Red Cell Transfusion in unique patient populations: Sickle Cell Disease and the Thalassemias

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Outline

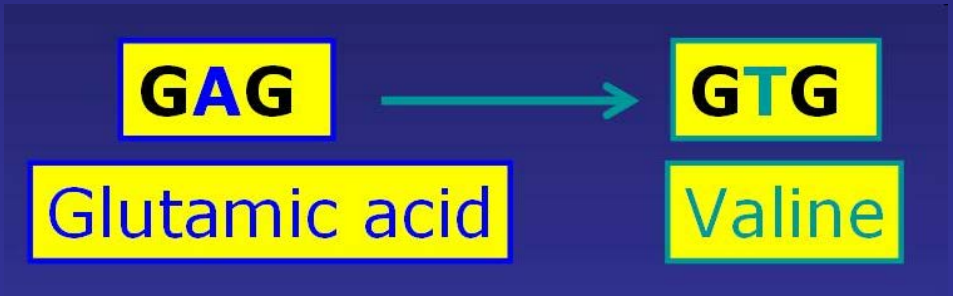
- Pathogenesis of Sickle Cell Anemia
- When to transfuse in SCD?
- Acute Chest Syndrome (XC or ST?)
- Literature regarding chronic transfusion to prevent primary strokes in kids
- Complications of Transfusion in SCD
- Brief Overview of Thalassemias
- When to transfuse in Thalassemia?

Sickle Cell Disease (SCD)

- Hgb SS — Sickle Cell Anemia
- Hgb SC
- Hgb S/β^0 — β thal major
- Hgb S/β+ — β thal minor

<u>βs Mutation</u>

- 6th Codon of the β Globin Gene



- Same mutation found in all βs genes around the world

SCD tissue damage: Two proposed, different, overlapping mechanisms

- Hemolysis → Free hemoglobin in plasma
  Free hemoglobin binds NO
  ↓ NO → vasoconstriction →
  pulmonary hypertension, leg ulcers, priapism, stroke
  (these events occur in the thalassemias – no sickle Hb)

- Hypoxia and/or inflammatory agents → vasculopathy
  Vasculopathy → endothelial adhesion of WBC, RBC
  Adhesion → vaso-occlusion →
  pain crisis, acute chest, avascular necrosis, bone infarcts

Mark Gladwin and Elliot Vichinsky, NEJM 2008 359:2254

Variability in SCD: genetic modulation of phenotype by epistatic genes

- Haplotype -> HbS mutation occurred at least 5 times -> Five different haplotypes in Africa, Mediterranean, Middle East & India: Different haplotypes have mild/mod/severe S/S disease
- Hemoglobin F -> HbF varies <1% to >20% in S/S pts: 1% severe, 20% almost asymptomatic
- Alpha Thalassemia inheritance is independent of HbS inheritance, 1, 2 or 3 gene deletion: alpha thal lessens severity proportional to number of deletions (decreases MCHC -> decrease in polymerization)
- Hgb Sβ^0 thal have a wide range of severity depending on thalassemia gene
- Hgb SC is milder for hemolytic-related events (longer RBC half life) but can be worse for vasculopathy-related events (higher Hct)

Steinberg M. Management of Sickle Cell Disease, NIH Publ 04-02117:173, 2004

Cooperative Study of Sickle Cell Disease (CSSCD)

Natural History of SCD: prevalence of clinical events

Prospective cohort of ~ 3800 pts enrolled (1979-99)

Third Phase completed in 1999: Newborn cohort of 694 babies

Published > 40 papers w/ this data

Trial	Therapy Tested (Type of Trial)	Outcome (Reference)
PROPS I	Prophylactic penicillin in infants (Phase III)	Pneumococcal sepsis prevented in infants (8)
PROPS II	Prophylactic penicillin in children (Phase III)	Penicillin prophylaxis can be safely stopped at age 5 (40)
Hydroxyurea Phase II Trial	Hydroxyurea in adults (Phase II)	Hydroxyurea can be safely given to adults with SCD-SS (41)
MSH Trial	Hydroxyurea in adults with severe sickle cell anemia (Phase III)	Hydroxyurea lowered rate of painful events, blood transfusions, acute chest syndrome, and hospitalizations by 50 percent (42,43)
PED HUG (HUG KIDS)	Hydroxyurea in children (Phase II)	Hydroxyurea can be safely given to children between the ages of 5 and 15 (47)
Perioperative Transfusion Trial	Simple blood transfusions to raise the total Hb level to 10 g/dL regardless of Hb S concentration, compared to aggressive blood transfusions to suppress Hb S level to below 30 percent at time of surgery in children and adults (Phase III)	Simple blood transfusions can be safely given during the perioperative period to raise Hb concentration to 10 g/dL (48)
STOP Trial	Blood transfusions to prevent stroke in children (Phase III)	First-time stroke can be prevented in children found to be at risk by periodic blood transfusions to suppress Hb S concentraion to less than 30 percent (49)

Transfusion Considerations in SCD

- SCD patients have normal or increased total blood volume -> Vasodilated -> Volume sensitive
- Increased viscosity of deoxy or oxy sickle blood
- Transfusion of normal RBCs to sickle pt increases viscosity when HbS is > 60%
- Tissue oxygenation reduce in SCD patients when transfused hct >30%

