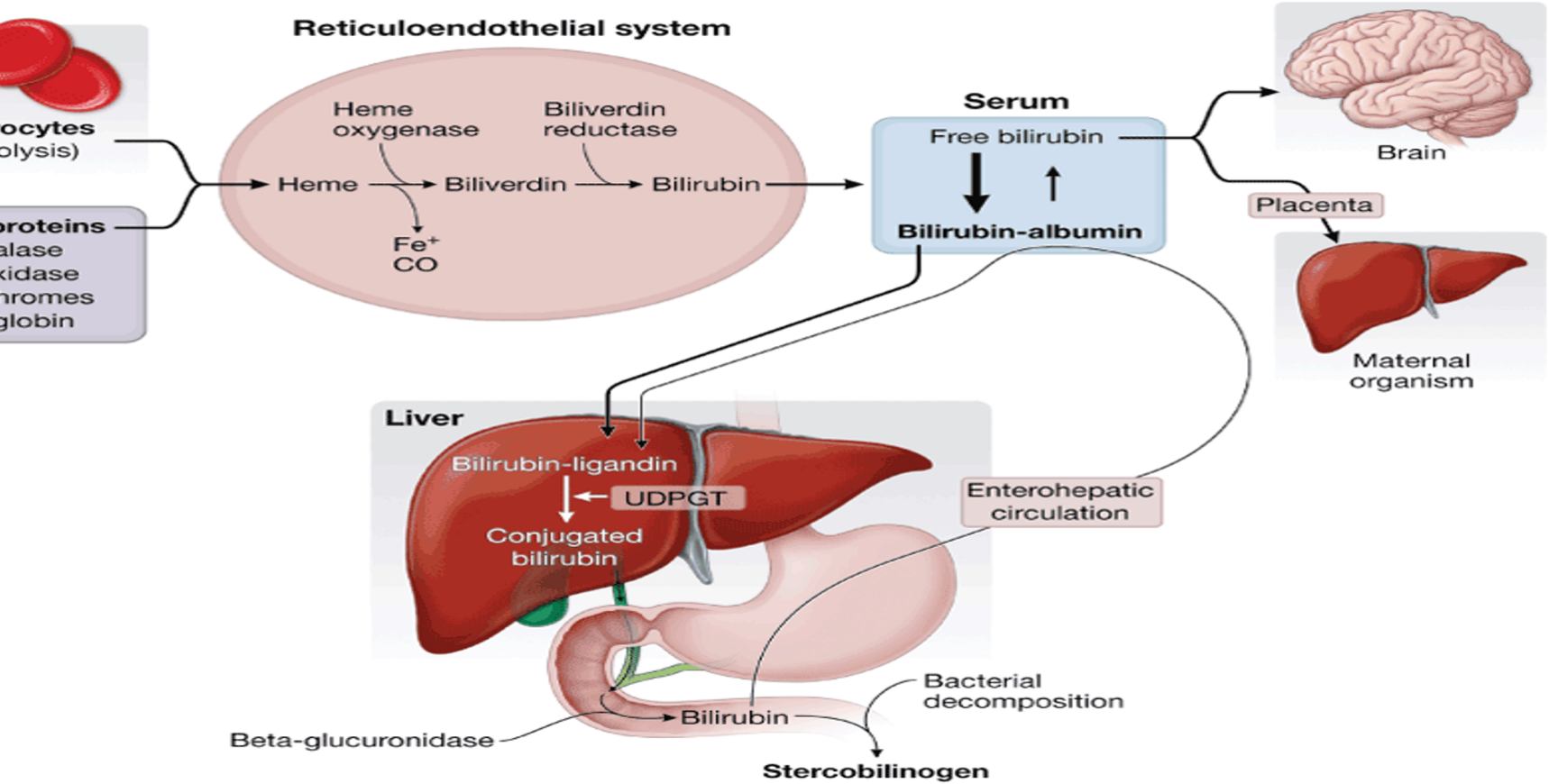
Hyperbilirubinemia

.....Yellow, it’s me



venson DK, Maisels MJ, Watchko JF: *Care of the Jaundiced Neonate*:
pediatrics.com

