

Management of Neonatal Rh Disease

OB/Peds Conference: Case Presentations

September 13, 2002

Mark Kadrofske

Neonatology Fellow

Management of Neonatal Rh Disease

Treatment of Hyperbilirubinemia.

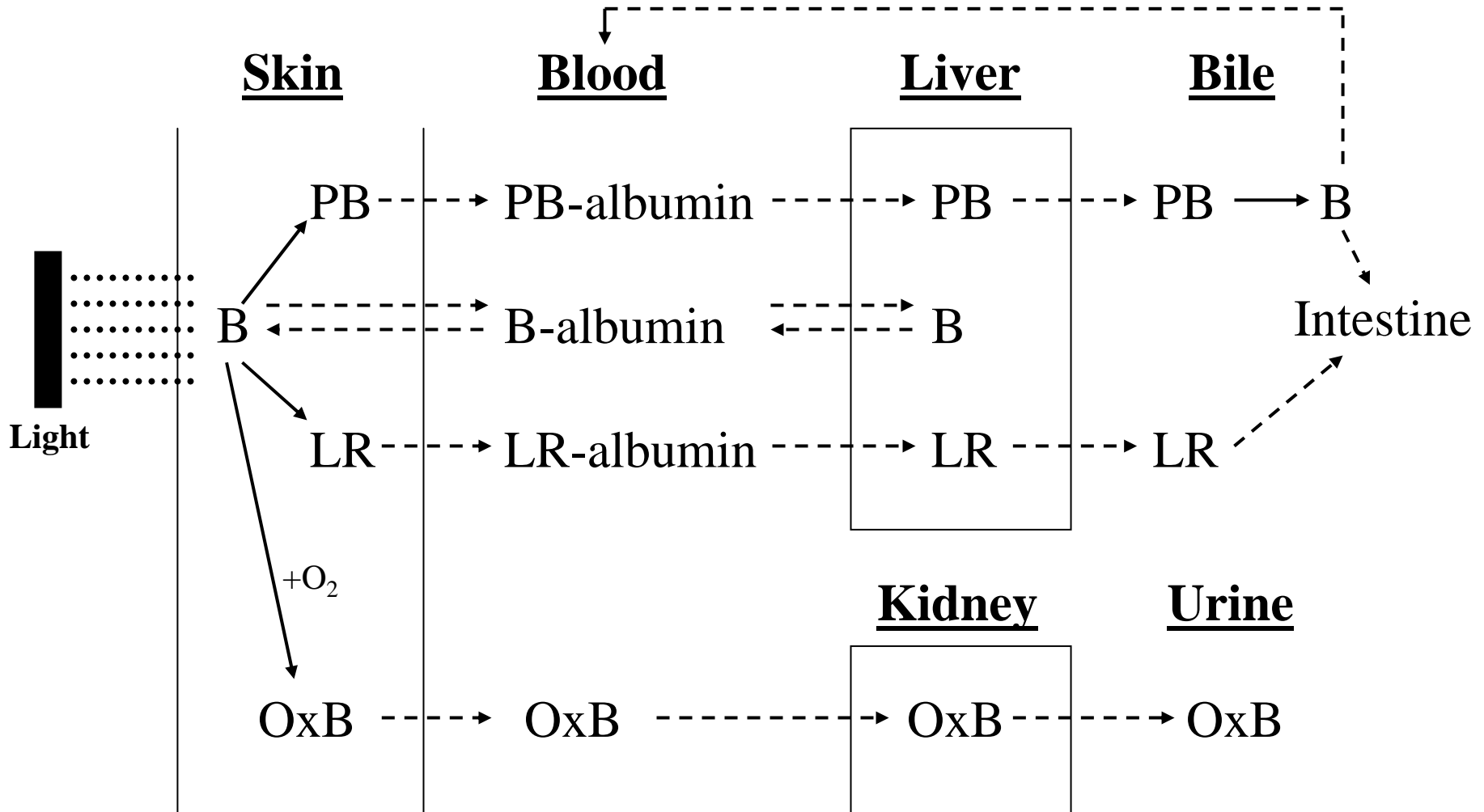
1. Phototherapy.

