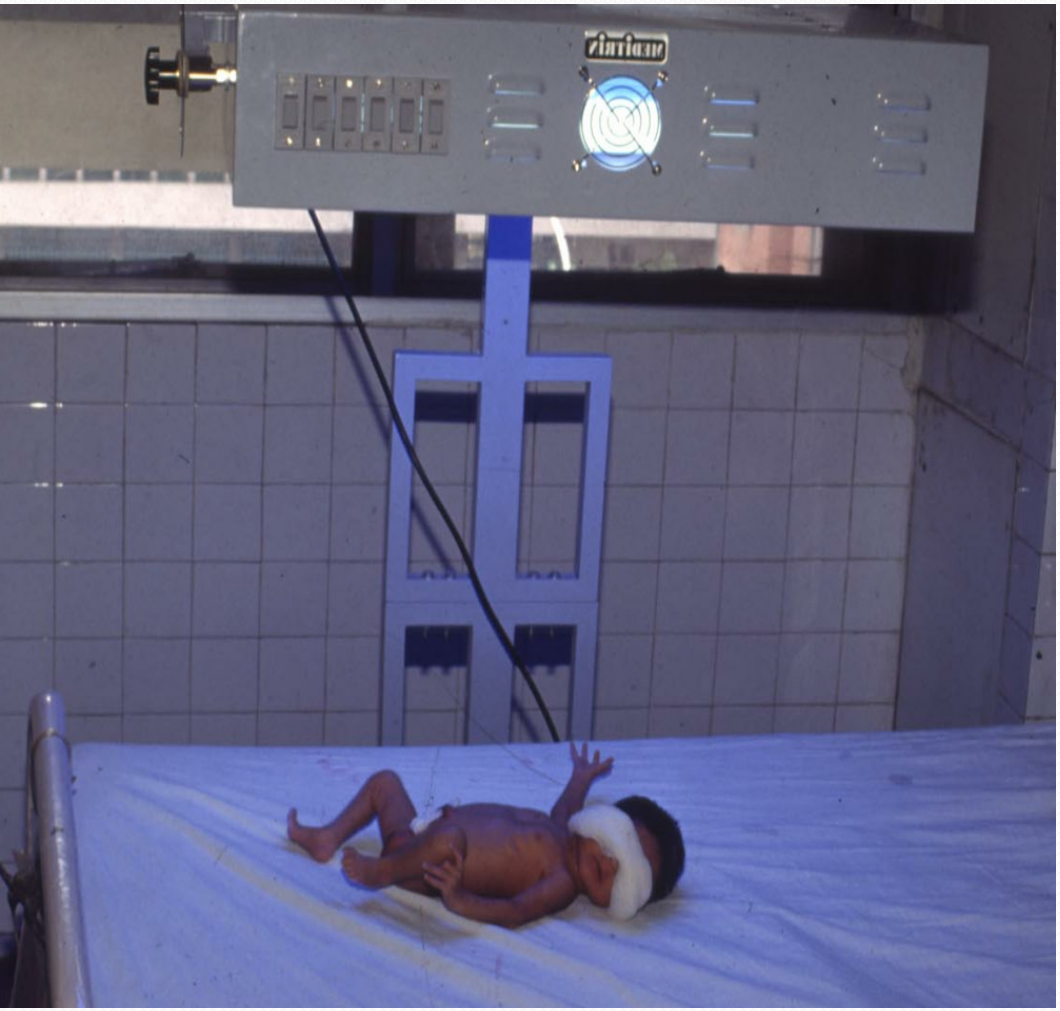
Prevention

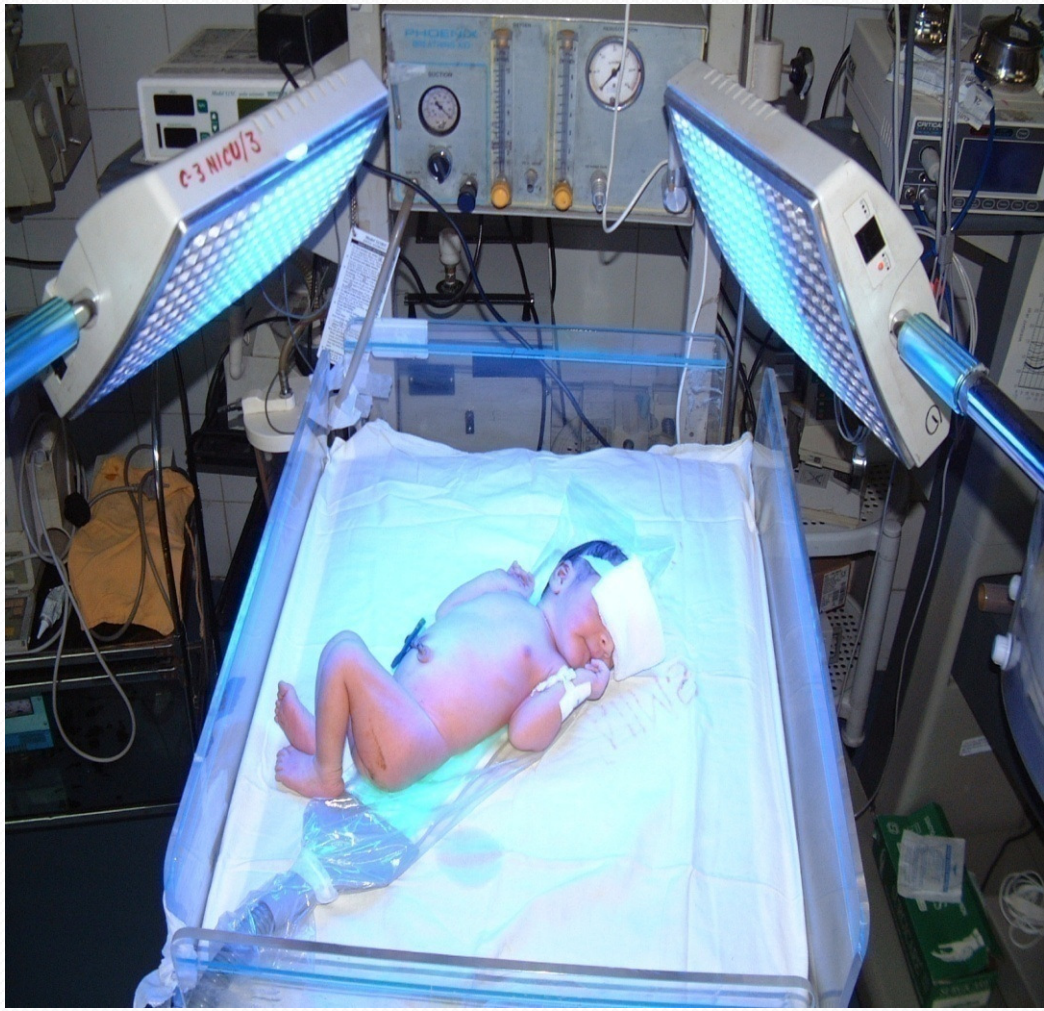
- Breastfeeding
  - Should be encouraged for most women
  - 8-12 times/day for 1st several days
  - Assistance and education
  - Avoid supplements in non-dehydrated infants

Prevention

- Ongoing assessments for risk of developing severe hyperbilirubinemia
  - Monitor at least every 8-12 hours
  - Don't rely on clinical exam
  - Blood testing
    - Prenatal (Mom): ABO & Rh type, antibody
    - Infant cord blood
      - Mom not tested, Rh (-): Coomb's, ABO, Rh
      - Mom O or Rh (+): optional to test cord blood

Babies under phototherapy





Why Phototherapy is effective?

- ***Three reactions*** can occur when bilirubin is exposed to light :

  1- photooxidation

  2- Configurational isomerization

  3- Structural isomerization

Principle of phototherapy

The initial and most rapid reactions occurring as a result of phototherapy produce ***configurational isomers .***The most prominent of these configurational isomers is called 4Z,15E bilirubin (native bilirubin being 4Z,15Z bilirubin).

The second most rapid photochemical reaction leads to the formation of **structural isomers**, the most prominent known as ***lumirubin .***But because lumirubin is cleared from the serum much more rapidly than the 4Z,15E isomer, it is likely that lumirubin formation is **mainly responsible** for the phototherapy induced decline in serum bilirubin in the human infant.

The slow process of **photo-oxidation** converts bilirubin to small polar products that are excreted in the urine. It is the least important reaction for lowering bilirubin levels.

Factors That Affect the Dose and Efficacy of Phototherapy

- Wavelength
- Irradiation level
- Distance
- Bilirubin concentration
- Nature and character of the light source

Wavelength

Bilirubin absorbs light primarily around 400 to 500 nm

- The most effective lights for phototherapy are those with high energy output near the maximum absorption peak of bilirubin (**450–460 nm**).
- Special blue lamps with a peak output at **425 to 475 nm** are the most efficient for phototherapy.
- Cool white lamps has a principal peak at **550 to 600** nm

Irradiation level

- ***Conventional phototherapy should deliver spectral irradiance at the infant's level of 8 to 10 µW/cm2/nm***

Intensive phototherapy delivers atleast

30-40 µW/cm2/nm.

