Kidz Medical Services  
Exchange Transfusion

**Purpose:**
To provide the clinicians of Kidz Medical Services with guidelines for the consistent treatment of newborns requiring exchange transfusions.

**Guideline:**
I. General:
   A. Exchange transfusion is a procedure used most often to maintain serum bilirubin below neurotoxic levels, but may also be used to control other conditions.
   B. Three types of exchange transfusions
      1. 2-volume exchange (replaces 87% of the infant’s blood volume with new blood)
      2. Isovolumetric 2-volume exchange
      3. Partial exchange (<2 volume) with normal saline, 5% albumin in saline or Plasmanate.

II. Indications:
   A. Hyperbilirubinemia:
      1. Exchange transfusion used to treat hyperbilirubinemia when serum bilirubin levels of any origin near or exceed a level that puts the infant at risk for neurotoxicity (kernicterus).
      2. 2-volume exchange transfusion taking 50-70 minutes are recommended for less stress on cardiovascular system and may enhance removal and reduction of bilirubin (efficiency of bilirubin removal is increased in slower exchanges because of extravascular and intravascular bilirubin equilibration).
      3. Appendix A has chart to follow for bilirubin levels at exchange levels.

   B. Hemolytic disease of the newborn:
      1. Exchange transfusion aids in removing antibody-coated RBCs as well as removing potentially toxic bilirubin levels.
      2. Immediate exchange transfusion generally indicated if:
         1. Cord Bili >4.5mg/dL and the cord hemoglobin level is under 11g/dL.
         2. Bili is rising >1mg/dL/hour despite phototherapy.
         3. Hgb level is between 11-13 g/dL and the bili level is rising >0.5 mg/dL/hour despite phototherapy.
         4. There is a progression of anemia in the face of adequate control of bilirubin by other methods (phototherapy).
      3. Repeated 2-volume exchanges may be needed if RBC destruction is rapid.

   C. Polycythemia:
      1. Usually best to give a partial exchange using normal saline because the normal saline will reduce both the polycythemia and the hyperviscosity.

   D. Sepsis:
      1. May be used when neonatal sepsis with associated with shock due to bacterial endotoxins.
2. 2-volume exchange may help remove bacteria, toxins, fibrin split products, and lactic acid. It may provide immunoglobulins, complements, and coagulation factors.

E. Disseminated Intravascular Coagulation (DIC):
   1. A 2-volume exchange is preferred but depending on the infant’s condition any of the exchange methods may provide necessary coagulation factors and help reduce the underlying cause of abnormal coagulation.
   2. Repletion of clotting factors by FFP (10-15ml/kg) transfusion may be all that is needed in mild cases of DIC.

F. Metabolic disorders causing severe metabolic acidosis:
   1. Partial exchanges are usually acceptable.

G. Severe fluid or electrolyte imbalance (i.e. hyperkalemia, fluid overload):
   1. Isovolumetric partial exchanges are recommended to prevent large electrolyte fluctuations with each aliquot of blood exchanged.

H. Severe anemia causing cardiac failure as in Hydrops Fetalis (normovolemic or hypervolemic)
   1. Partial exchange using red blood cells may be beneficial

III. Blood preparation:
- A. If bilirubin approaching dangerous levels consider time needed to prepare blood and start preparation of blood in a timely manner.
- B. CMV safe blood preferred.
- C. Irradiated blood preferred.
- D. Blood should be negative for Hgb S
- E. In infants, blood collected in citrate phosphate dextrose (CPD, CPD2, or CPDA-1) preferred
  1. Glucose concentration of CPD blood is 300mg/dL.
- F. PRBC should be less than 5 to 7 days old.
- G. For hydrops fetalis and asphyxia the blood should be less than 24 hours old. 
   (AABB does not specify, blood less than 24 old is usually not available. The only way to get a blood product this quickly would be to accept it before results of testing are available...many consents to sign) Donna’s comment so should we remove this whole line than Jorge?
- H. Transfusion Service should prepare reconstituted whole blood made from red blood cells and FFP to the desired HCT of 45-60%.
- I. Blood should be stored in citrate phosphate dextrose (CPD, CPD2, or CPDA-1)
- J. Use no more than 1 unit per exchange.
- K. Potassium levels in the donor blood should be determined if the infant is asphyxiated or in shock and renal impairment is suspected, if K levels >7 consider using a unit of blood that has been collected more recently or a unit of washed RBCs.
- L. Hyperbilirubinemia, metabolic imbalance or hemolysis not caused by isoimmune disorders
  1. Blood must be cross-matched against the infant’s plasma and RBCs, O or type specific, Rh specific.
- M. Infants with Rh incompatibility:
1. Blood must be O or type specific (ABO compatible with the mother), Rh negative, low titer anti-A, low titer anti-B blood.
2. If the blood is prepared before delivery of infant, it should be type O, Rh negative and crossmatched with the mother.
3. If the blood is prepared after delivery, it may also be crossmatched with the infant.