- Reduces or blunts the rise of U-bili regardless of maturity, presence or absence of hemolysis, or degree of skin pigmentation.
- No (reported) serious side effects, despite extensive use in U.S. and Europe; no (known) adverse outcomes.
- Demonstrated to reduce the need for exchange blood transfusions.
- *Mechanisms*>
 1. Geometric photoisomerization (Z-->E isomer; E isomer more soluble and can be excreted by liver into bile without need for conjugation).
 2. Intramolecular cyclization (bilirubin-->lumirubin)
 3. Oxidized byproducts (minor)

Management of Neonatal Rh Disease

1. Phototherapy

• *Mechanisms, cont>*



Management of Neonatal Rh Disease

1. Phototherapy

Technique>

- *Wavelengths (to induce photoisomerization):*

Bilirubin absorption between 420-500 nm (blue range);

Maximum: 460 (B-albumin), 440 (free B);

[Daylight 550-600 max]

Special blue lamps 420-480 peaks (but can't assess skin color and causes vertigo and nausea in caregivers)

- *Energy (or irradiance) ($\mu\text{W}/\text{cm}^2/\text{nm}$):*

Measured with photometer (“bili-meter”)

Minimum = $5 \mu\text{W}/\text{cm}^2/\text{nm}$

Maximum (saturation point) = $11 \mu\text{W}/\text{cm}^2/\text{nm}$

Remember--> $I \sim 1/\text{distance}^2$

Management of Neonatal Rh Disease

1. Phototherapy

Technique, cont.>

- *Surface area:*

The greater the surface area, the greater the effectiveness. Additional lights (double PT) NOT for increased I, but for increased surface area exposure.

White blanket around baby may reflect light onto relatively underexposed areas.

- *Fiberoptic phototherapy (“bili-blankets”):*

Halogen lamp-->fiberoptic bundle to a blanket.

(The AAP does NOT endorse home phototherapy)

- *“Off-time”:*

Intermittent breaks (feeds, bathing, etc.) OK since skin bilirubin pool takes 1-3 hours to restore.

Management of Neonatal Rh Disease

1. Phototherapy

•*Complications*>

1. Retinal degeneration (animal studies after prolonged use).
2. Increased insensible water loss (increased ~20-25%).
3. Increased GI fluid loss (stools looser and more frequent).
4. Upsets the usual maternal-infant bonding.
5. Bronze baby syndrome> occurs with conjugated hyper-bili or with cholestasis; exact mechanism unknown-->likely retention of photoproduct by skin.

Management of Neonatal Rh Disease



Management of Neonatal Rh Disease



Management of Neonatal Rh Disease

2. Double Volume Exchange Transfusion.

- Performed to correct anemia in infants severely affected with erythroblastosis and/or to prevent or correct hyperbilirubinemia that might lead to kernicterus.
- The infant's antibodies and the partially hemolyzed or antibody-coated RBC are washed out.
- Bilirubin is removed from the extravascular space because of equilibration and binding to the albumin in the exchanged blood.
- Leaves ~13% of the baby's original RBCs. After transfusion, bili declines ~50%; frequently rises to ~60% original level within one hr secondary to influx from extravascular space.

Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

- Hypoalbuminemia and acidosis should be corrected prior to exchange transfusion.
- Infants under intense phototherapy while a decision to exchange is being made.

Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

•*Early exchange* > indicated in the presence of hydrops and often indicated by a history of previously severely affected infants or a known sensitized infant.

