2-okt-11

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Blood and Beyond

Sikkelcelziekte en transfusiebeleid

Wanneer (niet)?

Jean-Louis Kerkhoffs

Transfusie specialist Sanquin

Internist-Hematoloog HagaZiekenhuis

INTRODUCTION

- SCD in brief
- Acute indications for transfusion of RBCx in SCD
- Chronic indications for transfusion of RBCx in SCD
- Risks of transfusions in SCD
- Exchange versus simple RBC transfusions
- General remarks with regard to type and dose of RBCs
- Summary of indications

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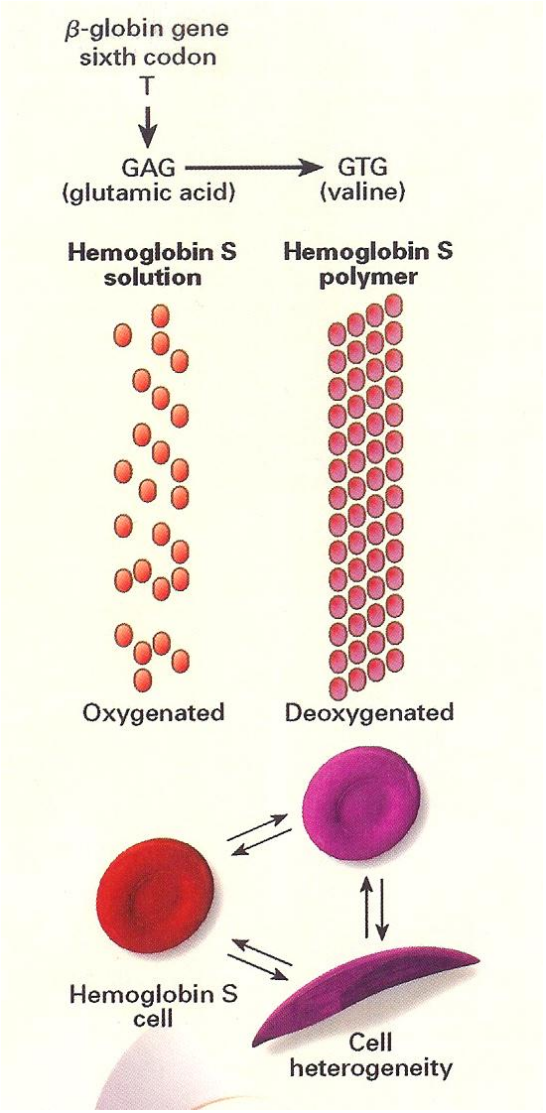
SICKLE CELL DISEASE (SCD)

- Caused by a glu-val substitution at the 6the codon of the beta-globine gene
- One of the most prevalent inherited disorders world wide
- HbS polymerizes at deoxygenation causing hemolysis and “stiff” red cells
- Leading to several acute and chronic complications and a reduced life expectancy

TRANSIT TIME!



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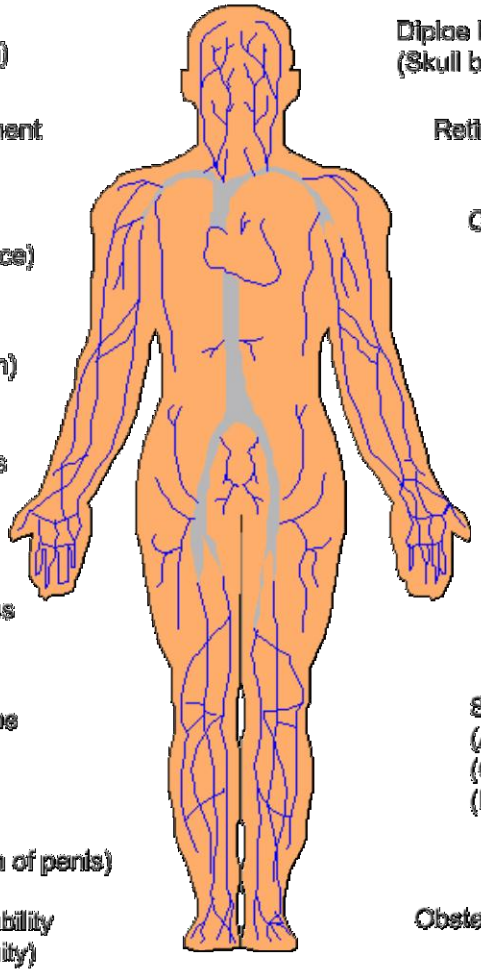
COMPLICATIES