Distance

- Distance should be kept at distance of

  45 cm

  and *can be reduced to 15-20* to provide more effective or intensive phototherapy.

- Energy delivered decreases with increasing distance .

Nature and character of the light source

- Quartz halide spotlights
- Green light
- Blue fluorescent tubes
  - ***Narrow-spectrum***
  - ***Ordinary***
- White (daylight) fluorescent tubes
- White quartz lamps
- Fiberoptic light

Lamps Beneficial for Phototherapy

- **Narrow spectrum blue fluorescent tube.**
- White fluorescent tubes
- White quartz lamp.
- Quartz lamps with single or double banks of 3-4 bulbs attached.
- Fibreoptic light.

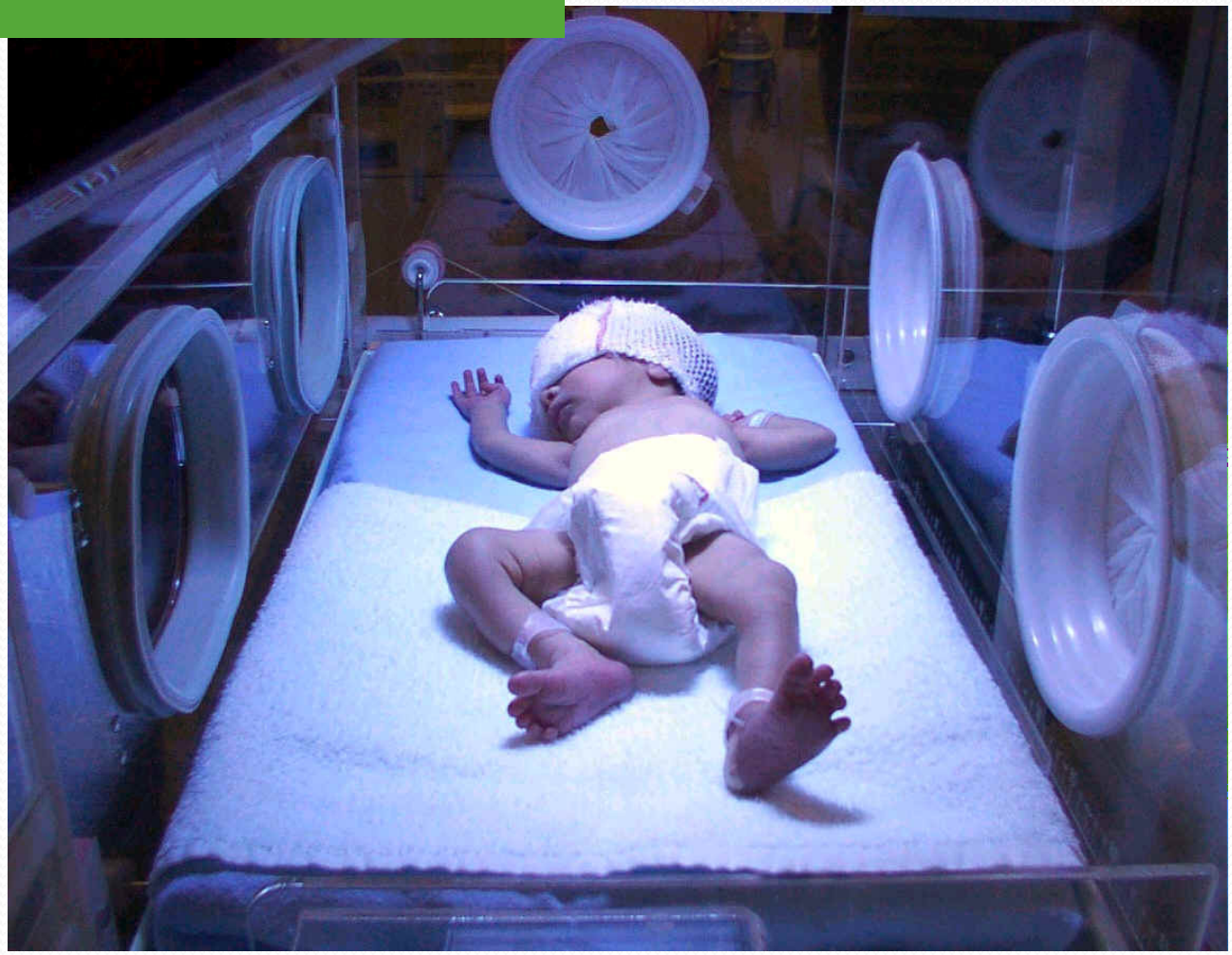
Phototherapy

Technique

- Perform hand wash
- Place baby naked in cradle or WARMER
- Fix eye shades
- Keep baby at least 45 cm from lights, if using closer monitor temperature of baby
- Start phototherapy