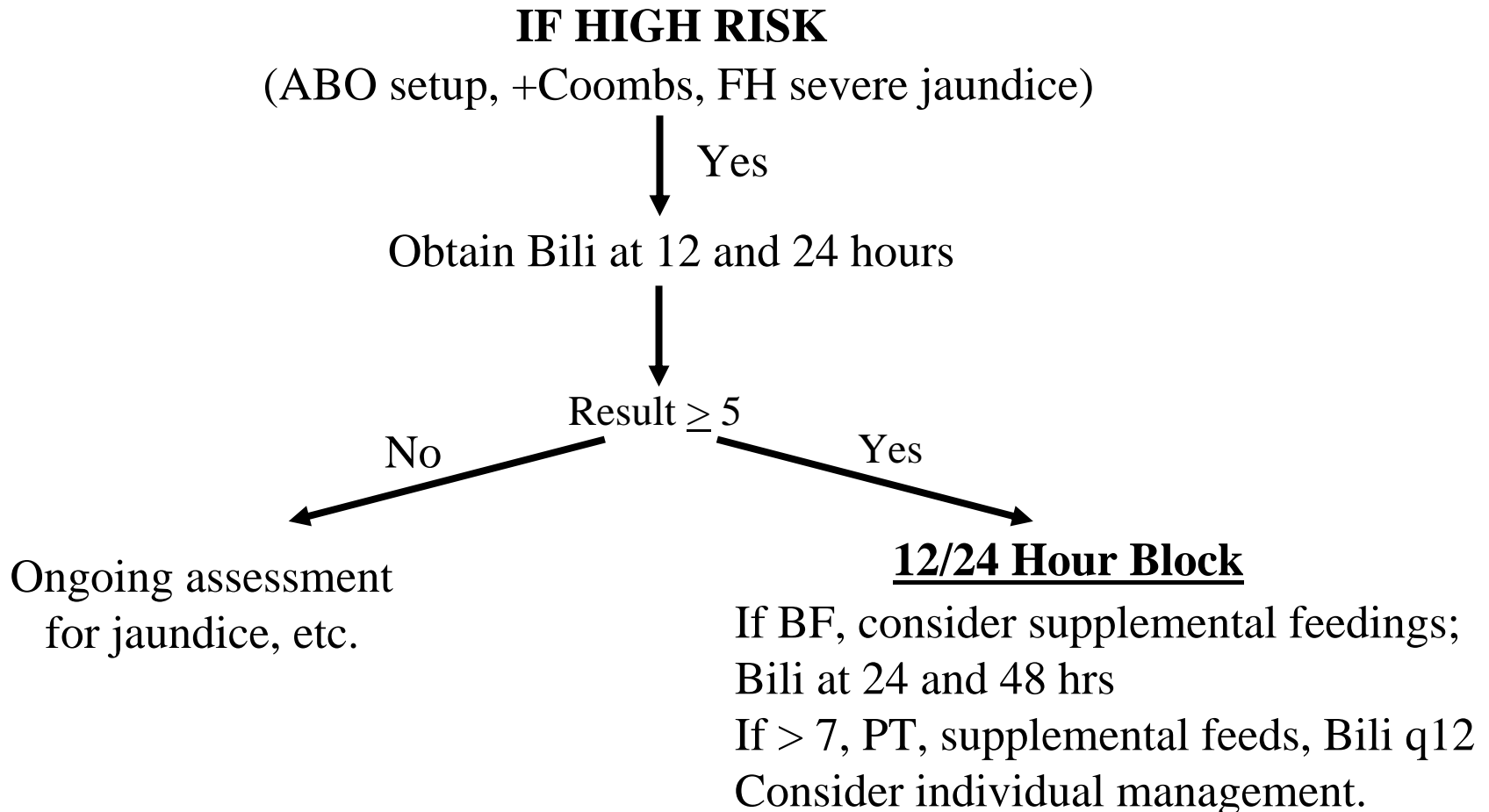
•General guidelines >

1. Bilirubin rising over 1 mg/dl/hr despite PT
2. The Hgb is between 11-13 gm/dl and the bilirubin level is rising over 0.5 mg/dl/hr despite PT
3. The bilirubin level is 20 mg/dl or it appears that it will reach 20 mg/dl at the rate it is rising.
4. Progressive (severe) anemia in the face of adequate control of bilirubin levels by PT.

Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

- MHMC guidelines (Hyperbilirubinemia)>



Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

- MHMC NICU guidelines (Hyperbilirubinemia)>

Preterm infants: Exchange level ~ 1% of BW in grams; may be lower if rate of rise >0.5 mg/dl/hr

Term infants**:

<u>Age in hours</u>	<u>Total bilirubin (mg/dl)</u>
24-48	20-25
48-72	25-30
>72	25-30

**To be individualized; exchange at lower level if hyperbili secondary to hemolytic process

Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

- Blood used in exchange: collected in citrate-phosphate-dextrose (CPD), not acid-citrate-dextrose secondary to high acid load; request a Hct ~50-55%.
- For Rh disease, use type O Rh-negative blood (or other ABO compatible blood, cross-matched against infant, if available). Sometimes O cells are used with AB plasma to lower the anti-A or anti-B antibody levels.