Physiologic Jaundice

- Non-pathologic, unconjugated hyperbilirubinemia
- 50-60% of well newborns
- Peaks at 3-5 days; later in Asian, pre-term (5-7 d)
- **Breast milk jaundice is mild, prolonged jaundice due to Pregnenalone inhibition of glucuronyl transferase. Can last 3-12 weeks. Not harmful.**
- **Breast feeding jaundice is due dehydration/inadequate intake, increased enterohepatic circulation**

Pathologic (Non-physiologic) jaundice

- 1st 24 hours
- Rate of rise > 0.2 mg/dL/hr
- Total > 15 mg/dL; direct fraction > 2.0 mg/dL
- Clinical jaundice beyond 7 days

NOTE: Jaundice lasting beyond 2 weeks (formula-fed) or 3 weeks (BF) should have a total/direct Bili check.

Bath tub analogy

Imagine level of jaundice as a tub filled with yellow water

Goal is to avoid it spilling over the top

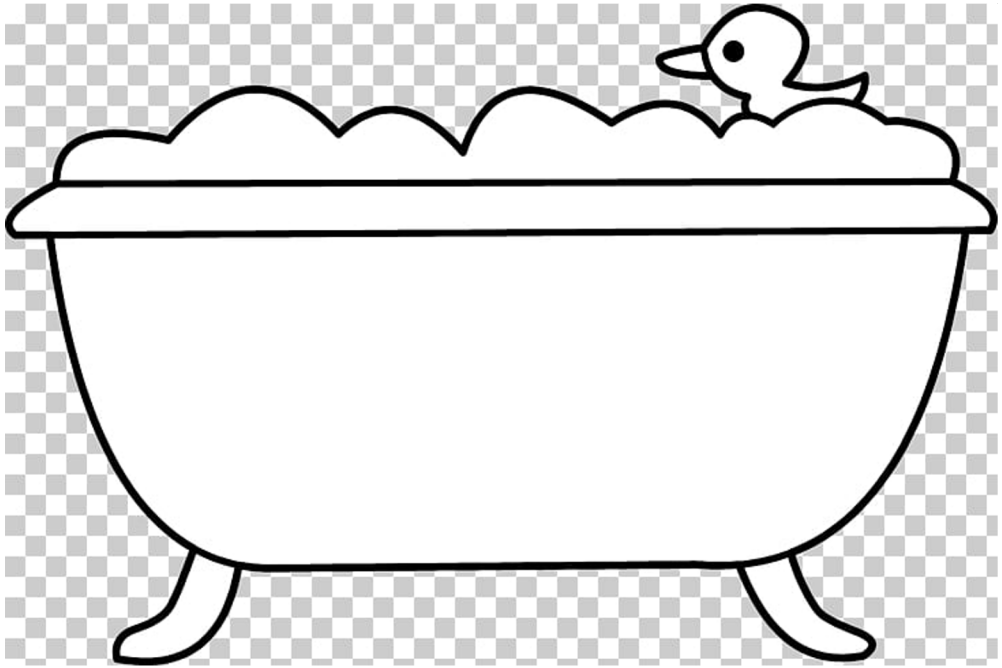
Faucet = breakdown of RBC's

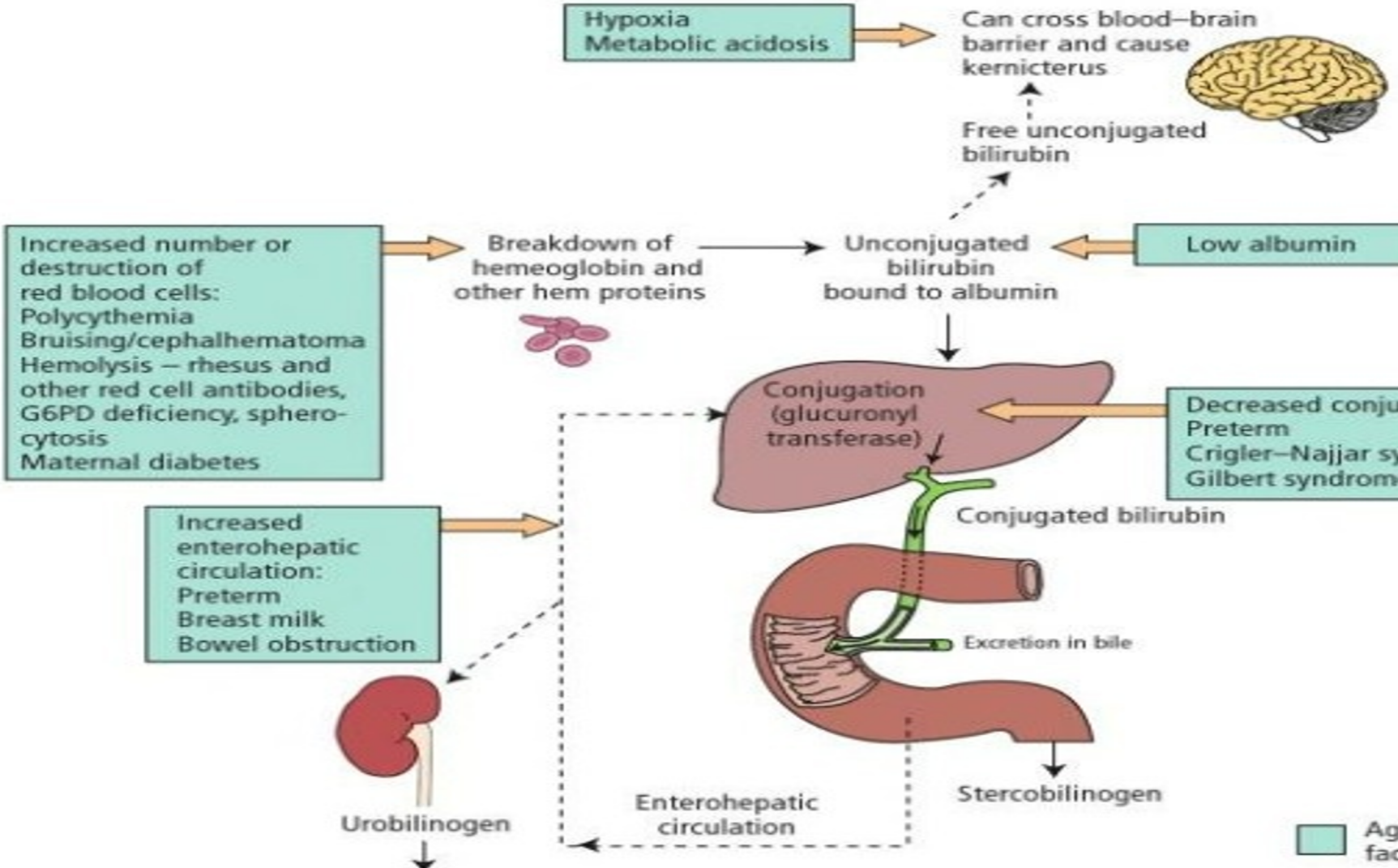
Drain = liver -> gut -> stool

Phototherapy = bucket

Tub gets taller over time (i.e. we can tolerate higher