Cerebral Vascular Bleeding (Stroke)

Gnanopathy
(Gnasher teeth)

Auditory Impairment

Hepatomegaly
(Cholelithiasis, jaundice)

Growth Impairment
(Endocrine dysfunction)

Renal Pathology
(e.g. Haematuria, Enuresis
Papillary necrosis)
(Sequestration)

Micro-Vascular Occlusions
(e.g. Mesenteric)

Hand Foot Syndrome
(Dactylitis)

Priapism
(involuntary erection of penis)

Physical Disability
(Bony deformity)

Diploe Expansion
(Skull bone expansion)

Retinopathy

Cardiomegaly

Chest Syndrome
(Pulmonary)

Splenomegaly

Delayed Puberty

Reduced Fertility

Skeleto-pathology
(Aplastic crisis)
(Osteonecrosis)
(Leg ulcers)

Obstetric Complications

Immuno-suppression
Chronic haemolytic anaemia
Psychosocial implications

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INDICATIONS (GENERAL)

- Anemia related
- Related to vasculopathy
- Related to vaso-obstruction
- Specific circumstances

- Triggers are usually: Hb/Ht and HbS%

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ACUTE INDICATIONS

1. **Hb triggered**
   a) Splenic sequestration
   b) Aplastic crisis
   c) Hemolytic crisis
2. **HbS triggered**
   a) ACS
   b) CVA
   c) MOF

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SPECIAL CONDITIONS

- Surgery

- Pregnancy

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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.,

TAPS ??

Koshy et al (N Engl J Med 1988; 319: 1447–52.)

- **72 pregnant females were randomized; 36 received prophylactic RBCx and 36 received RBCx on demand.**
- **Perinatal outcome: n.s. different.**
- **The occurrence of a perinatal death in a previous pregnancy and the presence of twins in the present pregnancy were two major risk factors for an unfavorable outcome.**
- **Prophylactic transfusion significantly reduced the incidence of painful crises of sickle cell disease ($P<0.01$) and substantially reduced the cumulative incidence of other complications of this disorder ($P = 0.07$).**
- **Increases in costs, the number of hospitalizations, and the risk of alloimmunization were disadvantages of prophylactic transfusion.**

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CHRONIC INDICATIONS

1. Hb triggered: none
2. HbS triggered:
   a) CVA secondary prevention
   b) Abnormale TCD
   c) Recurrent ACS
   d) Recurrent vaso-occlusion

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STOP TRIAL

- n = 130 children, age 8.3 ± 3.3 years with increased blood-flow velocity measured using TCD (velocity > 200 cm/sec) were randomized to receive chronic transfusions to reduce HbS below 30% (n = 63) versus standard care (n = 67).

- Outcome measure: the incidence of stroke

- Trial was terminated early

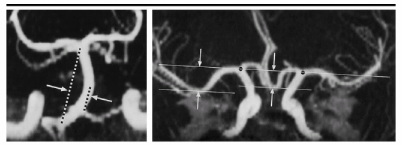

Figure 1. Coronal MR angiograms (34/5; field of view, 20 cm; flip angle, 20°; matrix, 192 × 256) show how measurements were made to establish whether a child had arterial tortuosity. (a) Image shows characterization of basilar artery bowing by means of drawing the basilar chord (left dotted line) from the point of junction of the vertebral arteries to the point of bifurcation of the posterior cerebral arteries. Then a perpendicular distance (between the lines at the arrows) was measured from the basilar chord to a line drawn down the center of the basilar artery (right dotted line) at a point where the artery was farthest from the basilar chord. (b) Image shows characterization of middle cerebral artery bowing by means of locating points (dots) at the confluence of the A1 segment of the anterior cerebral artery and the M1 segment of the middle cerebral artery on each side of the brain, so that a line of reference (upper line) could be drawn through these points. This compensates for head tilt, which could otherwise corrupt the measurement, in the subject. Then the perpendicular distance was measured from the line of reference to the midpoint of the artery (at the point of farthest bowing) of the A1 segment (right arrows) and M1 segment (left arrows) on both sides of the circulation.