Nursing Responsibilities:

-cover eyes and sex organ



Phototherapy

- Frequent extra breast feeding every 2 hourly
- Turn baby after each feed
- Temperature record 2 to 4 hourly
- Weight record- daily(small infants weighe twice daily)
- Monitor urine frequency
- Monitor bilirubin level every 12-24 hours

Maisel's chart

<table>
<tr><th rowspan="2">Sr Bilirubin (mg/dl)</th><th rowspan="2">Birth weight</th><th colspan="4">Age in hrs</th></tr>
<tr><th>< 24</th><th>24 – 48</th><th>49 – 72</th><th>>72</th></tr>
<tr><td><5</td><td>All</td><td></td><td></td><td></td><td></td></tr>
<tr><td>5-9</td><td>All</td><td>Phototherapy if hemolysis</td><td></td><td></td><td></td></tr>
<tr><td rowspan="2">10-14</td><td>< 2500g</td><td rowspan="2">Phototherapy if hemolysis</td><td colspan="3">PHOTOTHERAPY</td></tr>
<tr><td>> 2500g</td><td></td><td colspan="2">Investigate if bilirubin > 12mg%</td></tr>
<tr><td rowspan="2">15-19</td><td>< 2500g</td><td colspan="2" rowspan="2">EXCHANGE</td><td colspan="2">Consider Exchange</td></tr>
<tr><td>> 2500g</td><td colspan="2">Phototherapy</td></tr>
<tr><td>≥ 20</td><td>All</td><td colspan="4">EXCHANGE</td></tr>
</table>

TABLE 35-29 GUIDELINES FOR THE USE OF PHOTOTHERAPY AND EXCHANGE TRANSFUSION IN LOW-BIRTH-WEIGHT INFANTS BASED ON BIRTH WEIGHT

	Total bilirubin level (mg/dL [μmol/L][a])	
Birth Weights (g)	Phototherapy[b]	Exchange Transfusion[c]
≤1,500	7-9	12-15
1,500-1,999	10-12	15-18
2,000-2,499	13-15	18-20

TABLE 35-30 GUIDELINES FOR USE OF PHOTOTHERAPY AND EXCHANGE TRANSFUSION IN PRETERM INFANTS BASED ON GESTATIONAL AGE

Total bilirubin level (mg/dL [μmol/L])

		Exchange Transfusion	
Gestational Age (Weeks)	Phototherapy	Sick[a]	Well
36	14.6 (250)	17.5 (300)	20.5 (350)
32	8.8 (150)	14.6 (250)	17.5 (300)
28	5.8 (100)	11.7 (200)	14.6 (250)
24	4.7 (80)	8.8 (150)	11.7 (200)

[a]

When discontinuation of phototherapy?

- When serum bilirubin levels falls below the level that triggered the initiation of phototherapy.

- Phototherapy is usually dis-continued at mean bilirubin levels of **13 ± 0.7 mg/dL** in term and **10.7± 1.2** mg/dL in preterm infants.

- Serum bilirubin levels often ***rebound*** , and follow-up tests should be obtained within ***6-12 hours*** after discontinuation.

Side effects of phototherapy

- Increased insensible water loss
- Redistribution of blood flow
- Watery diarrhea and increased fecal water loss
- Low calcium levels
- Retinal damage
- Tanning of the skin of black infants
- “Bronze baby” syndrome
- Mutations, sister chromatid exchange, and DNA strand breaks have been described in cell culture.
- Tryptophan is reduced in amino acid solutions exposed to phototherapy.
- Upsets maternal baby interaction

EXCHANGE TRANSFUSION

With this technique, the equivalent of two neonatal blood volumes **(160 mL/kg of body weight)** is replaced in aliquots not to exceed 10% of the total blood volume.

This results in the replacement of approximately 85% of the circulating RBCs.

In the **push–pull method**, blood is removed in aliquots that are tolerated by the infant. This usually **is**

5 mL for infants <1,500 g
10 mL for infants 1,500 to 2,500 g
15 mL for infants 2,500 to 3,500 g
20 mL for infants >3,500 g.

Serum bilirubin concentrations are usually reduced by 50%.
The procedure usually takes 1 to 2 hours.

Indications for exchange transfusion

1.When phototherapy fails to prevent a rise in bilirubin to toxic levels

2.To correct anemia and improve heart failure in hydropic infants with hemolytic disease.