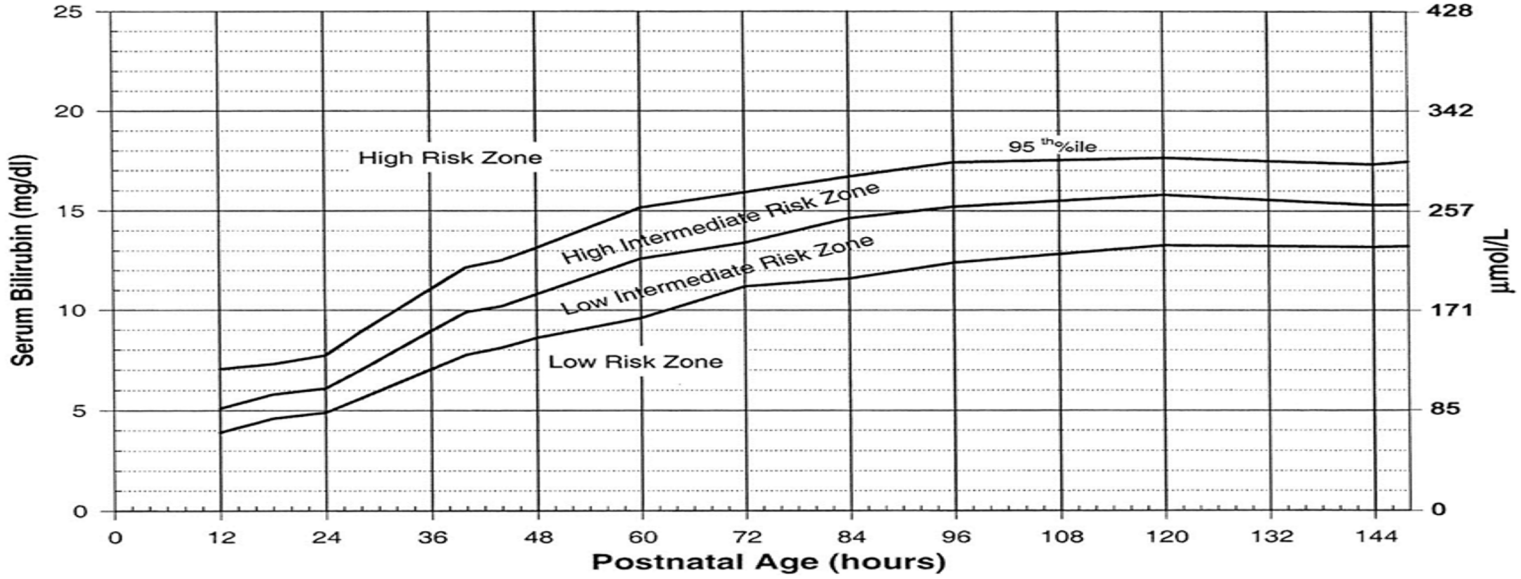
Bili levels at a greater age)




Hypoxia
Metabolic acidosis
Can cross blood–brain barrier and cause kernicterus
Free unconjugated bilirubin
Increased number or destruction of red blood cells:
Polycythemia
Bruising/cephalhematoma
Hemolysis – rhesus and other red cell antibodies, G6PD deficiency, spherocytosis
Maternal diabetes
Breakdown of hemeoglobin and other hem proteins
Unconjugated bilirubin bound to albumin
Low albumin
Conjugation (glucuronyl transferase)
Decreased conjugation:
Preterm
Crigler–Najjar syndrome
Gilbert syndrome
Conjugated bilirubin
Increased enterohepatic circulation:
Preterm
Breast milk
Bowel obstruction
Excretion in bile
Urobilinogen
Enterohepatic circulation
Stercobilinogen
Aggravating factors

How high is too high? (Bhutani nomogram)

Nomogram for designation of risk in 2840 well newborns at 36 or more weeks' gestational age with birth weight of 2000 g or more or 35 or more weeks' gestational age and birth weight of 2500 g or more based on the hour-specific serum bilirubin values.



Subcommittee on Hyperbilirubinemia et al. Pediatrics 2004;114:297-316

PEDIATRICS®

Bilitool ™

- Enter age of baby in hours, total Bili level
- Risk zone based on Bhutani nomogram
- Risk stratified into low/med/high risk for hyperbili (i.e. when to re-check) AND if phototherapy is indicated (based on low/med/high risk for BIND)
- Web site also has link to Exchange Transfusion nomogram

Risk for hyperbili: jaundice in first 24 hrs, ABO incompatibility with (+)Coombs/other hemolytic dz, prior sib requiring phototx, 35-36 week GA, cephalhematoma/bruising, exclusive BF, large wt loss, Far East Asian race (Chinese/Japanese/Korean/Mongolian/Taiwanese) and South East Asian (Laotian, Cambodian, Filipino, Indonesian, Vietnamese). Note: Indian, Pakistani, other South Asian are not at higher risk. Risk for readmission: GA < 37wks > Far East > SE Asian > Coombs(+) > Primipara

Bentz, et al Hospital Pediatrics May 2018, 8 (5) 269-273; DOI: https://doi.org/10.1542/hpeds.2017-0234