Management of Neonatal Rh Disease

2. Exchange Transfusion, cont.

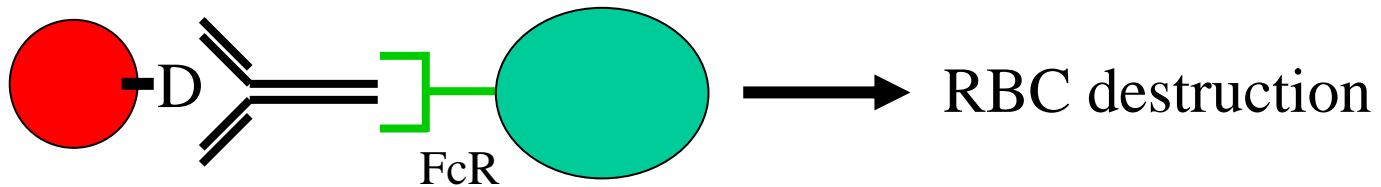
•Side effects/complications>

1. Hypocalcemia and hypomagnesemia from CPD buffer.
2. Hyperglycemia from CPD buffer.
3. Hyperkalemia (or hypokalemia, if pRBC washed): may wish to stat check K before use.
4. pH of donor blood is low; given citrate (metabolized by liver to bicarb) may get rebound alkylolysis; but if ill infant, may become acidotic (also, if mixing with plasma, this contains ACD buffer).
5. Thrombocytopenia and bleeding (secondary to deficient clotting factors).
6. Volume overload and CHF.
7. Transient maculopapular rash.
8. Line complications (thrombus, air embolus).

Management of Neonatal Rh Disease

3. Intravenous Immunoglobulin (IVIG)

- Anti-Rh antibodies do not fix complement and do not induce intravascular hemolysis; antibody sensitized RBC are bound to Fc receptor-bearing cells of the RES (similar to ITP):



- IVIG therapy in neonates with severe Rh disease may be a reasonable adjunct to PT
- 1992 Rubo et al. Multicenter, randomized, controlled study (not blinded), N =32 (16 in treatment group; 16 in control); Pts enrolled “as soon as direct Coombs test was positive.” All pts received standard phototherapy and ivf.

Management of Neonatal Rh Disease

3. Intravenous Immunoglobulin (IVIG), cont.

- Treatment group received one dose 500 mg/kg IVIG over 2 hrs.
- Treatment group > 2/16 (13%) required exchange transfusion;
Control group > 11/16 (69%) required ET (P < 0.005)
- Treatment failures (N=2) believed to be secondary to suboptimal management
- IVIG side effects > None reported; (general: hypotension, tachycardia, fever, hypersensitivity).

Management of Neonatal Rh Disease

4. Phenobarbital.

- Phenobarbital believed to accelerate bilirubin clearance by increasing its uptake by the liver, increasing its conjugation by UDP-glucuronyl transferase, and increasing the excretion of conjugated bilirubin by increasing bile flow.
- BUT, takes 3-7 days to reach full effectiveness, and may take longer in premature infants....
- 5-8 mg/kg q 24 hrs
- Side effects > lethargy, slow feeding, (neuronal development?)

Management of Neonatal Rh Disease

References>

1. Peterec, S.M. Management of Neonatal Rh Disease. 1995. *Clinics in Perinatology* Vol 22, pp 561-590.
2. Page, S. Rh Hemolytic Disease of the Newborn. 1989. *Neonatal Network*. Vol. 7 pp 31-41.
3. Cloherty, J.P. Neonatal Hyperbilirubinemia. In: *Manual of Neonatal Care*, ed: Stark, A.R. and Cloherty J.P. 1991. 3rd ed. pp 298-334.
4. MHMC NICU “*Black book*” ed: Collin, M. 2002.
5. Rubo, J., Albrecht, K, Lasch, P., et al. High-dose Intravenous Immune Globulin Therapy for Hyperbilirubinemia Caused by Rh Hemolytic Disease. 1992. *J Pediatrics* Vol 121, pp 93-97.