**Principle**

This policy is to ensure that all patients with Sickle Cell Disease receive:

A. Correctly selected blood products (Sickledex negative, phenotypically matched)
B. Receive simple transfusions when medically indicated
C. Receive exchange transfusions when medically indicated
D. Are placed on chronic transfusion programs when medically indicated
E. Receive appropriate perioperative transfusion management
F. Appropriate screening preoperatively by Sickledex testing or Hemoglobin electrophoresis
G. Receive transfusions during pregnancy only when medically indicated
H. Appropriate use of medical devices
I. Are monitored and treated for transfusional iron overload

A patient with Sickle Cell Disease includes all of the following: SS disease, SC disease, S-Beta Thalassemia. **Only Sections F and H apply to patients with Sickle Cell Trait** (Hemoglobin AS).

**Patient Safety**

All patients with Sickle Cell Disease must be identified prior to transfusion. If a diagnosis is lacking for any transfusion recipient a concerted effort shall be made by the blood bank to determine the patient’s diagnosis prior to transfusion. **It is critical that the physician communicates this information to the blood bank or hematology consultation service at the time of admission.**

**Selection of Blood Products**

**Sickledex Negative Blood**

Sickle trait blood should not be transfused to patients with sickle cell disease. In emergency situations blood may be transfused to a patient with Sickle Cell Disease prior to Sickledex testing. Sickledex positive blood may be used at the discretion of the Medical Director if phenotypically compatible Sickledex negative units are not available from CBS.

**Red Cells < 14 Days Old**

Red blood cells less than 14 days from collection are preferable, but not mandatory. Fresh red blood cells may deliver oxygen more efficiently.

**Phenotypically Matched PRBC**

All patients should be registered with the Canadian Blood Services Phenotyping Program. Any sickle cell patient unknown to Canadian Blood Services Phenotyping Program shall be registered by the Blood Bank. RBC should be preferably matched for the following antigens:

(1) Rh (D, C, E)
(2) Kell (K1)
Not Required:

- CMV negative blood products (unless patient has a co-existing indication for CMV-negative blood products)
- Irradiated blood products (unless patient has another co-existing indication for irradiated blood products) – note that allogeneic bone marrow transplant is performed occasionally in the treatment of patients with Sickle Cell Disease.

**Indications for Simple Transfusion**

Simple packed red blood cell transfusions are indicated for the following indications. **Transfusion above a hemoglobin of 100 g/L or hematocrit of 0.30 should be avoided due to concerns of increasing blood viscosity.**

1. Acute anemia – transfusion usually is required with a fall in hemoglobin > 20% from baseline. Common precipitators: infection (e.g. sepsis, pneumonia, parvovirus B19), bleeding, and drug-related hemolysis due to G-6-PD deficiency.
2. Splenic sequestration – a life-threatening emergency characterized by sudden onset of painful massive splenomegaly, an abrupt decrease in hematocrit level and platelet count, and hypovolemic shock. Patients should be watched for the ‘over shoot’ phenomenon – transfusion triggers the spleen to release trapped erythrocytes leading to a higher hematocrit than expected based on the amount of transfused blood. The rate and volume of transfused blood required should be determined by the starting vital signs.
3. Preoperatively patients shall be transfused to a hemoglobin of 100 g/L prior to a general anesthesia or eye surgery to prevent perioperative complications.

**Transfusions should not be given in the treatment of the acute painful episode or uncomplicated pregnancy, unless other clear-cut indications for their use are present.**

**Acute Exchange Transfusion**

Red blood cell exchange is designed to reduce the level of hemoglobin S to less than 20% by 24 hours.

A single volume RBC exchange = HC ti x TBV (usually lowers HbS to < 30%). A double volume exchange = 2 x HC ti x TBV (usually lowers HbS to < 10%).

