

Improved Survival of Children with Sickle Cell Anemia and Stroke who Continue Blood Transfusion after Transition into an Adult Program

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Cardeza Foundation

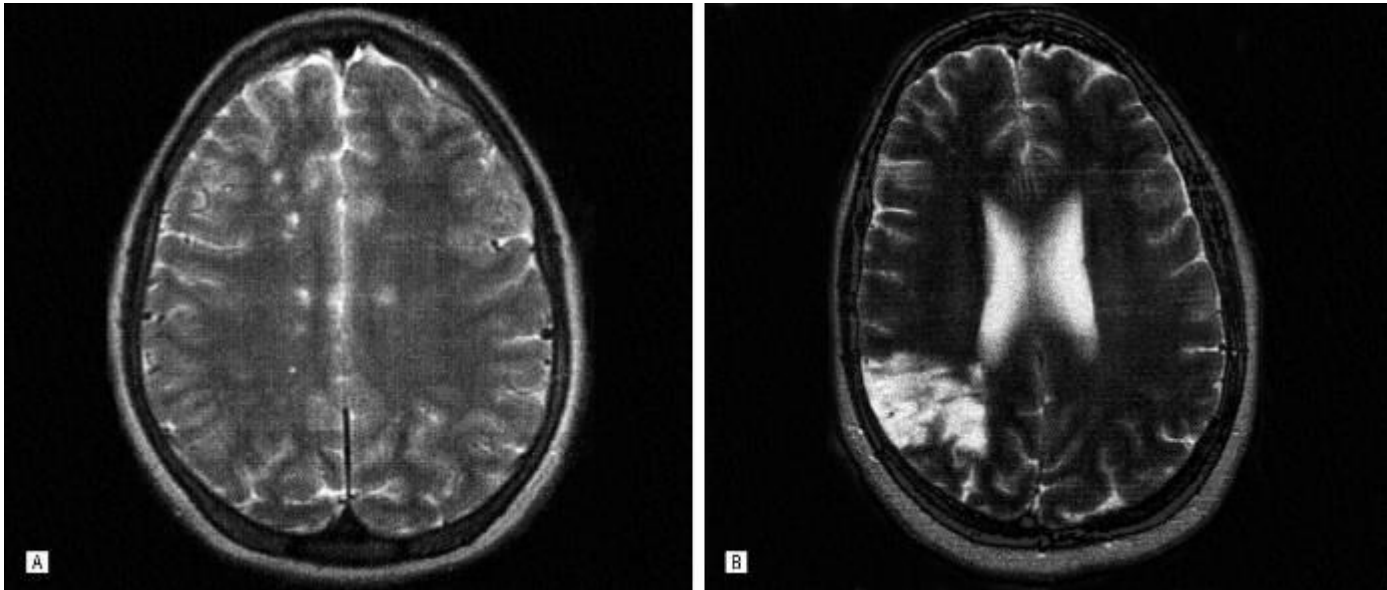
Thomas Jefferson University

Philadelphia, PA

Stroke (Cerebral Vasculopathy) in SCD

- **Incidence:** About 10% in Children < 20 Y with SS
- **Types:** Overt, Silent
- **Overt Stroke:**
 - Signs & Symptoms: Sensory, motor, seizure
 - Types: Infarctive, Moyamoya, Hemorrhagic,

Silent infarcts (A) versus ischemic infarct (B)



