Transfusion Support for Sickle Cell Disease

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DISCLOSURES

- Research support from Canadian Blood Services
Objectives

1. Outline the principles of RBC transfusion in sickle cell disease

2. Define acceptable indications for RBC transfusion in sickle cell disease

3. Recognize the importance of prophylactic antigen matching of RBCs, and the transfusion complication of hyperhemolysis
Oxygen Delivery: Macrocirculatory vs Microcirculatory Perspectives

Oxygen-carrying capacity

Small vessel perfusion
Oxygen Delivery: Macrocirculation

- **Oxygen carrying capacity** ($\text{CaO}_2$) of blood determined predominantly by hemoglobin concentration
  - Much smaller proportion dissolved in plasma
- Oxygen delivery in turn is the oxygen carrying capacity multiplied by rate of blood flow. Rate of blood is determined by cardiac output
- Under normal conditions, oxygen consumption is 200-300 mL/min, which is 4-5x less than what is delivered
Oxygen Delivery: Microcirculation

- While *total* blood flow defined by cardiac output, flow in any particular blood vessel determined by *vascular resistance* and pressure difference between ends of the vessel.

- By Hagen–Poiseuille equation Vascular resistance defined by radius and length of the blood vessel, and the viscosity of the fluid flowing through it.

\[
\text{velocity} = \frac{\pi \rho r^4}{8 \eta} = \frac{\pi (\text{pressure}) (\text{radius of the tube})^4}{8 (\text{length of tube}) (\text{viscosity})}
\]

- Blood viscosity determined primarily by the hematocrit.
Oxygen Delivery: What is the Optimal Hct?

- Given the competing effects of red cell mass on oxygen delivery (increases oxygen carrying capacity but decreases blood flow), is there an *optimal* hematocrit that maximizes oxygen delivery?

- Physiologic studies define this optimal point as the Hct at which any further increases result in a proportionally larger increase in viscosity (e.g., optimal Hct = maximal Hct/viscosity ratio)
While oxygenated sickle blood is already more viscous than normal blood, viscosity increases dramatically when deoxygenated.

Result is apparent optimal Hct of 25% even at high shear; even if HgbS diluted to 25%, no further benefit in increasing Hct past 30%

Alexy T, Transfusion 2006;46:912
Implications of Viscosity Studies

- In vascular beds with low shear, particularly those with low oxygen tension (e.g., post-capillary venules, bone marrow), any increase in oxygen delivery achieved by transfusion is likely offset by increases in viscosity.

- This would suggest that top-up transfusions are unlikely to be of benefit as treatment for vaso-occlusive crises manifesting as bony pain.
Implications of Viscosity Studies

- In vascular beds with high shear (e.g., brain, kidneys, lungs), oxygen delivery may be optimized by increasing the Hct, but with deoxygenated sickle blood there is likely little benefit and possibly harm of transfusing to exceed a Hct of 30%, even if patient’s own blood has already been diluted by 75%.

- Moreover, any improvements in oxygen delivery achieved by transfusion in high-shear vascular beds may result in worsened oxygen delivery in low shear beds.
Implications of Viscosity Studies: Rules of Thumb

1. In most cases, the benefits of transfusing a patient with sickle cell disease will come from decreasing the viscosity of their blood rather than by increasing its oxygen-carrying capacity.
   - **Goal of transfusion is to decr HgbS%, not incr total Hgb.**

2. Transfusing a patient with sickle cell disease to Hgb > 100-110 g/L may worsen their condition, particularly if the patient is already in a hyperviscous state (dehydrated, low-flow, hypoxic).
   - **Target HgbS% may only be safely achievable by removing patient’s own blood prior to transfusing = EXCHANGE TRANSFUSION.**
Transfusing to Increase the Oxygen Carrying Capacity
Transfusing for CaO$_2$

- Remember: O2 dissociation curve is right-shifted in sickle cell: what seem like symptoms of anemia may in fact reflect medication effects (eg., fatigue), hypovolemia (eg., tachycardia, hypotension), or other disease (eg., dyspnea)

- Prophylactic transfusions to prevent complications of anemia in sickle cell disease not advised unless Hgb < 50 g/L!