Goals of Transfusion for SCD

- Improve oxygen carrying capacity
- Decrease blood viscosity and improve blood flow by diluting RBCs with hgbS
- Suppress endogenous hgb SS erythropoiesis by increasing tissue oxygenation

Exchange Transfusion

- Advantages
  - Can remove 66% of patient RBCs with a single volume exchange
  - 95% of patient RBCs with a 2 volume exchange
  - Minimizes iron accumulation/overload
  - Rapid reduction of Hb S percent
  - Eliminates risks of increase viscosity
- Disadvantages
  - Requires venous access
  - Multiple units of RBCs
  - Requires trained, skilled ahperesis RNs

Transfusion Indications in SCD

Simple Transfusion

Acute	Chronic**
Acute Chest Syndrome	Prevention of first stroke in kids
Symptomatic anemia	Prevention of recurrent strokes in kids
Prior to surgery requiring general anesthesia	Complicated pregnancy
Red Cell Aplasia	Chronic hypoxic lung dz
Splenic sequestration	Chronic heart failure
Hepatic sequestration	Chronic renal failure
Acute Organ Failure	
Sepsis & Mengitis	

Exchange Transfusion (RBC)

- Acute Chest Syndrome
- Acute Neurologic Event
- Acute Multiorgan failure
- Prior to surgery for CNS and posterior segment of the eye

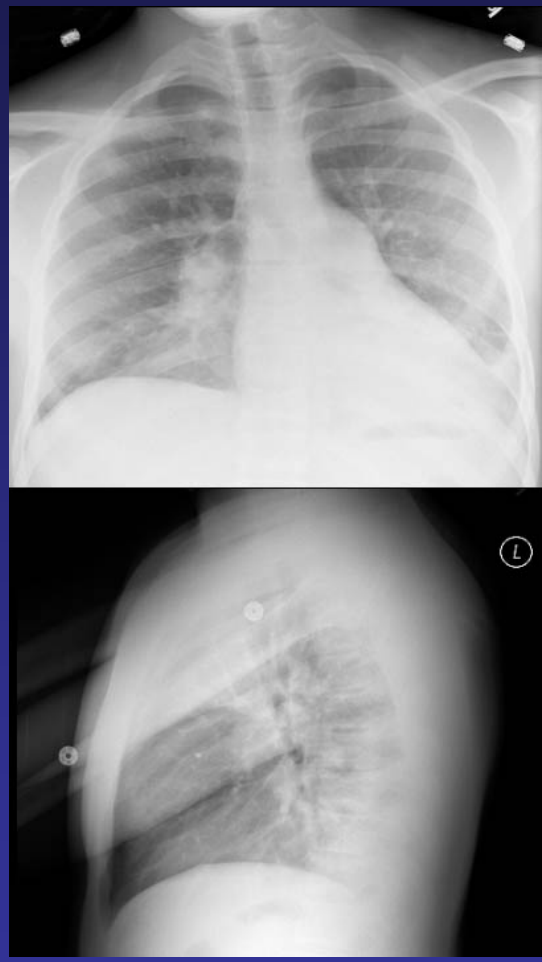
**transfusions q3-4 wks with primary goal to maintain hgb S [ ] 30% or less

Controversial Indications for Acute or Chronic Transfusion in SCD

- Recurrent Acute Chest Syndrome
- Prevention of Pulmonary Hypertension / Cor Pulmonale
- Priaprism
- Acute pain episodes
- Normal Pregnancy
- Leg Ulcers

Acute Chest Syndrome (ACS)

- Occurs in 40- 50 % of Hb SS pts
- Leading cause of morbidity and mortality in sickle cell disease
- Pathogenesis unclear
- 1. Presence of a new pulmonary infiltrate, not due to atelectasis, involving at least one complete lung segment
- 2. Chest Pain
- 3. Temp > 38.5 C
- 4. Tachynea, wheezing, cough
- 5. Hypoxia



Etiology of ACS

Unknown Cause	46% overall
Pulmonary infarction	16%
Fat embolism with or w/o infection	9%
Chlamydia pneumoniae	7%
Mycoplasma pneumoniae	7%
Viral infection	6%
Mixed infections	4%
Other pathogens	1%

Management of ACS

- Primarily supportive
- Antibiotics
- Supplemental oxygen
- Bronchodilators
- Hydration
- Simple Transfusion with HbS neg RBCs
- Exchange Transfusion with HbS neg RBCs
- Goal HbS <30%
- Goal Hct is 30%

Exchange versus simple transfusion for acute chest syndrome in sickle cell anemia adults

Volume 49, May 2009 **TRANSFUSION**

Jeff M. Turner, Jason B. Kaplan, Hillel W. Cohen, and Henny H. Billett

- Retrospective study from single institution (Montefiore)
- Selected first 20 pts either SS or SB^0 received exchange transfusion (XC) for Acute Chest Syndrome
- Control group: First 20 pts either SS or SB^0 received simple transfusion (ST) for Acute Chest Syndrome
- Primary Outcome: Post-procedure length of stay
- Underpowered Study
- 9 out of the 20 XC patients received ST at least 24 hours before the XC

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice–Evidence-Based Approach from the Apheresis Applications Committee of the American Society for Apheresis