Stroke in SCD

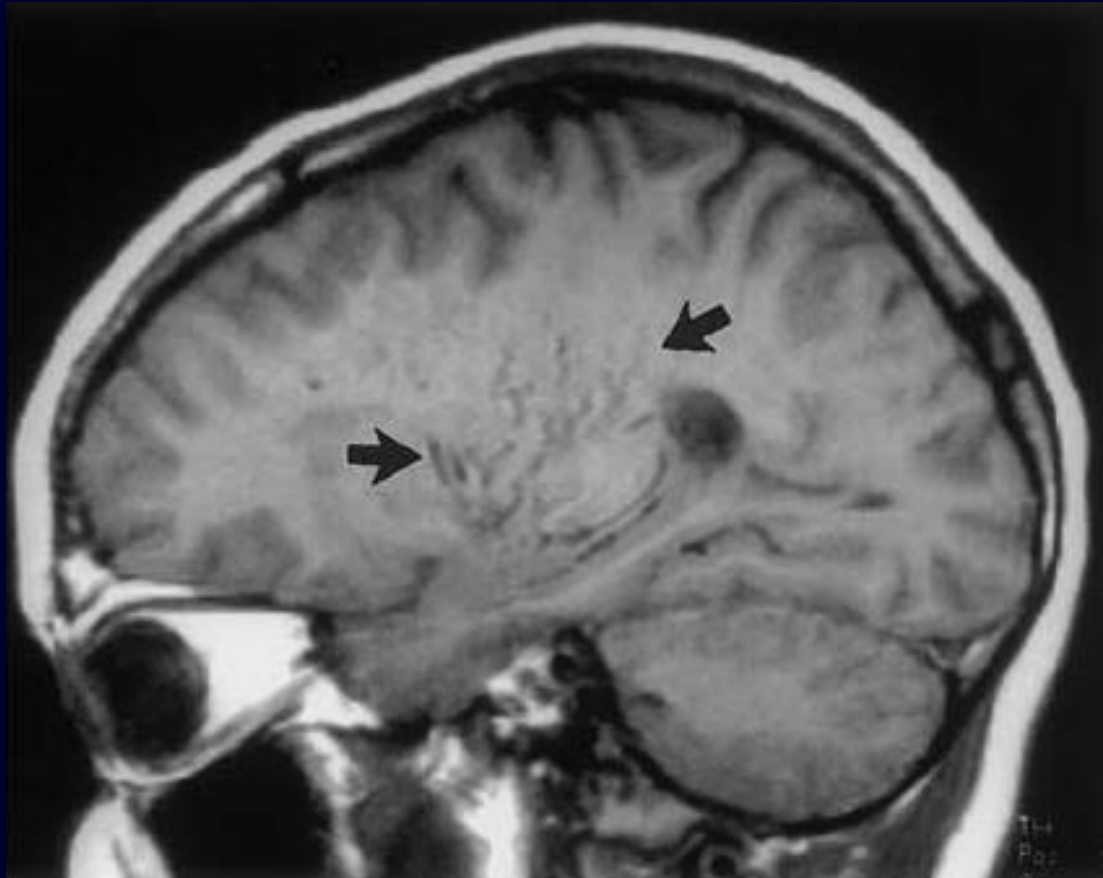
- **Infarctive**

- An acute neurological syndrome resulting from impaired cerebral blood flow without evidence of hemorrhage.

- **Moyamoya**

- Abnormal vascular network (“puff of smoke” appearance) indicative of collateral circulation secondary to stenosis or occlusion of large cerebral arteries

Cerebral Scan of Adult SCD Patient With Moyamoya Lesions



JAMA[®]

The Journal of the American Medical Association

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Stroke in SCD

- **Management**

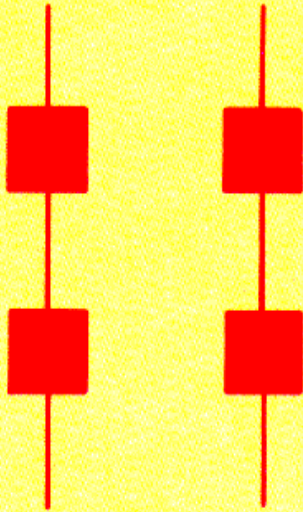
- Blood Transfusion/Exchange on a Regular Basis without Interruption
- Failure to Transfuse Results in Recurrence of Stroke
- Problems Arise after Transition to Adult Programs
- Little or no Data after transition

- **This Study** Reports the outcome of 22 Pts with SS and Stroke after transition to our Adult Program: 1993-2009

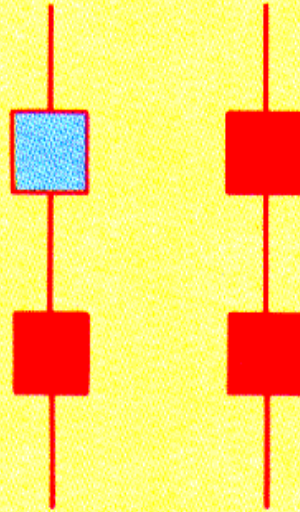
Patients & Methods

- **Records** were kept prospectively.
- **Blood Bank/Transfusion** data were computerized according to FDA and AABB regulations.
- **Blood counts** and **% Hb S** were done before and after each transfusion.
- Hb S was kept below 30% & total Hb 9-10 g/dl
- **Metabolic profiles** were done every 6 months or more often if needed.
- **Molecular diagnostics** including alpha genotypes and beta globin haplotypes were done by described methods.
- **Statistical analysis** was by the 2-tailed *t* test