N. Infants with ABO incompatibility:
   1. Blood must be O, Rh-compatible (with mother and the infant) or Rh-negative
   2. Blood must be low titer anti-A, low titer anti-B blood, and crossmatched with mother and/or infant

O. Other blood group incompatibilities:
   1. Blood must be O or type specific(ABO compatible with the mother)
   2. Blood must be antigen negative for the maternal antibody, and crossmatched with the mother’s blood, if available, or the infant

IV. Equipment needed for procedure:
   A. Radiant warmer
   B. Equipment and medication for resuscitation should be readily available.
   C. Cardiorespiratory, oxygen saturation and blood pressure monitoring
   D. Immediate access to blood gas analysis.
   E. Peripheral intravenous access for administration of glucose or medications.
   F. Soft restraints for arms and legs if needed.
   G. Equipment for umbilical vein and artery catheterization.
   H. Exchange transfusion tray.
   I. NPO at least 4 hour prior if possible otherwise OG/NG tube placement to evacuate the stomach before initiating the exchange.
   J. A temperature-controlled device must be used to warm the blood before and during the exchange. The blood should be warmed to 37ºC.
   K. An assistant to help monitor infant and record the procedure volumes should be present throughout procedure.
   L. Calcium gluconate

V. Labs studies to be obtained before and after procedure:
   A. Bilirubin levels 2, 4, 6 hr after exchange then at 4-6 hr intervals
   B. Blood chemistries- Ca, Na, K, CL, Mag, blood gas, glucose
      1. Monitor bedside glucose frequently especially after transfusion for rebound hypoglycemia
   C. Hematologic studies- CBC with diff and platelets
   D. Blood culture

VI. Procedure:
   A. 2-volume Exchange Transfusion
      1. Normal blood volume in a term infant is 80ml/kg.
      2. Normal blood volume in preterm or low birth weight infant may be up to 95-100 ml/kg
      3. Twice this volume of blood is exchanged in a 2-volume transfusion
      4. Perform exchange in a NICU setting
      5. Place on C/R and O2 sat monitors
6. Consider OG tube placement
7. Have emergency resuscitation equipment and medication readily available
8. Insert an umbilical vein catheter – confirm placement before blood obtained
9. Check blood types of donor and infant
10. Warm the blood using a blood warmer.

11. **Check Hct of blood (lab?)**
   1. Agitate blood regularly throughout procedure to maintain constant Hct

12. Establish volume of each aliquot:

<table>
<thead>
<tr>
<th>Infant's weight</th>
<th>Aliquot (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 kg</td>
<td>20</td>
</tr>
<tr>
<td>2-3 kg</td>
<td>15</td>
</tr>
<tr>
<td>1-2 kg</td>
<td>10</td>
</tr>
<tr>
<td>850 g-1000 g</td>
<td>5</td>
</tr>
<tr>
<td>&lt;850 g</td>
<td>1-3</td>
</tr>
</tbody>
</table>

13. Slow steady pace: 3-5 minutes per pass with push-pull technique
14. Avoid excessive suction when withdrawing and excessive pressure when infusing

B. Isovolumetric 2-volume exchange transfusion:
   1. Same steps as 2-volume exchange with addition of placing umbilical artery catheterization
   2. Is performed using double setup with infusion via the umbilical vein and withdrawal via the umbilical artery

C. Partial exchange transfusion
   1. If a partial exchange is for polycythemia (using normal saline) or anemia (using PRBC) use the following formula:
   
   \[
   \text{Volume of exchange (ml)} = \text{Estimated blood volume (ml)} \times \text{weight (kg)} \times \frac{\text{observed hct} - \text{desired hct}}{\text{Observed hct}}
   \]

VII. Administration of Calcium Gluconate:
   A. The citrate buffer binds calcium and transiently lowers ionized calcium levels.
   1. Some physicians routinely administer 1-2 ml of 10% calcium gluconate by slow infusion after 100-200ml of exchange donor blood.
   2. Others maintain that this treatment has no therapeutic effect unless hypocalcemia is documented by electrocardiogram showing a change in the QT interval.