**Guidelines on red cell transfusion in sickle cell disease**

**Part II: indications for transfusion**

“Transfusion is not recommended in uncomplicated painful crises but should be considered if there is a substantial drop in Hb from baseline (e.g. >20 g/l or to Hb <50 g/l), haemodynamic compromise or concern about impending critical organ complications (Grade 1C).”
Is there ever a need to increase $\text{CaO}_2$?

- Three major causes of acute anemia exacerbations in sickle cell disease ($\text{Hgb decre} > 20 \text{ g/L from baseline} \pm \text{Hgb} < 50 \text{ g/L}$):
  - Aplastic crisis
  - Sequestration crisis
  - Hyperhemolysis

*excluding hemorrhage or artefact from overly aggressive hydration
Aplastic crisis

- Most commonly due to erythrovirus (parvovirous B19)
  - 1 week latency from infection, then fever (90%), pain (60%), acute splenic sequestration (20%), and acute chest syndrome (10%)\(^1\)
  - 2 weeks later: erythematous rash and arthropathy x 2-3d, then severe reticulocytopenia (< 50 x 10\(^9\)/L)
- Reticulocytopenia lasts 1 week and then recovers as virus cleared by neutralizing antibodies
- Lifelong immunity following infection (~75% by age 20)
- As patients with sickle cell disease have RBC lifespan of only 16-20d, severe anemia may occur during interim (Hgb decr > 30 g/L)

\(^{\text{Smith-Whitley, Blood 2004;103:422}}\)
Aplastic crisis

- As fall in hemoglobin occurs over days, plasma volume has time to increase in compensation

- Further transfusions therefore risk volume overload; administer slowly and consider prophylactic diuretics

- For patients with humoural immunodeficiency IVIG 0.5 mg/kg weekly x 4 is reasonable

- Most patients with SCD have self-limiting disease

Anderson D, Trans Med Rev 2007;21(S1):S9
Splenic Sequestration Crisis

- Trapping of sickle erythrocytes in sinusoids results in massive enlargement of spleen (abd pain and distension) and severe anemia over a period of hours, accompanied by reticulocytosis.
  - May also be accompanied by thrombocytopenia and leukopenia.
- If untreated, can cause death from hypovolemic shock/anemia.
  - Hepatic sequestration rarer and less severe (liver not as distensible).
- ~25% incidence in pts with sickle cell disease, most common first 2 years of life, very rare after puberty.
- Chronic transfusions do not appear to decrease the risk of recurrence, which occurs in 50% of patients, although mortality rate decreases over time.

Owusu-Ofori, Cochrane Database 2002; CD003425.
Splenic Sequestration Crisis

- Post-transfusion hemoglobin levels often higher than expected, suggesting autotransfusion: sequestered RBCs released back into circulation
- Care must therefore be taken not to accidentally induce polycythemia with attendant risks of hyperviscosity; in children, advisable to administer transfusions in smaller than normal aliquots (eg., 3-5 mL/kg)
- Often a single transfusion is sufficient to reverse a sequestration crisis
Hyperhemolysis

- Broadly defined as a marked fall in hemoglobin with evidence of increased hemolysis and no other cause
- “Hemolytic crises” often observed in sickle patients in setting of vaso-occlusive pain episodes, or following exposure to certain medications
- More recently: recognition of a type of severe delayed hemolytic transfusion reaction in which post-transfusion RBC destruction accompanied by fall in Hgb to below pre-transfusion levels
  - Sometimes accompanied by transient “abnormally normal” reticulocyte count
- Cases may initially present as fever and pain: fall in hemoglobin occurs shortly after
- Two types
  - Acute (<7 days post-transfusion): often no evidence of new antibodies
  - Delayed (>7 days post-transfusion): new antibodies often detected in serum or eluate
Hyperhemolysis

- Serial hemoglobin electrophoresis demonstrates rapid clearance of transfused HgbA-containing RBCs.
- If only transfused RBCs cleared, however, then post-transfusion Hgb should be same as pre-transfusion level.
- Further fall in Hgb suggests “innocent bystander” autologous RBCs are also being destroyed at increased rate.
  - Increased complement sensitivity?
  - Macrophage activation syndrome?
- Furthermore, even in cases triggered by a delayed hemolytic transfusion reaction, matching for the new antibody doesn’t help: *transfusions just make the anemia worse*. 
Hyperhemolysis