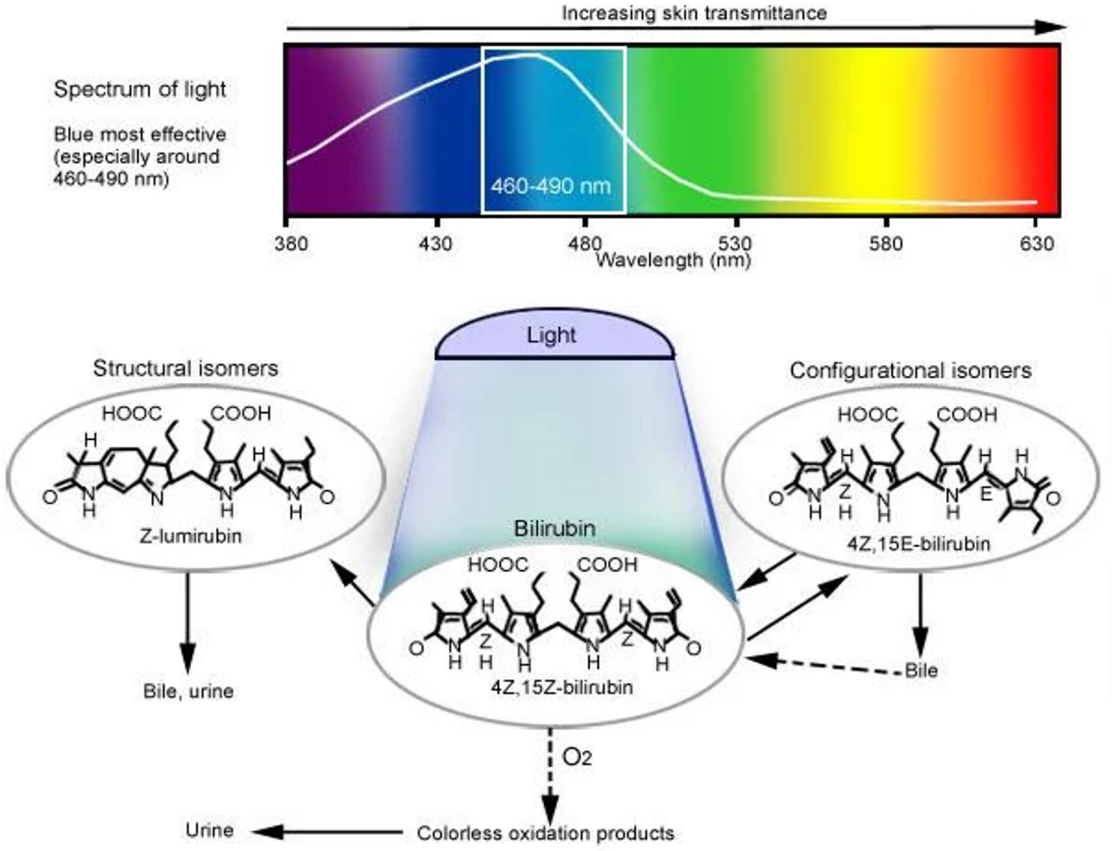
Initial Evaluation

- Total/direct bili
- Maternal Blood type and Rh, Ab status
- Baby Type and Coombs/DAT if mother is Type O or Rh (-)

Other tests: CBC with retic (hemolysis/polycythemia), RBC smear (spherocytosis), Albumin, G6PD activity, HgbEP, BCx, Urinalysis/UCx, thyroid levels