Zbigniew M. Szczepiorkowski,[1*†] Jeffrey L. Winters,[2*] Nicholas Bandarenko,[3*] Haewon C. Kim,[4*] Michael L. Linenberger,[5*] Marisa B. Marques,[6*] Ravindra Sarode,[7*] Joseph Schwartz,[8*] Robert Weinstein,[9*] and Beth H. Shaz[10*]

Journal of Clinical Apheresis 25:83–177 (2010)

Incidence: 289 per 100,000 African-Americans, 89.8 per 100,000 Hispanics primarily from Caribbean islands (1 in 375 for Hb SS, 1 in 835 for Hb SC, 1 in 1,667 for Hb S/β-thalassemia among African-American live births)

Procedure	Recommendation	Category
RBC exchange	Grade 1C	I (Acute stroke)
		II (Acute chest syndrome)
RBC exchange	Grade 1C	II (Prophylaxis for primary or secondary stroke prevention of transfusional iron load)
RBC exchange	Grade 1C	
RBC exchange	Grade 2C	III (Multiorgan failure)

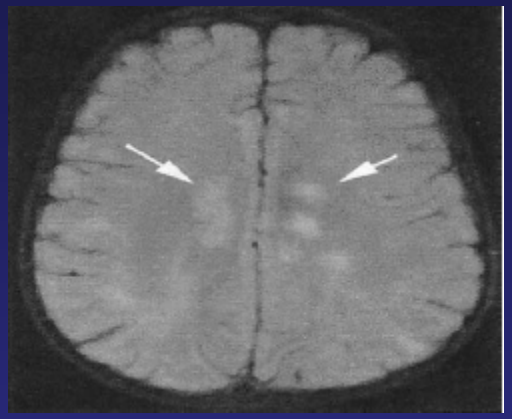
# of reported patients*: >300

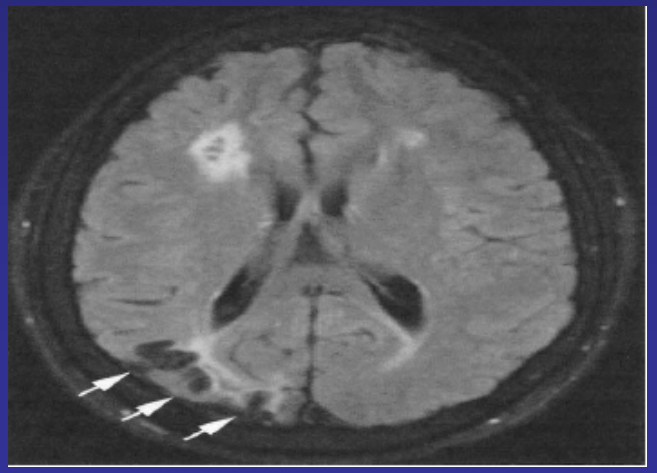
	RCT	CT	CS	CR	Type of evidence
Acute stroke	0	0	7 (160)	7 (9)	Type II-3
Acute chest syndrome	0	0	12 (142)	8 (8)	Type II-3
Prophylaxis for primary or secondary stroke prevention of transfusional iron load	0	0	18 (310)	3 (3)	Type II-3
Multiorgan failure	0	0	3 (10)	2 (2)	Type II-3

Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Stroke in Sickle Cell Disease:

- Second leading cause of death in kids with SCD
- Affects 15-25% of patients with Hb SS
  - Thrombotic peak age 7-10 yrs
  - Hemorrhagic (subarachnoid) more common in the second decade of life



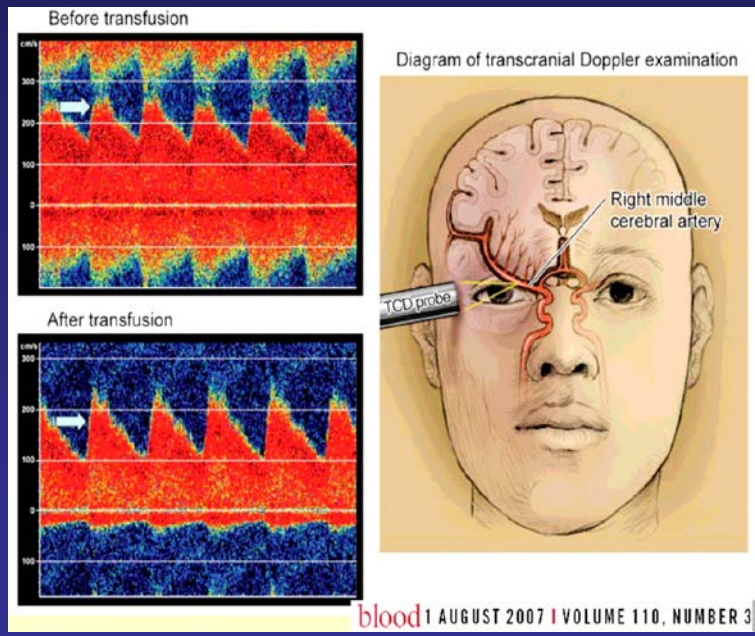


PREVENTION OF A FIRST STROKE BY TRANSFUSIONS IN CHILDREN WITH SICKLE CELL ANEMIA AND ABNORMAL RESULTS ON TRANSCRANIAL DOPPLER ULTRASONOGRAPHY

ROBERT J. ADAMS, M.D., VIRGIL C. MCKIE, M.D., LEWIS HSU, M.D., PH.D., BEATRICE FILES, M.D., ELLIOTT VICHINSKY, M.D., CHARLES PEGELOW, M.D., MIGUEL ABBOUD, M.D., DIANNE GALLAGHER, M.S., ABDULLAH KUTLAR, M.D., FENWICK T. NICHOLS, M.D., DUANE R. BONDS, M.D., AND DONALD BRAMBILLA, PH.D.