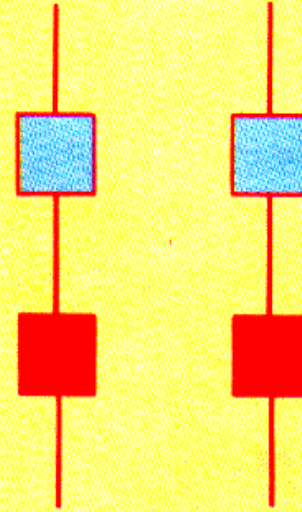
Normal



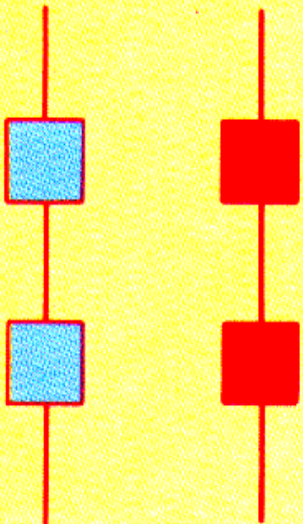
α^+ trait



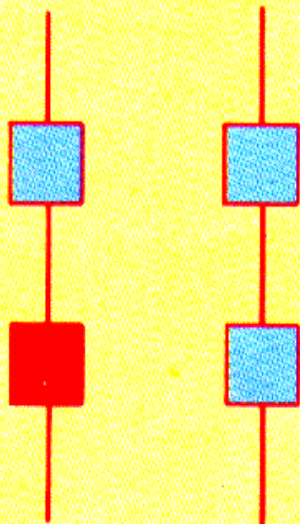
Homozygous α^+ trait



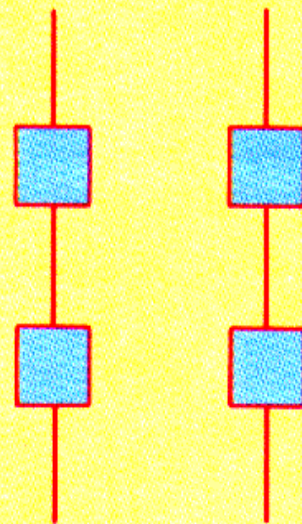
α^0 trait

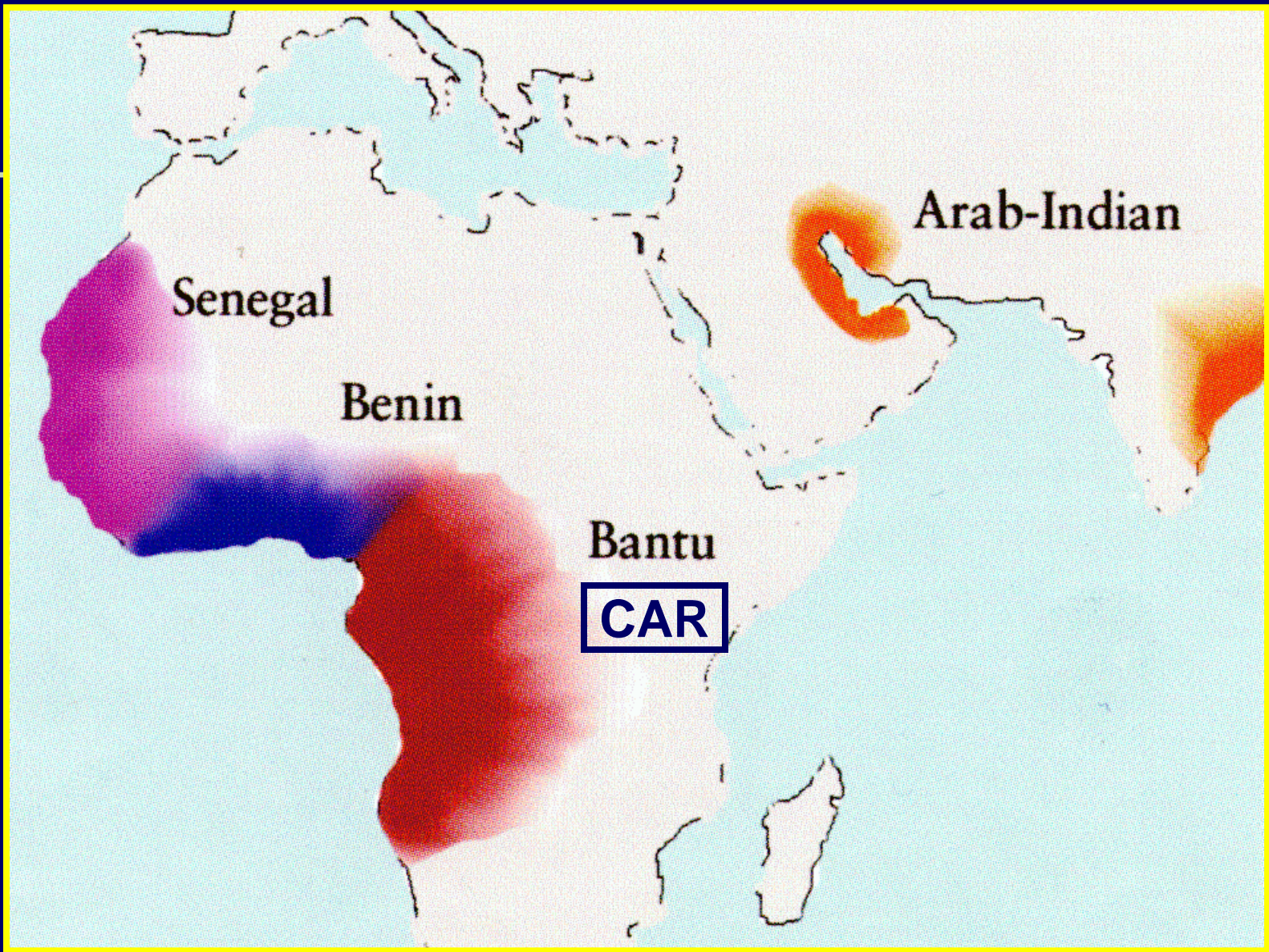


Hb H disease



Hydrops fetalis





Results-Continued

- No **alpha gene** deletion was detected in 18 (82%) patients, 4 had one alpha gene deletion and none had 2 alpha gene deletion.
- The Ben/CAR **haplotype** was found in 7 patients, Ben/Ben in 5, Ben/Sen in 4 and other combinations in 6 patients; 21 patients were heterozygous for the Ben haplotype.
- **Hb F** was 1.0-7.0% except for one patient on hydroxyurea (HU) with 20% Hb F.

Results

- All patients were kept on the same regimen of transfusion they had as children
- 15 were kept on exchange transfusion two of whom were non-compliant
- Two were kept on simple transfusion plus HU
- The remaining 5 refused to have chronic blood transfusion and were kept on standard care. One of these 5 patients agreed to be on HU.
- All patients had ischemic strokes during childhood
- One had hemorrhagic stroke superimposed on cerebral infarction.
- Two patients developed moyamoya after transition.

Table 1. Demographics of Patients Studied

Variable	Males	Females	Total
Number	10	12	22