- Case reports suggest beneficial effect of IVIG and high-dose steroids, with erythropoietin of potential benefit if accompanying reticulocytopenia
- In cases accompanied by acute organ failure, some have advocated
  - Eculizumab to mitigate hemolysis
  - Rescue transfusion preceded by rituximab if evidence of serologic incompatibility
- Once diagnosed, hyperhemolysis is a relative contraindication to all future transfusions

Win, Trans Med Rev 2010;24:64
Pirenne, Blood 2018; epub ahead of print
Transfusing to Decrease Whole Blood Viscosity
Transfusing to Decr HgbS%  

- Traditional goal of therapy is to decr HgbS to < 30% while keeping total Hgb < 110 g/L  
  - In patients with HgbSC, may be preferable to state goal as HgbA > 70%  

- Available RCT evidence limited to ability of transfusion to prevent complications in variety of high-risk settings:  
  - Pregnancy  
  - Perioperative  
  - Stroke prevention  

- Guidelines for *treatment* of complications based largely on observational studies and case series  
  - In some cases (eg., acute chest syndrome), there may no longer be clinical equipoise: placebo-controlled RCTs may be unethical
Transfusing to Decrease Whole Blood Viscosity

PROPHYLAXIS
Pregnancy

- HgbSS pts < 28 weeks gestation enrolled
  - Excluded if history of neurologic dysfunction or chronic disease of kidney, liver, lung, or coagulation
- All provided very close obstetric follow-up (bi-weekly until last month of pregnancy, then weekly)
- **Intervention**: 36 pts randomized to transfusion with goal of HgbS < 35% and total Hgb 100-110 g/L, starting weekly x 3 or until goals met
- **Control**: 36 pts randomized to receive transfusion only if Hgb < 60 g/L and retics < 3%, or in response to “medical or obstetrical indications”

Koshy, NEJM, 1988;319:1447
Pregnancy

- Chronic transfusion support resulted in
  - More RBC exposure (mean 12 units/pt vs 6.5 in control arm)
  - No significant decrease in adjusted gestational age or other obstetric complications
    - Trend towards worse outcomes with transfusion (perinatal death 15% vs 5%, neonatal death 6% vs 0%, stillbirth 10% vs 5%)
  - Far fewer maternal pain crises (14% vs 50%) and other non-pain sickle complications (19% vs 42%)
  - Note that maternal opioid exposure results in increased risk of neonatal abstinence syndrome (Am J Hematol. 2016;91:416)

- Conclusion: chronic transfusion useful to prevent maternal morbidity but no benefit to fetus, so long as very close obstetrical care provided

Koshy, NEJM, 1988;319:1447
Pregnancy

- Meta-analysis of RCT and observational data suggest there may yet be benefit to fetus, but quality of evidence poor
- Current guidelines discourage *routine* provision of transfusion support to pregnant women, but still support it for:
  - Women previously on hydroxyurea because of severe disease
  - Previous or current medical, obstetric or fetal problems related to sickle cell disease
  - Multiple pregnancy

Malinowski, Blood 2015;19:126
BCSH, Br J Haem 2017;176:192
Perioperative

- **TAPS Trial**: Patients with HgbSS/Sβ° undergoing low-moderate risk surgery randomized to two different perioperative transfusion strategies
  - 33 pts to supportive care only (no transfusion)
  - 34 pts to pre-op transfusion within 10d of procedure: top-up if Hgb < 90 g/L, partial exchange if Hgb > 90 g/L (goal of HgbS < 60%)
- 81% mod risk (eg., cholecystectomy, joint replacement), 19% low risk (eg., adenoidectomy, inguinal hernia repair)
- Exclusions included Hgb < 65 g/L, history of ETT for ACS
- Recommended perioperative management
  - IV fluids if NPO > 2 hrs pre-op
  - Keep SpO₂ >96%
  - DVT prophylaxis if immobile > 24 hrs