N Engl J Med 1998;339:5-11.

- STOP I Stroke Prevention Trial in Sickle Cell Anemia
- 130 kids at risk for stroke with abnormal transcranial doppler (TCD)
  - 63 randomized to receive transfusions
  - 67 randomized to receive standard care

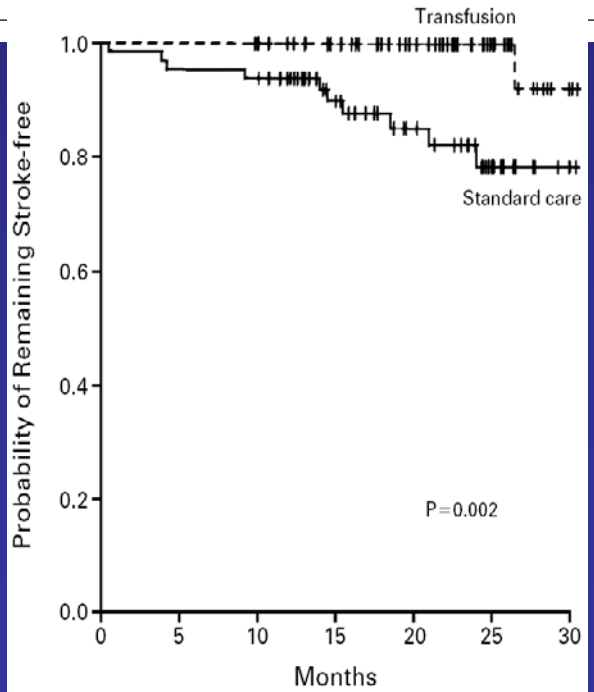


STOP I Stroke Prevention Trial in Sickle Cell Anemia

- Elevated TCD velocity associated with increased stroke risk (10% per yr)
- Chronic pRBC transfusions produces a 90% reduction in the rate of first time strokes in children with a high risk TCD velocity.

TABLE 2. LENGTH OF FOLLOW-UP AND NUMBER OF PRIMARY EVENTS.

VARIABLE	TOTAL (N=130)	TRANSFUSION (N=63)	STANDARD CARE (N=67)
Follow-up (mo)			
Total	2550	1321	1229
Median	21.1	22.2	18.3
Mean ±SD	19.6±6.5	21.0±5.7	18.3±7.0
No. of strokes	12	1	11
Cerebral infarction	11	1	10
Intracerebral hematoma	1	0	1



Discontinuing Prophylactic Transfusions Used to Prevent Stroke in Sickle Cell Disease

The Optimizing Primary Stroke Prevention in Sickle Cell Anemia (STOP 2) Trial Investigators*

N ENGL J MED 353;26 WWW.NEJM.ORG DECEMBER 29, 2005

- How long should kids with SCD who high risk TCD velocities be continued on prophylactic transfusion?
- Randomized to continue or halt transfusions after 30 months
- 14/41 in transfusion-halted group developed high risk TCD and 2 had strokes.
- None of the 38 kids in the continued transfusion group had a stroke or reversion to high risk TCD results
- Cessation of transfusion is associated with high risk of TCD reversion or stroke

Alloimmunization in SCD

- Well recognized & documented complication of transfusion therapy in SCD
- SCD pts have higher rates (15 - 40%) of alloimmunization compared to other groups receiving multiple transfusion
- Impart due to racial differences between red cell antigen frequency in donor and recipients
- Alloantibodies may be found in the circulation for yrs

Transfusion and Alloimmunization in Sickle Cell Disease

By Wendell F. Rosse, Dianne Gallagher, Thomas R. Kinney, Oswaldo Castro, Harvey Dosik, John Moohr, Winfred Wang, Paul S. Levy, and the Cooperative Study of Sickle Cell Disease

Blood, Vol 76, No 7 (October 1), 1990: pp 1431-1437

- 1814 SCD pts received transfusion
- Overall rate of alloimmunization of 18.6%
- Alloimmunization increased exponentially with the number of transfusions
- Alloimmunization occurred with < 15 units of pRBCs
- Most common antibodies were to E, C, Kell, Fya, Jkb and Lewis antigens