Red cell exchange should be performed by red cell apheresis method (available at Toronto General Hospital or St. Michael’s Hospital), where possible, and if in the extremely rare event where this is unavailable, by manual exchange. Indications for exchange transfusion include the following: (1) ischemic stroke, (2) hemorrhagic stroke, (3) acute chest syndrome, (4) acute multiple organ damage syndrome, (5) retinal artery occlusion. Priapism should be managed by surgical intervention (aspiration of blood from the corpora cavernosa and irrigation with dilute epinephrine solution under local anesthesia; Mantadakis E, et al. Blood 2000) [1], however, red cell exchange may be performed on the advice of the treating hematologist if surgical management fails. Contact the Blood Bank immediately if an exchange transfusion will be required.
Method for Manual Red Cell Exchange

To be performed by the Hematologist on call, or his/her delegate

1. One unit of appropriately selected RBC labeled for the patient should be available at the bedside.
2. Standard bedside check shall be performed.
3. Patient must have a correct identification band.
4. Patient vitals should be measured and recorded in the patient record every 15 minutes during the procedure and for 2 hours after completion. (HR, RR, blood pressure, temperature)
5. Start a large bore intravenous in the antecubital fossa (14 or 16 gauge needle).
6. Infuse 25 mL of normal saline to ensure patency of intravenous line.
7. Insert needle from autologous collection set into 1st IV port.
8. Inflate BP cuff to 90 mmHg.
9. Clamp IV immediately above the first IV port.
10. Phlebotomize the first unit of blood (450 ml) utilizing rocker from the autologous blood collection room (ensure checked by the autologous RN prior to use).
11. Infuse 300 mL of normal saline over 15 minutes.
12. Phlebotomize the second unit of blood (450 ml) as above.
13. Start the first unit of allogeneic blood.
14. Infuse a total of 5 units of RBC over the next 10 hours, approximately 1 U over each 2-hour period.
15. At the end of the last unit draw a specimen for hemoglobin electrophoresis.

Chronic Transfusion

A program of chronic transfusions may be embarked on for the following indications:

1. Hemorrhagic or ischemic stroke – after acute exchange transfusion, hemoglobin S should be maintained less than 30% for the first 4 years after a stoke, thereafter, the hemoglobin S should be maintained less than 50% indefinitely.
2. Leg ulcers – until complete healing is observed.
3. Chronic symptomatic anemia – consider concurrent treatment with hydroxyurea.
4. Debilitating veno-occlusive disease that is unresponsive to hydroxyurea.
5. Complicated pregnancy – severe sickle-related complications, history of recurrent fetal loss, multiple gestation, or chronic fetal distress (Intrauterine growth retardation/IUGR).

The volume of transfused RBC is approximately 15 ml/kg q3-4 weeks (maintaining the Hb below 100 g/L). Where a Hb S of less than 30% is required, a hemoglobin electrophoresis should be performed prior to each transfusion until the hemoglobin S fraction is less than 0.30 on 2 consecutive occasions, and q3 months thereafter.

Perioperative Transfusion & Perioperative Management

Patients with sickle cell disease have a very high rate of perioperative complications. Approximately 35% of Sickle Cell patients experience a complication in the immediate perioperative period (Infection, painful crisis, or acute chest syndrome). Acute chest syndrome is the most common postoperative complication (10% of patients; Vichinsky EP, et al. N Engl J Med 1995) [2]. Patients who undergo major surgery without preoperative transfusions are at a substantial increased risk of major complications, particularly pulmonary complications affecting 35% of un-transfused patients [3]. 7% of all deaths from Sickle Cell Disease are directly related to surgery and therefore optimal management is critical. The mortality rate at 30 days following cholecystectomy is 1.1%. Perioperative transfusion and anesthetic management should include all of the following:
1. Ensure the patient is not in an active crisis, veno-occlusive or chest crisis.
2. Simple transfusion to increase the hemoglobin to 100 g/L for all patients undergoing a general anesthetic, major surgery, or eye surgery. This results in a 50% reduction in the perioperative complication rate [2, 4].
3. Consider exchange transfusion for patients with a history of severe perioperative complications, such as the acute chest syndrome.
4. Consider starting hydroxyurea 3 or more months preoperative for patients who require this therapy for other reasons (more than 3 sickle crises per year requiring admission to hospital, severe symptomatic anemia, or severe vaso-occlusive complications).
5. Hydration for 12 to 24 hours preoperative to avoid preoperative dehydration.
6. Incentive spirometry pre-op and until discharge.
7. Avoidance of hypoxia.
8. Avoidance of hypothermia – options include warming the operating room, use of warming blankets, and/or the use of blood warmers.
9. Consider laparoscopic surgery where appropriate. Regional anesthesia may be associated with a higher complication rate than general anesthesia.
10. Aggressive remobilization post-op to prevent thromboembolic complications and atelectasis.
11. Thromboembolism prophylaxis with low molecular weight heparin.
12. Consideration should be given to intensive monitoring for 48 hours postop in the Critical Care Unit.