Phototherapy

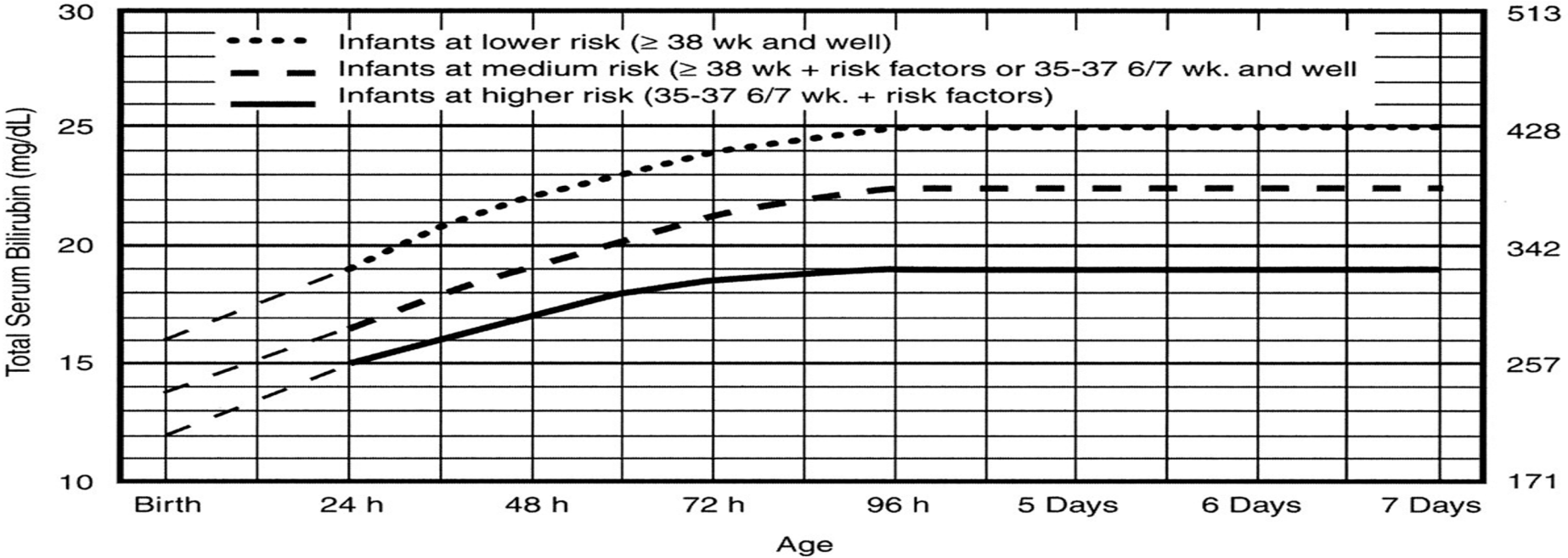
- Blue light (460-490 nm)
- Causes configurational or structural change in molecule, increasing water solubility



Neurotoxicity Risk Factors

- Isoimmune hemolytic disease
- G6PD Deficiency
- Asphyxia
- Significant Lethargy, Temp instability
- Acidosis
- Sepsis
- Albumin < 3.0 g/dL

Exchange Transfusion



- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 µmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend)

BIND (Bilirubin-Induced Neurological Dysfunction)

- Only caused by free serum Bilirubin
- Less common in Black race (exception:G6PD deficiency)

Acute Bilirubin Encephalopathy (ABE)

- Reversible
- Est. 2-10% risk in infants with TB > 30.
- BIND-M score: 0-3 pts in 4 domains (max 12 pts): mental status, muscle tone, cry, loss of upward gaze (sundowning); 1-4 pts = mild/reversible; > 7 = severe, likely irreversible

Bilirubin Induced Neurological Dysfunction (BIND)

Chronic Bilirubin Encephalopathy (Kernicterus)

- Athetoid CP, dystonia, myoclonus
- SNHL/Deafness (dx. ABR)
- Vestibular instability
- Dental enamel hypoplasia
- ? Cognitive delays
- Kernicterus refers to yellow staining of motor nuclei in brain seen on autopsy (Globus Pallidus) - can be seen on MRI
- Kernicterus was labelled a Serious Reportable Event by National Quality Forum (NQF) in 2002

Direct Hyperbilirubinemia - Cholestasis

- Direct/Conjugated Bili represents Bili that has been processed in liver but then returns to serum. This is a normal occurrence.
- Some rise in direct bili is normal as free bili gets processed. Direct fraction should remain < 20% of total.

Caused by:

A. **Hepatocellular damage** (hepatitis: infectious/chemical/ischemic, TPN, Metabolic d/o, UTI)

B. **Biliary tree abnormalities** (biliary atresia, paucity of bile ducts (Alagille), choledochal cyst, bile plug/inspissated bile)

Cholestasis - Initial w/u

- Direct/total bili
- ALT, AST, GGT (more sensitive for cholestasis)
- Hepatic U/S
- Hepatitis panel
- Involve GI early

Biliary Atresia

- Progressive, fibro-obliterative dz. of intra-, extra-hepatic bile ducts, tree
- Occurs in 1:12,000
- Not hereditary
- Sl higher in female, Asian, African American
- Early discovery and surgery (Kasai HPE)
- Kasai < 60d ⇒ 70% establish bile flow
- Kasai > 90d ⇒ 25%
- > 50% of pts. will require liver XP