Volume 322 JUNE 7, 1990 Number 23

ALLOIMMUNIZATION IN SICKLE CELL ANEMIA AND TRANSFUSION OF RACIALLY UNMATCHED BLOOD

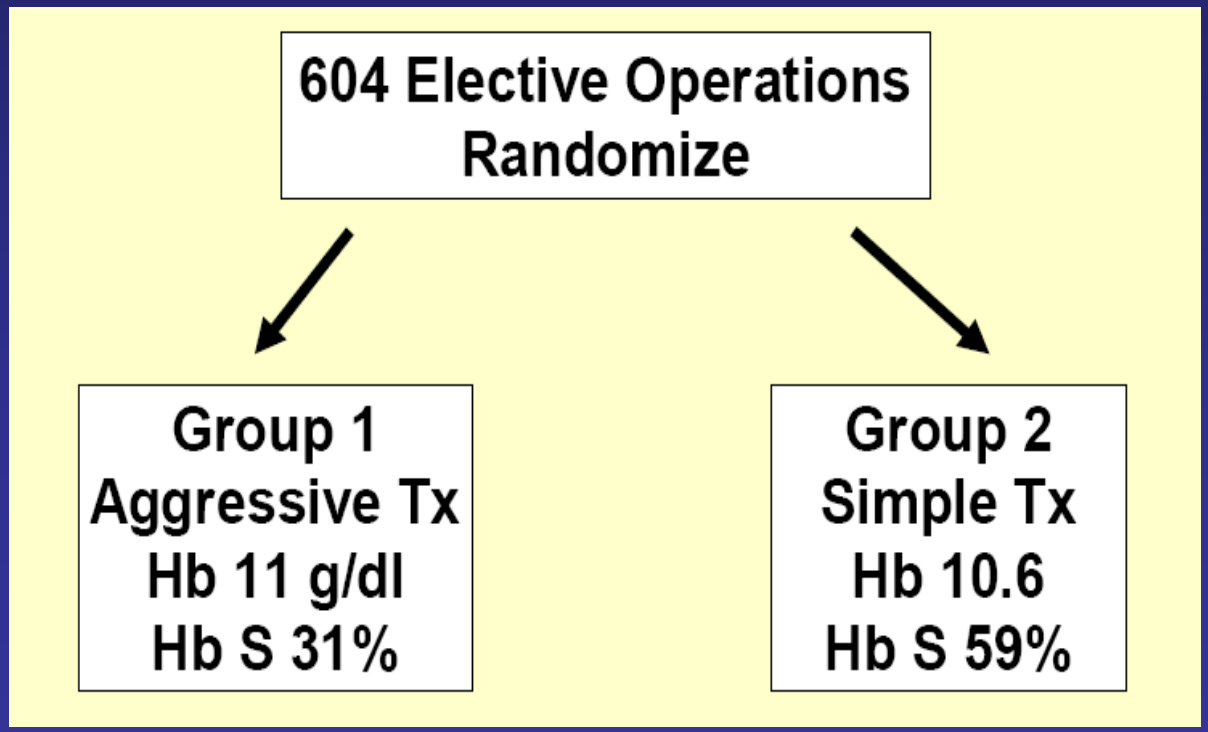
ELLIOTT P. VICHINSKY, M.D., ANN EARLES, P.N.P., ROBERT A. JOHNSON, M.D., M. SILVIJA HOAG, M.D., AMBER WILLIAMS, M.T., AND BERTRAM LUBIN, M.D.

- Prospective study of 107 transfused AA pts with SCD
- Control group: 51 nontransfused AA with SCD & 19 Caucasians multiply transfused
- Average alloimmunization rate was 30% compared with 5% with multiply transfused
- None of nontransfused SCD pts developed alloab
- 66% of all alloab directed against C, E, K antigens
- Increased alloimmunization rate in SCD pts due to RBC antigenic differences btwn AA & white donors

A COMPARISON OF CONSERVATIVE AND AGGRESSIVE TRANSFUSION REGIMENS IN THE PERIOPERATIVE MANAGEMENT OF SICKLE CELL DISEASE

ELLIOT P. VICHINSKY, M.D., CHARLES M. HABERKERN, M.D., LYNNE NEUMAYR, M.D., ANN NOONAN EARLES, R.N., P.N.P., DENNIS BLACK, PH.D., MABEL KOSHY, M.D., CHARLES PEGELOW, M.D., MIGUEL ABBOUD, M.D., KWAKU OHENE-FREMPONG, M.D., RATHI V. IYER, M.D., AND THE PREOPERATIVE TRANSFUSION IN SICKLE CELL DISEASE STUDY GROUP*