3. To stop hemolysis and bilirubin production by removing antibody and sensitized RBCs.

4. In hemolytic disease, immediate exchange transfusion is usually indicated if:

a. The cord bilirubin level is >4.5 mg/dL and the cord hemoglobin level is under 11 g/dL

b. The bilirubin level is rising > 1 mg/dL/hour despite phototherapy.

c. The hemoglobin level is between 11 and 13 g/dL, and the bilirubin level is rising > 0.5 mg/dL/hour despite phototherapy.

d. The bilirubin level is 20 mg/dL, or it appears that it will reach 20 mg/dL at the rate it is rising.

e. There is progression of anemia in the face of adequate control of bilirubin by other methods (e.g., phototherapy).

5. Repeat exchanges are done for the same indications as the initial exchange. All infants should be under intensive phototherapy while decisions regarding exchange transfusion are being made.

Choice of blood for exchange blood transfusion

- **ABO incompatibility**
  - Use **O blood of same Rh type**, ideal O cells suspended in AB plasma
- **Rh isoimmunization**
  - Emergency **o -ve** blood , Ideal o -ve suspended in AB plasma or baby's blood group but Rh –ve
- **Other situations**
  - Baby's blood group

TABLE 35-39 POTENTIAL COMPLICATIONS OF EXCHANGE TRANSFUSION	
Cardiovascular	Arrhythmias
	Cardiac arrest
	Volume overload
	Embolization with air or clots
	Thrombosis
	Vasospasm
Hematologic	Sickling (donor blood)
	Thrombocytopenia
	Bleeding (overheparinization of donor blood)
	Graft-versus-host disease
	Mechanical of thermal injury to donor cells
Gastrointestinal	Necrotizing enterocolitis
	Bowel perforation
Biochemical	Hyperkalemia
	Hypernatremia
	Hypocalcemia
	Hypomagnesemia
	Acidosis
	Hypoglycemia
Infectious	Bacteremia
	Virus infection (hepatitis, cytomegalovirus)
	Malaria
Miscellaneous	Hypothermia
	Perforation of umbilical vein
	Drug loss
	Apnea

Pharmacologic Treatment

Phenobarbital

Phenobarbital is a potent inducer of microsomal enzymes that increases bilirubin conjugation and excretion and increases bile flow. When given in sufficient doses
to the mother, the infant, or both, phenobarbital is effective in lowering serum bilirubin levels in the first week of life. However, concerns about longterm toxicity when given to pregnant women militate against its use for this purpose

Tin Mesoporphyrin

Decreasing Bilirubin Production by Inhibiting Heme Oxygenase drug is still awaiting FDA approval

Inhibiting the Enterohepatic Circulation of Bilirubin

charcoal,agar, orlistat and cholestyramine,have been administered in the infants but they have failed to produce clinically significant reductions in TSB

Decreasing Bilirubin Production by Inhibiting Hemolysis

Intravenous Immunoglobulin

Controlled trials have confirmed that the administration of IVIg to infants with Rh hemolytic disease will significantly reduce the need for exchange transfusion

Prolonged indirect jaundice

Causes

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

Conjugated hyperbilirubinemia

Suspect

- High colored urine
- White or clay colored stool

Caution

☞Always refer to hospital for investigations so that biliary atresia or metabolic disorders can be diagnosed and managed early

Conjugated hyperbilirubinemia

Causes

- **Liver cell injury (normal bile ducts)**

1. a. Toxic. Prolonged use of PN
2. b. Infection. Viral: hepatitis (B, C), giant cell neonatal hepatitis, rubella, CMV, herpes, Epstein-Barr virus, etc. Bacterial: syphilis, Escherichia coli, group B hemolytic strepto-coccus, listeria, tuberculosis, staphylococcus. Parasitic: toxoplasma.
3. c. Metabolic. α1-antitrypsin deficiency, cystic fibrosis, galactosemia, tyrosin-emia, hypermethionemia, fructosemia, storage diseases (Gaucher, Niemann-Pick, glycogenosis type IV, Wolmans), Rotor syndrome

- Excessive bilirubin load (inspissated bile syndrome)

- Bile flow obstruction (biliary atresia, extrahepatic or intrahepatic).

Physiologic Role of Bilirubin

Bilirubin is a powerful ***antioxidant in vitro*** and there is a positive relationship between serum bilirubin levels and antioxidant activity in term and preterm infants

Bilirubin may have a physiologic role as an antioxidant in the human neonate

In sick neonates who have circulatory failure, asphyxia or sepsis, the rate of rise of TSB is less than in control infants suggesting that **bilirubin is consumed to cope with oxidative stress**

Thank You