VIII. Post Exchange:
   A. Resume phototherapy
   B. Monitor labs as above
   C. Cross-match with mother and/or infant if repeat exchange required. Original unit will expire in less than 24 hours after receipt so it will probably be a separate unit and will need cross-match
   D. Remedication:
      1. Patients receiving antibiotics and anticonvulsants need to remediacted.
2. Unless cardiac status is deteriorating or serum digoxin levels are too low, patients receiving digoxin should not be remedicated.
3. Determination of drug levels after exchange is advisable.
4. Antibiotic prophylaxis should be considered on an individual basis.
   Infection is uncommon but is the most frequent complication.

IX. Complications
A. Infection: Bacteremia, hepatitis, CMV infection (unit should be CMV negative), malaria and AIDS have been reported
B. Vascular Complications: Clot or air embolism, arteriospasm of lower limbs, thrombosis, and infarction of major organs may occur.
C. Coagulopathies: May result from thrombocytopenia or diminished coagulation factors. Platelets may decrease by 50% after a 2-volume exchange transfusion.
D. Electrolyte imbalance:
   1. Hyperkalemia- K levels elevated in stored Red Blood Cells but washing the cells removes the excess K. If blood greater than 24 hours consider checking K level.
   2. The citrate in CPD blood binds ionic CA and MAG.
      1. Hypocalcemia treat if EKG changes or clinical symptoms present.
      2. Hypomagnesemia related to exchanges have not been associated with clinical problems.
E. Hypoglycemia: more likely in infant of diabetic mother and erythroblastosis fetalis.
F. Metabolic acidosis: from stored donor blood, less likely with CPD blood
G. Metabolic alkalosis: may occur as a result of delayed clearing of citrate preservative from the donated blood by the liver.
H. Hypothermia or hyperthermia with inappropriate blood temperature
I. Hypoxemia
J. Cardiovascular:
   1. Hypovolemia/hypervolema if inaccurate replacement
   2. Arrhythmias related to electrolyte imbalance
   3. Cardiac arrest

References:


AAP Guidelines and recommendations regarding exchange transfusions and hyperbilirubinemia:

- 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)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

**Fig 4. Guidelines for exchange transfusion in infants 35 or more weeks’ gestation.**

Note that these suggested levels represent a consensus of most of the committee but are based on limited evidence, and the levels shown are approximations. See ref. 3 for risks and complications of exchange transfusion. During birth hospitalization, exchange transfusion is recommended if the TSB rises to these levels despite intensive phototherapy. For readmitted infants, if the TSB level is above the exchange level, repeat TSB measurement every 2 to 3 hours and consider exchange if the TSB remains above the levels indicated after intensive phototherapy for 6 hours.

The following B/A ratios can be used together with but in not in lieu of the TSB level as an additional factor in determining the need for exchange transfusion:

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>B/A Ratio at Which Exchange Transfusion Should be Considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants ≥38 0/7 wk</td>
<td>TSB μmol/L/Alb, μmol/L</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
</tr>
<tr>
<td>Infants 35 0/7–36 6/7 wk and well or ≥38 0/7 wk if higher risk or isoimmune hemolytic disease or G6PD deficiency</td>
<td>7.2</td>
</tr>
</tbody>
</table>
TABLE 3. Example of a Clinical Pathway for Management of the Newborn Infant Readmitted for Phototherapy or Exchange Transfusion

Treatment

Use intensive phototherapy and/or exchange transfusion as indicated in Figs 3 and 4 (see Appendix 2 for details of phototherapy use)

Laboratory tests

TSB and direct bilirubin levels
Blood type (ABO, Rh)
Direct antibody test (Coombs’)
Serum albumin
Complete blood cell count with differential and smear for red cell morphology
Reticulocyte count
ETCO₂ (if available)
G6PD if suggested by ethnic or geographic origin or if poor response to phototherapy
Urine for reducing substances
If history and/or presentation suggest sepsis, perform blood culture, urine culture, and cerebrospinal fluid for protein, glucose, cell count, and culture