Perioperative Transfusion in Sickle Cell Disease Study



Group 1
57% got XC
5 RBCs

Group 2
2.5 RBCs

Alloimmunization rates in Perioperative Transfusion in Sickle Cell Disease Study

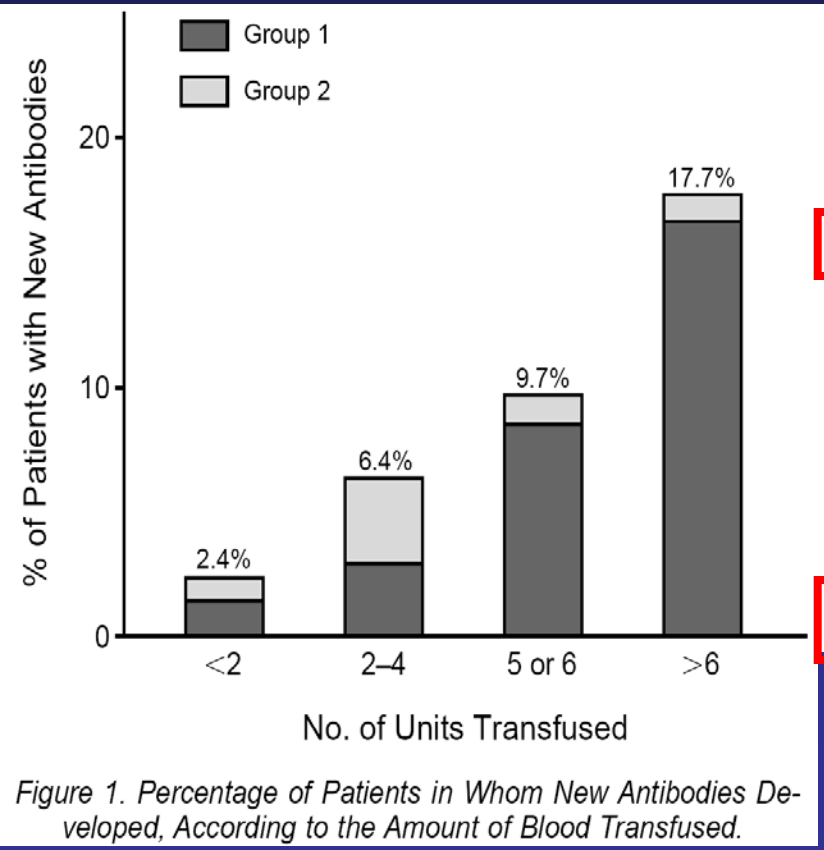


Figure 1. Percentage of Patients in Whom New Antibodies Developed, According to the Amount of Blood Transfused.

*Table 5. Transfusion-Related Complications.**

Complication	Group 1 (N = 303)	Group 2 (N = 301)	Odds Ratio (95% CI)
	no. of operations (%)		
New alloantibody†	31 (10)	14 (5)	2.33 (1.21–4.49)
Hemolysis			
Immediate	3 (1)	0	
Delayed	16 (5)	4 (1)	
Allergic reaction	0	3 (1)	
Anaphylactic reaction	1 (<1)	0	
Fever	4 (1)	4 (1)	
Fluid overload resulting in respiratory distress	3 (1)	0	
Other‡	3 (1)	0	
Any complication	41 (14)	22 (7)	2.15 (1.23–3.77)

Selection of Blood for SCD Patients

- Prophylactic limited phenotype matching (C, E, K) for all SCD pts
- Try to “honor” all clinically significant alloantibodies
- Prophylactic extended phenotype matching (usually Kidd & Duffy) for all SCD pts with alloantibodies
- Sickle negative pRBCs
- Leuko-reduced pRBCs
- Use of fresh pRBC (less than 7 days old)

Antibodies to High Incidence Antigens in Sickle Cell Patients

- Anti-U
  - 1/100 (1%) of Blacks lack U antigen
  - Virtually all whites have U antigen (U+)
  - Allo anti U can cause severe HTR and HDN
- Anti-hr^B (e variant)
  - 2% of all populations lack the hr^B antigen
  - Most hr^B negative individuals are Black
  - Presents as allo e in persons who are e+

Alloimmunization & Autoantibodies in SCD

- 7-10% of alloimmunized SCD patients developed auto-antibodies
- Typically IgG
- Panagglutinin
- Mimic allo like specificity
- Associated with development of AIHA

Factors to Consider in Providing "Matched" Red Cell Units in SCD

- Immunogenicity of the antigens:

  % of an antigen negative individuals who will make antibodies after single exposure to the antigen in question
- Ability of antibody to cause hemolysis (HDN or HTR)

Antigen	Immunogencity
Rh (D)	80
K	10
c,E	3
Fya	0.4
Jka	0.1

Factors to Consider in Providing "Matched" Donor Units in SCD

- Availability of antigen negative units is inversely proportional to antigen frequency in the donor population
  - the less common the antigen, the easier to find antigen negative units

- Differences in frequency of antigen expression between donor and recipients
  - (E-, C-, K-, Fya- Jkb- unit is 93% more likely to be found in an African American donor & only 8% likely in a white donor)
  - In NYC, only 8% of donors self identify as AA (Latinos ~ 12%)

Phenotype Matching of Donor Red Blood Cell Units for Nonalloimmunized Sickle Cell Disease Patients

A Survey of 1182 North American Laboratories

Arch Pathol Lab Med—Vol 129, February 2005

Melanie Osby, MD; Ira A. Shulman, MD

- 1182 labs in US & Canada
- 743 did not perform phenotype matching at all
- 330 matched for at least C E, Kell

Blood bank management of sickle cell patients at comprehensive sickle cell centers

Volume 47, November 2007 **TRANSFUSION**

Araba Afenyi-Annan, Monte S. Willis, Thomas R. Konrad, and Richard Lottenberg

- 49 academic centers in US & Canada surveyed in 2004
- 36 / 49 responded
- 27 (89%) used “matched” C E Kell
- 15 / 24 matched for additional antigens most commonly c e

Delayed Hemolytic Transfusion Reaction (DHTR)

- Especially problematic in SCD patients
- DHTR can mimic a pain crisis
- DHTR can even lead to a pain crisis
- Must have a high index of suspicion
- New alloantibody is detected in a recently transfused SCD pt, esp if DAT is positive

  -> consider DHTR.