Perioperative Screening for Sickle Cell Disease & Sickle Cell Trait

Individuals with sickle cell TRAIT may develop sickling at extreme hypoxia or have difficulty concentrating their urine (isosthenuria). Two recent reports suggest that preoperative screening for sickle cell trait is no longer warranted [5, 6]. Individuals from high-risk groups (Blacks, Africans, Arabs, India) should be aware of their sickle cell status. If unknown, these individuals should be tested and informed of their carrier status for prevention of Sickle Cell Disease in their children. Sickle Cell Carrier status is not required information preoperatively, unless the patient is undergoing intrathoracic surgery, cardiopulmonary bypass, or a tourniquet will be used. These patients may be at risk of sickling complications due to extreme hypoxia post-operatively and require more intensive monitoring intra-operatively and post-operatively. Individuals with Sickle Cell Disease shall be identified by history and physical exam, and where necessary, confirmed by hemoglobin electrophoresis.

Pregnancy

Patients with Sickle Cell Disease are at a greater risk of obstetrical complications including: 16% intrauterine growth retardation, 15-20% stillbirths, premature delivery, and increased perinatal mortality. Maternal mortality has not been documented to be greater than non-pregnant individuals with Sickle Cell Disease and therefore MDs caring for women with Sickle Cell Disease should support them if they desire to have children [7]. Simple transfusions appear not to affect maternal or fetal outcome measures [8]. Role of simple transfusions prior to Caesarean section has not been formally evaluated in studies. Patients during labour and delivery should be monitored in a high-risk setting. Anemia with consequent high cardiac output is aggravated by the periods of uterine contraction. Complications can be minimized by the use of (1) epidural anesthesia, (2) judicious use of oxygen, (3) adequate hydration, (4) continuous fetal monitoring, (5) anti-embolic stockings and early ambulation, (6) shortening of the duration of labour, (7) exchange transfusion for serious sickle complications (e.g. acute chest syndrome). All infants at risk should be tested by hemoglobin electrophoresis prior to discharge from hospital [9].
Use of Medical Devices

1. Tourniquet – avoid where possible. If deemed required careful exsanguination of the extremity prior to application is warranted. Avoid prolonged use of tourniquet. One study showed safe use of this device in Sickle Cell Disease, albeit of the less severe Indian-Arab haplotype [10].


4. Cardiopulmonary Bypass – if required other centres have utilized the following options to minimize the perioperative complication, of which none have been extensively studied: preoperative transfusion, preoperative exchange transfusion, and priming the pump with RBC. Patients with Sickle Cell TRAIT may be at elevated risk of veno-occlusive complication perioperatively for patients with sickle cell disease. Small studies have shown that normothermic cardiac surgery can be performed in AS patients without preoperative transfusions.

Prevention of Iron Overload

Iron overload related complications are expected to occur with the deposition of 20 g of iron (or 80 transfusions of RBC). Screening for iron overload should commence after the transfusion of more than 20 transfusions. Patients with ferritin levels greater than 1000 ng/ml should be considered at risk for tissue iron overload and should undergo a liver biopsy for liver iron quantification. The target for liver iron is to maintain the liver iron between 3 to 7 mg/g dry liver weight or less.

Complications of Transfusion

1. RBC Alloimmunization – 47% of adult patients with SSD have alloantibodies. The risk per unit is 3.1% without phenotypically matched blood compared to 0.5% with matched [12].

2. RBC Autoantibodies – approximately 10% of patients have autoantibodies, in addition to alloantibodies. These autoantibodies can cause difficulty with detection of clinically significant RBC alloantibodies.

3. Iron overload – see above.

4. Hyper-hemolysis syndrome – characterized by hemolysis of donor and recipient RBCs. Markers of hemolysis are elevated, including bilirubin and LDH. The most important feature is relative reticulocytopenia, and usually the DAT is negative. Continuation of RBC transfusions can be life threatening. Therapy may include corticosteroids, IVIG, hemoglobin based oxygen carriers, and withholding of RBC transfusions.

5. Delayed hemolytic transfusion reactions due to new RBC alloantibodies.
References