Howard, Lancet 2013; 381: 930
Perioperative

- Trial stopped early due to incr rate of serious adverse events in untransfused arm (33% vs 3%)
  - Most significantly acute chest syndrome: 9/33 if untransfused, 1/34 if transfused
  - Only 1 patient developed acute chest syndrome after low-risk surgery
- Median time to post-operative complications = 2.5 d
- Of patients in untransfused arm, 12% were transfused intraoperatively anyway, another 27% post-operatively (most for sickle complications, e.g. ACS)

Howard, Lancet 2013; 381: 930
Perioperative

- Surgeries without pre-op transfusion complicated by post-operative acute chest syndrome (9 of 33 patients)
  - Adenoido-tonsillectomy (3)
  - Laparoscopic cholecystectomy (2)
  - Tonsillectomy (1)
  - Laparoscopic splenectomy (1)
  - Umbilical hernia repair (1)
  - Shoulder arthroplasty and subacromion decompression (1)
- A 10th patient developed intra-operative bleeding requiring conversion of laparoscopic to open cholecystectomy, followed by acute chest syndrome
- 2/10 patients required ICU admission

Howard, Lancet 2013; 381: 930
# Perioperative: General Guidelines

<table>
<thead>
<tr>
<th>Risk</th>
<th>Example</th>
<th>Pre-op transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>• Skin, eyes, nose, ears, dental</td>
<td>Not required</td>
</tr>
<tr>
<td></td>
<td>• Distal extremities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Perineal, and inguinal areas</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>• Abdominal or orthopedic procedures</td>
<td>Top-up transfusion to 100 g/L (approx HgbS 60%); exchange if Hgb &gt; 90g /L</td>
</tr>
<tr>
<td></td>
<td>• Oropharyngeal procedures</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>• Intracranial, cardiovascular, or intrathoracic procedures</td>
<td>Exchange transfusion to HgbS of 30% (HgbA 70%)</td>
</tr>
<tr>
<td></td>
<td>• Scleral buckling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Intermediate-risk procedures in patients with significant comorbidities (eg., chronic pulmonary disease), or with baseline Hgb &gt; 90g/L</td>
<td></td>
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</tbody>
</table>
Stroke prevention

- **STOP**: maintaining HgbS < 30% in children with high MCA or ICA blood flow results by transcranial doppler results in 92% reduction in symptomatic stroke risk vs routine care

- **STOP2**: discontinuing transfusion results in rapid reversion to high-risk flows rates and 5% incidence of stroke within average of 4.5 months

- **SIT**: maintaining HgbS < 30% in children with normal TCDs but ≥ 1 silent infarct by MRI results in 57% decrease in new clinical or radiologic infarct

- **SWITCH**: in children with previous stroke, combination of hydroxyurea and phlebotomy (HgbS ~60%) not as effective as exchange transfusion (HgbS ~30%) in preventing stroke (10% vs 0% incidence)

- **TWITCH**: in children with high TCD flow and no previous stroke (or severe cerebral vasculopathy,) transitioning from ≥ 1 year of exchange transfusion to HU/phlebotomy resulted in improved TCDs and less iron overload

Adams, NEJM. 1998;339:5
Adams, NEJM. 2005;353:2769
Ware, Blood. 2012;119:3925
DeBaun, NEJM. 2014;371:699
Ware, Lancet. 2016;13;387
Stroke prevention

Conclusion

- Transfusion remains first line therapy for primary and secondary stroke prevention in children with sickle cell disease and pending further evidence should be continued indefinitely.

- In patients being transfused for secondary prophylaxis, must maintain HgbS% of <30% indefinitely (and continue monitoring: may not be sufficient to completely prevent progressive disease).

- In patients being transfused for primary prophylaxis, careful transition to hydroxyurea after > 1 year of transfusion may be feasible.

- No equivalent evidence to guide initiation of stroke prophylaxis in adults: if no obvious other explanation (e.g., cardioembolism) prudent to initiate chronic transfusion support.

- Implications of SIT trial are enormous (25-35% of SSD children have silent infarcts!) For now, initiation of transfusions should be considered on case-by-case basis (BCSH, Br J Haem 2017;176:192).
Transfusing to Decrease Whole Blood Viscosity

TREATMENT
Acute Chest Syndrome

- Standard definition encompasses a broad range of disease severity: new pulmonary infiltrates on CXR accompanied by respiratory symptoms, chest pain or fever.
- May be triggered by infection or marrow embolism; specific cause not identified in ~60% of cases despite extensive investigations.