Age Stroke Diagnosed	10 ± 4.78 (3 – 18)	9.3 ± 3.25 (4-16)	9.6 ± 4.03 (3-18)
Age Transitioned	23.2 ± 2.32 (20-28)	21.7 ± 3.47 (18-29)	22.4 ± 3.10 (18-29)

Table 2. Characteristics of patients Studied

Variable	Patients with Transfusion	Patients with Standard Care
Number	17	5
Nonadherent	2	5
Admissssions /y	3.7 ± 0.94	5.7 ± 5.00 *
Deceased n,%	2, 12%	5, 100%
Age of Deceased n,age	(2) 28.5 ± 1.5	(5) 26.4 ± 3.44
Age of living	35.4 ± 5.92 **	N/A

*p<0.025

**p<0.001

Table 3. Characteristics of patients Studied

Variable	Patients with Transfusion	Patients with Standard Care
Number	17	5
Units Transfused/Y	47±17(11-120)	15±5.5(6-22)
# Alloimmunized	10	2
Antibodies	1-6	1-6
Serum Ferritin ng/ml	1405	4005*

* p <0.05

Alloimmunization

- 12 Patients were alloimmunized with 36 Antibodies
 - Number per patient varied from 1-6
- Most common Ab's were:
 - Anti-K (6), -E(5), -Go^a(3), -HLA(3), -C(3), -D(2), -Cold(2)
AND
- One Ab Each of:
 - Anti-A1, Jk^b, Fy^a, Kp^a, Sd^a, I, M, Le^a, V-VS, Rg^a, Warm and unknown specificity

Causes of Death

- Patients Without Regular Transfusion

- Massive infarct 1
- Massive intraventricular hemorrhage 1
- Sudden during crisis 3

- Nonadherent Patients

- ARDS 2

Signa 1.5T SYS#KBR0000

Thomas Jefferson Univ Hosp MRI

Ex:7331

A110

PICKARD, ARTHUR I.