Interventions

If TSB ≥25 mg/dL (428 µmol/L) or ≥20 mg/dL (342 µmol/L) in a sick infant or infant <38 wk gestation, obtain a type and crossmatch, and request blood in case an exchange transfusion is necessary

In infants with isoimmune hemolytic disease and TSB level rising in spite of intensive phototherapy or within 2–3 mg/dL (34–51 µmol/L) of exchange level (Fig 4), administer intravenous immunoglobulin 0.5–1 g/kg over 2 h and repeat in 12 h if necessary

If infant’s weight loss from birth is >12% or there is clinical or biochemical evidence of dehydration, recommend formula or expressed breast milk. If oral intake is in question, give intravenous fluids.

For infants receiving intensive phototherapy

Breastfeed or bottle-feed (formula or expressed breast milk) every 2–3 h
If TSB ≥25 mg/dL (428 µmol/L), repeat TSB within 2–3 h
If TSB 20–25 mg/dL (342–428 µmol/L), repeat within 3–4 h. If TSB <20 mg/dL (342 µmol/L), repeat in 4–6 h. If TSB continues to fall, repeat in 8–12 h.

If TSB is not decreasing or is moving closer to level for exchange transfusion or the TSB/albumin ratio exceeds levels shown in Fig 4, consider exchange transfusion (see Fig 4 for exchange transfusion recommendations).

When TSB is <13–14 mg/dL (239 µmol/L), discontinue phototherapy.

Depending on the cause of the hyperbilirubinemia, it is an option to measure TSB 24 h after discharge to check for rebound.

RECOMMENDATION 7.1.1: In using the guidelines for phototherapy and exchange transfusion (Figs 3 and 4), the direct-reacting (or conjugated) bilirubin level should not be subtracted from the total (evidence quality D: benefits versus harms exceptional).

In unusual situations in which the direct bilirubin level is 50% or more of the total bilirubin, there are no good data to provide guidance for therapy, and consultation with an expert in the field is recommended.

RECOMMENDATION 7.1.2: If the TSB is at a level at which exchange transfusion is recommended (Fig 4) or if the TSB level is 25 mg/dL (428 µmol/L) or higher at any time, it is a medical emergency and the infant should be admitted immediately and directly to a hospital pediatric service for intensive phototherapy. These infants should not be referred to the emergency department, because it delays the initiation of treatment (evidence quality C: benefits exceed harms).

RECOMMENDATION 7.1.3: Exchange transfusions should be performed only by trained personnel in a neonatal intensive care unit with full monitoring and resuscitation capabilities (evidence quality D: benefits versus harms exceptional).

RECOMMENDATION 7.1.4: In isoimmune hemolytic disease, administration of intravenous \( \gamma \)-globulin (0.5-1 g/kg over 2 hours) is recommended if the TSB is rising despite intensive phototherapy or the TSB level is within 2 to 3 mg/dL (34-51 µmol/L) of the exchange level (Fig 4). If necessary, this dose can be repeated in 12 hours (evidence quality B: benefits exceed harms).

Intravenous \( \gamma \)-globulin has been shown to reduce the need for exchange transfusions in Rh and ABO hemolytic disease. Although data are limited, it is reasonable to assume that intravenous \( \gamma \)-globulin will also be helpful in the other types of Rh hemolytic disease such as anti-C and anti-E.

Serum Albumin Levels and the Bilirubin/Albumin Ratio

RECOMMENDATION 7.1.5: It is an option to measure the serum albumin level and consider an albumin level of less than 3.0 g/dL as one risk factor for lowering the threshold for phototherapy use (see Fig 3) (evidence quality D: benefits versus risks exceptional.).

RECOMMENDATION 7.1.6: If an exchange transfusion is being considered, the serum albumin level should be measured and the bilirubin/albumin (B/A) ratio used in conjunction with the TSB level and other factors in determining the need for exchange transfusion (see Fig 4) (evidence quality D: benefits versus harms exceptional).

The recommendations shown above for treating hyperbilirubinemia are based primarily on TSB levels and other factors that affect the risk of bilirubin encephalopathy. This risk might be increased by a prolonged (rather than a brief) exposure to a certain TSB level. Because the published data that address this issue are limited, however, it is not possible to provide specific recommendations for intervention based on the duration of hyperbilirubinemia.