Hyperhemolysis

- Severe hemolysis following blood transfusion in the absence of detectable clinically significant antibodies (CSA)
- Associated with post transfusion Hb levels below pre-transfusion levels
- Syndrome is often worsened by further transfusion
- Occurs in spite of phenotypically matched leuko reduced cell blood

Pathogenesis of Hyperhemolysis

Not well understood

1. Removal of antigen-negative autologous red cells by “bystander” hemolysis
2. Transfusion suppresses production of EPO and can result in marked reticulocytopenia

Management of Hyperhemolysis

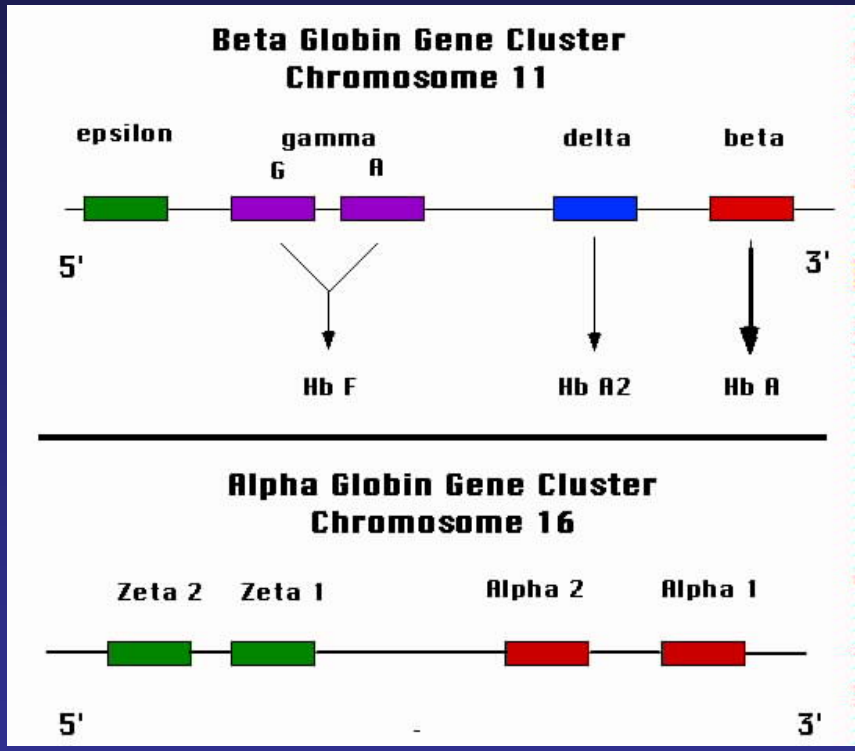
- Early recognition & diagnosis
- Monitoring of Hb S & Hb A levels may be beneficial in establishing the diagnosis.
- Avoid further transfusion if possible
- Steroid
- IVIG
- EPO

Summary

- Transfusion therapy has had a major impact in reducing morbidity & mortality of SCD
- 2/3 of patients with SCD do not become alloimmunized despite repeated stimulation
- Alloimmunization remains a controversial topic in which much of the debate centers around availability & cost of providing “matched” blood
- The major adverse outcome caused by transfusion in SCD is hyperhemolysis

Normal Hemoglobin

- Consist of 2 alpha-like chains & 2 non alpha chains
- Hb A = α2β2 97%
- Hb A2 = α2δ2 2.5%
- Hb F = α2γ2 0.5-1%
- 4 heme groups: one per globin: bind O_2
- Embryonic globins: zeta ξ epsilon ε



Mutations in Thalassemia

Beta Thalassemia

- Point Mutations (> 200)
  - Disrupt the regulatory sequences of beta globin production (decreased or absent)
- 90% are point mutations
- Genetic classification
  - β^0 absence of the synthesis of β globin
  - $\beta+$ reduction in the synthesis of β globin

Alpha Thalassemia

- Deletions involving segments of the alpha globin gene (s)
- Small DNA deletions remove one α gene
  - 3.7 rightward deletion
  - 4.2 left ward

  ($\alpha+$ phenotype)
- Large DNA deletions
  - Removes 2 α genes
  - Southeast Asian (SEA)

  (α^0 phenotype)

Clinical Classification of Beta Thalassemia

- β Thalassemia Major (Cooley's anemia)
  - β0 β0
  - Profound anemia (hgb < 7.0 d/dL)
  - Total transfusion dependence
- β Thalassemia Intermedia
  - β+ β0 or β+ β+
  - Thalassemia trait / carrier
  - Moderate to severe anemia
  - Occasional transfusion dependent
- β Thalassemia Minor
  - βA β0 or βA β+
  - Asymptomatic, very mild or no anemia
  - ↓ MCV, ↓ MCH, and ↑ HbA2 and HbF.