Vichsinky, NEJM 2000;342:1855
Wayne, Blood 1993;1811109
Acute Chest Syndrome

- Largest observational study of 671 episodes noted\(^1\)
  - 72\% of pts received transfusions, ~2/3 of them top-up transfusions
  - Transfusion associated with improvement in gas exchange (PO\(_2\) 68 → 71 mmHg and SpO\(_2\)% 91\% → 94\%)
  - Simple and exchange transfusions resulted in “similar” improvements (data not shown)
- However, an earlier case series reported that 40\% of patients referred for exchange transfusion for ACS had failed earlier attempt at top-up transfusion.\(^2\)
- Improvement usually occurs within 24 hours of transfusion

Vichsinky, NEJM 2000;342:1855
Wayne, Blood 1993;181109
Acute Chest Syndrome

In absence of RCT evidence, authorities recommend transfusions for all patients with symptomatic ACS and either a Hgb decr ≥ 10 g/L from baseline or worsening O2 requirements. Exchange transfusions for patients with poor prognostic markers.

Physical exam
- Altered mental status
- Persistent HR > 125/min
- Persistent RR > 30 or other evidence of incr work of breathing
- Temp > 40C
- Hypotension vs baseline

Lab/radiologic findings
- Arterial pH < 7.35
- SpO2 persistently < 88% despite aggressive ventilatory support
- Serial decline in SpO2% or A-a gradient
- Hgb decr by ≥ 20 g/L
- Plts < 200/fL
- Elevated BNP or troponin
- Evidence of multiorgan failure
- Pleural effusion
- Progressive pulm infiltrates

Johnson, Hematol Oncol Clin N Am 2005:19;857
Selection of RBCs
Prevention of Alloimmunization

- Approx 25% of patients with SSD will become alloimmunized from transfusion.
- Traditionally assumed to represent differences in antigen expression between typical donor and sickle cell patient.
- Evidence also emerging of a “responder” phenotype who sensitizes readily to transfusions.
- Episodic transfusion also seems to carry higher risk than chronic.

Table 3. Average Frequencies of RBC Alloantibodies Made By Transfused Patients With SCD

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Average frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-E</td>
<td>21</td>
</tr>
<tr>
<td>Anti-K</td>
<td>18</td>
</tr>
<tr>
<td>Anti-C</td>
<td>14</td>
</tr>
<tr>
<td>Anti-(\text{Le}^a)</td>
<td>8</td>
</tr>
<tr>
<td>Anti-(\text{Fy}^a)</td>
<td>7</td>
</tr>
<tr>
<td>Anti-(\text{Jk}^b)</td>
<td>7</td>
</tr>
<tr>
<td>Anti-D</td>
<td>7</td>
</tr>
<tr>
<td>Anti-(\text{Le}^b)</td>
<td>7</td>
</tr>
<tr>
<td>Anti-S</td>
<td>6</td>
</tr>
<tr>
<td>Anti-(\text{Fy}^b)</td>
<td>5</td>
</tr>
<tr>
<td>Anti-M</td>
<td>4</td>
</tr>
<tr>
<td>Anti-E</td>
<td>2</td>
</tr>
<tr>
<td>Anti-C</td>
<td>2</td>
</tr>
</tbody>
</table>

Josephson CJ, TMR 2007;21:118
Detection of Alloantibodies

- In patients with sickle cell disease, 30-50% of antibodies will be detectable on at least one occasion 1 year after they were first observed.
- Episodic transfusions in different hospitals increases risk of DHTRs and possibly hyperhemolysis.
- In one study, 4.2% of adult deaths in SSD were due to DHTRs!