Se:2/4

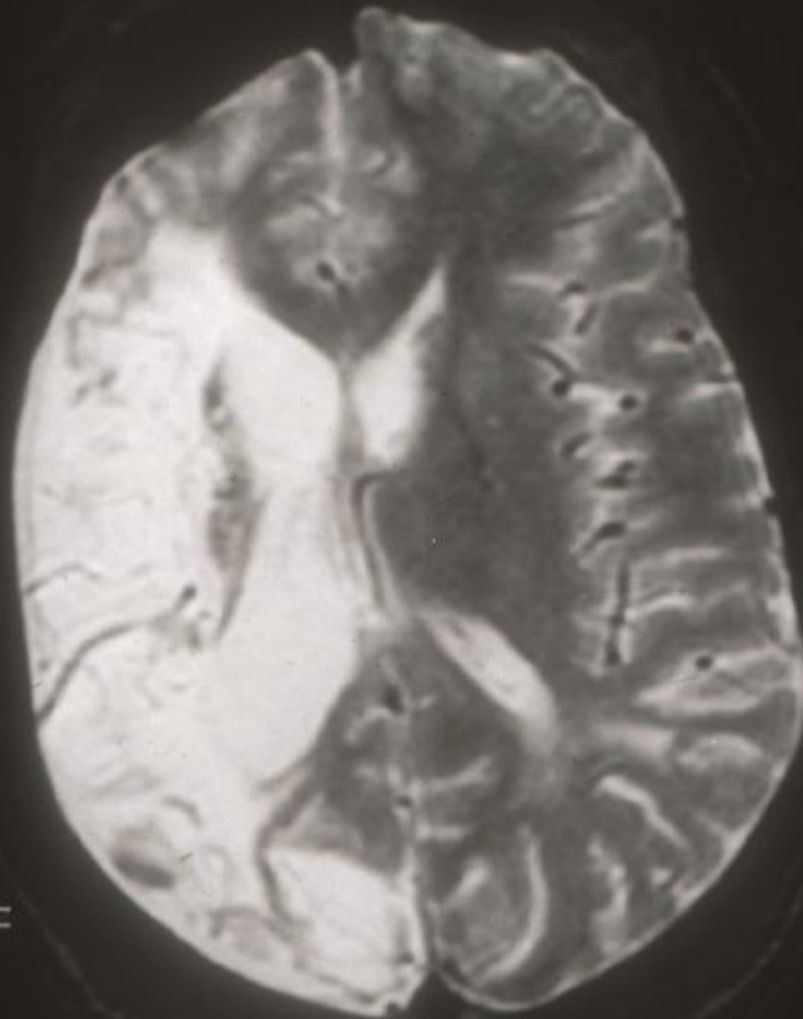
27 MAR 1992

Im:22/38

14/19/95

Ac:32.0

00:50



R
1
1
0

L
1
1
0

SF/V
TR:2316
TE:90
EC:2/2 4.81kHz

HEAD
FOV:22x16
5.0thk/2.5sp
38/05:01
256x192/1 NEX

P110

V↑

Summary

- **About one third (7/22) of patients with SS and Stroke died within 3 years after transition into an adult program**
- **About 12% (2/17) die if non-compliant with regular transfusion/exchange transfusion**
- **Mortality among patients who discontinued regular blood transfusion/exchange was 100% (5/5) within 3 years after transition**
- **Iron overload seems to be more common among patients who discontinue regular blood transfusion or who are non-compliant**

Conclusion

- **It is imperative that all efforts be made to maintain adequate chronic blood transfusion/exchange transfusion for children with SCD and stroke after transition to adult care.**
- **Strong recommendation for transfusion or exchange transfusion for children with SS and stroke was established before strong evidence became available by RCT with TCD (Stop I and II Trials)**

Thank YOU