Thalassemia Intermedia

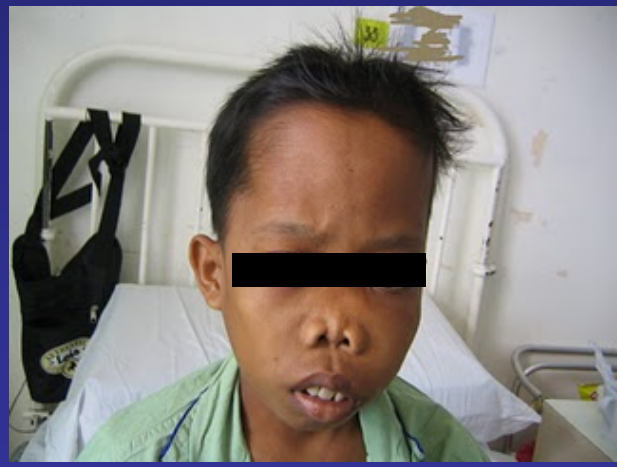
- Descriptive term
  - Includes β thalassemia with a broad spectrum of clinical phenotypes between the 2 extremes of asymptomatic thal trait to transfusion-dependent thal major
- From
  - Mild anemia (Hb 9-10 gm/dL) with or without splenomegaly
- To
  - Severe anemia (Hb ~6 gm/dL) and just capable of surviving without blood transfusions
    ? Severe thal intermedia or mild thal major

Normally refers to disorders of β rather than α thalassemia

Clinical Features of Beta Thalassemia Intermedia

Extremely Variable

- Anemia and jaundice, variable
  - Can present at 2-4 yrs -> transfusion dependent
  - Asymptomatic & diagnosis by chance hematological studies
- Splenomegaly
  - Usual but variable degree
- Growth and development
  - Normal to similar degree of retardation encountered in thal major
- Bone changes variable
  - None to severe



Thalassemia Intermedia - Management

1. Clinically guided with careful monitoring of:
   - Growth and development charts
   - Iron status
2. Folic acid supplementation
3. Blood transfusion as indicated
4. Iron chelation as indicated
5. Splenectomy may be indicated with falling hemoglobin levels & increasing spleen size
6. Treatment of extramedullary hemopoietic masses
   - Small doses radiotherapy
   - Hydroxyurea
   - Blood transfusion

Alpha Thalassemia Overview

Normal	αα/αα	
Silent Carrier	-α/ αα	
Alpha Thal Trait	-α/- α AA --/ αα SE Asian 2 gene deletion	Hgb range 10 – 11 gm/dL Microcytosis (MCV 65-75)
Hgb H β_4 tetramer	--/-α 3 gene deletion	Hgb range 6 – 9 gm/dL Microcytosis (MCV 55-65) HSM Some are Transfusion Dependent
Hgb Bart's Hydrops Fetalis γ_4 tetramer	--/-- 4 gene deletion	 Die in utero or shortly after birth Transfusion Dependent In Utero

Goals of Transfusion Therapy

- Increase oxygen carrying capacity by correcting anemia
- Preventing progressive hypersplenism
- Suppressing ineffective erythropoiesis
- Reducing GI absorption of iron

Indications for Transfusion

- Initiated in childhood when symptoms & signs of anemia are present including growth retardation & failure to thrive.

- Prevent facial & skull deformity

- Progressive hypersplenism to delay splenectomy

Beta Thalassemia	Alpha Thalassemia
β Thalassemia Major	Hydrops Fetalis
β Thalassemia Intermedia	Hemoglobin H disease

Deciding to Begin Transfusion Therapy in Thalassemia

- “The decision to initiate regular red blood cell transfusions is one of the most important—and sometimes most difficult—steps in the management of thalassemia. Regular red blood cell transfusions not only distinguish thalassemia major from thalassemia intermedia but also commit the patient to long-term chelation therapy to control the transfusional iron loading.”
- “Children who are growing poorly and developing disfiguring bone changes will benefit from regular transfusions even if their hemoglobin levels are 8 to 9 g/dL. On the other hand, children who are asymptomatic at hemoglobin levels of 7 to 8 g/dL may have little to gain from transfusions. Hemoglobin levels below 7 g/dL are usually associated with problems related to both the anemia and the compensatory erythropoiesis. When the hemoglobin level is consistently less than 7 g/dL, there is usually little to be gained from delaying transfusion.”

Patricia J. Giardina, Bernard G. Forget. Hoffman: Hematology: Basic Principles and Practice, 5th ed.

Guidelines for Transfusion in Thalassemia

1. Obtain a complete red blood cell antigen profile before the first transfusion.

2. Administer 10 to 15 mL/kg of red blood cells every 2 to 4 weeks to maintain the pretransfusion hemoglobin level above 9 to 10.5 g/dL.

3. Use leukoreduced washed red blood cells that have been stored for less than 7 to 10 days.

4. Avoid the use of first-degree relatives as blood donors.

5. For patients who come to a new center after receiving transfusions elsewhere, contact the previous blood bank for information about alloantibodies.

Patricia J. Giardina, Bernard G. Forget. Hoffman: Hematology: Basic Principles and Practice, 5th ed.

Chelation Therapy

- Serum Ferritin 1000 mcg/dL
- SQ infusion of desferoxamine over 8 to 12 hrs, 5 to 7 days a week
  - Neurosensory toxicity
- Deferasirox (Exjade) qD oral treatment
  - Neutropenia

Summary

- Thalassemia - Quantitative Globin Disorders
  - Pathophysiology results from globin chain imbalance
- Decreased Hb production leads to cardiovascular compromise, impaired linear growth & excessive marrow expansion
- Transfusion to suppress ineffective erythropoeisis is the mainstay of therapy