Vichinsky E, Semin in Hematol 2001;1(S1):14
Ngo Blood 2014;124(21):abstract 2715
Prevention of Alloimmunization

- Extensive matching has diminishing yields and can be challenging

<table>
<thead>
<tr>
<th>Matching protocol</th>
<th>% of immunizations that would have been prevented beyond ABO/D matching</th>
<th>% of transfused SSD who would never make an antibody</th>
<th>Frequency of required phenotype in Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh (C,c,D,E,e)</td>
<td>37.2%</td>
<td>82.3%</td>
<td>15%</td>
</tr>
<tr>
<td>Rh and K</td>
<td>53.3%</td>
<td>87.5%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Rh, K and S</td>
<td>55.5%</td>
<td>88.3%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Rh, K, S and Fy(^a)</td>
<td>62.8%</td>
<td>91.2%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Rh, K, S, Fy(^a), Jk(^b)</td>
<td>70.8%</td>
<td>93.4%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Note: in this study, only 137 of 351 (39%) of SSD patients transfused RBCs matched for just ABO/RhD made an alloantibody

Castro, Transfusion 2002;42:684
Prevention of Alloimmunization

- Generally accepted that prophylactic Rh and Kell system matching for common, clinically significant antibodies (D, C, c, E, e, K) is indicated for all sickle patients.
- More intensive prophylactic matching within other blood systems indicated for patients at higher risk, e.g.:
  - Alloantibody already detected
  - Previous DHTR, even without detectable antibody (e.g., rapidly cleared HgbA% on post-transfusion HPLC)
  - Unknown ability to tolerate transfusions (e.g., ≤ 12 unit exposure)

Pirenne, Blood 2018; epub ahead of print
Reasons for Failure of Prophylactic Matching

- Laboratory/transcription error in phenotype of either donor or recipient
- Failure to notify blood transfusion service of patient diagnosis or previous transfusion history
- Inability to source antigen-typed units for urgent transfusion
- Genotype/phenotype discrepancy (e.g., partial Rh antigens)
  - ~1/4 patients with will phenotype as C+ but will be capable of making an anti-C; of these patients, 30% will seroconvert when given C+ RBCs and are at risk of DHTR/hyperhemolysis! (Tournamille et al, Transfusion, 2010;50:13)
Other Considerations

- Transfusion of HgbS-containing units (e.g., from sickle trait donors) may confound attempts to monitor response to transfusion but does not itself pose any significant harm to patients.

- Transfusion of fresh RBCs (e.g., < 7-10 days) may prolong interval between transfusions.

- The above considerations are of lesser importance than the provision of antigen-typed units.

- Genotyping of donors may allow more careful selection of RBCs and may be only feasible method for supplier to meet growing demand for antigen typed units, particularly for SCD pts.
Other Considerations

- However, sickle cell patients still stand to benefit from implementation of “low-tech” solutions:
  - Judicious ordering of blood products by clinicians (e.g., not for asymptomatic anemia or uncomplicated pain crisis)
  - Increase recruitment of donors from ethnic minority groups
  - Better communication between clinicians and laboratory regarding patient diagnosis
  - Better communication between hospital blood transfusion services regarding patient phenotype and antibody history (*tell your blood bank if your patient has ever been transfused elsewhere*)
### QUESTIONS/COMMENTS?

#### PRINCIPLES
- **Decr HgbS%**, generally more important than increasing total Hgb
- Benefit only with high-shear vasculature
- Ceiling of Hgb ~100 g/L

#### WEAK EVIDENCE WITH PREGNANCY
- Available evidence suggests more benefit for mom than developing fetus
- There may be exceptions (eg., signs of placental insufficiency, prev IUGR)

#### CAUTION WITH SEVERE ANEMIA
- Aplastic crisis: *volume overload*
- Sequestration: *autotransfusion*
- Hyperhemolysis: *worsening anemia*

#### GOOD EVIDENCE FOR STROKE PREVENTION
- Transfusion indicated for all children with high-risk dopplers and history of stroke
- Smaller value for children with SCIs
- Limited evidence in adults; look for other causes, caution with hemorrhagic stroke

#### NUANCED APPROACH FOR SURGERY
- Usually not needed for low-risk patient with low risk procedure
- Indicated for everyone else, top-up vs exchange depends on comorbidity, procedure risk, baseline hemoglobin

#### THERAPEUTIC TRANSFUSION IF ACUTE ORGAN COMPROMISE
- Limited evidence, but consensus supports transfusion for acute stroke, acute chest syndrome, sickle hepatopathy
- Other situations: “if all else fails”

#### SELECTION OF RBCs MUST BE DONE WITH CARE!
- Tell your blood bank early that your patient has sickle cell, provide detailed transfusion history