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

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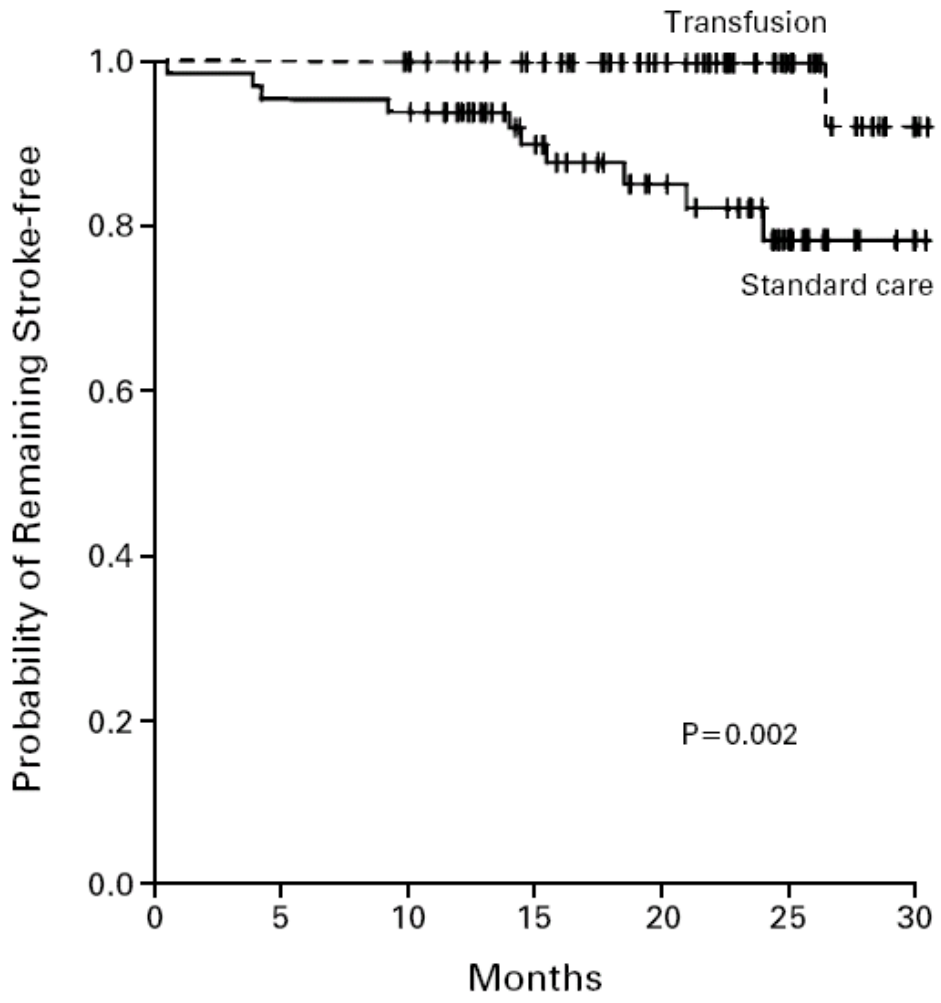

12 strokes in the standard care group versus 1 in the chronic transfusion group

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STOP - 2

- n = 79 children with a normalised TCD were randomized to either continue (n = 38) or stop chronic transfusion therapy (n = 41).

- Outcome measure: stroke or conversion to abnormal TCD.

- Trial was stopped early.

N Engl J Med 2005;353:2769-78.

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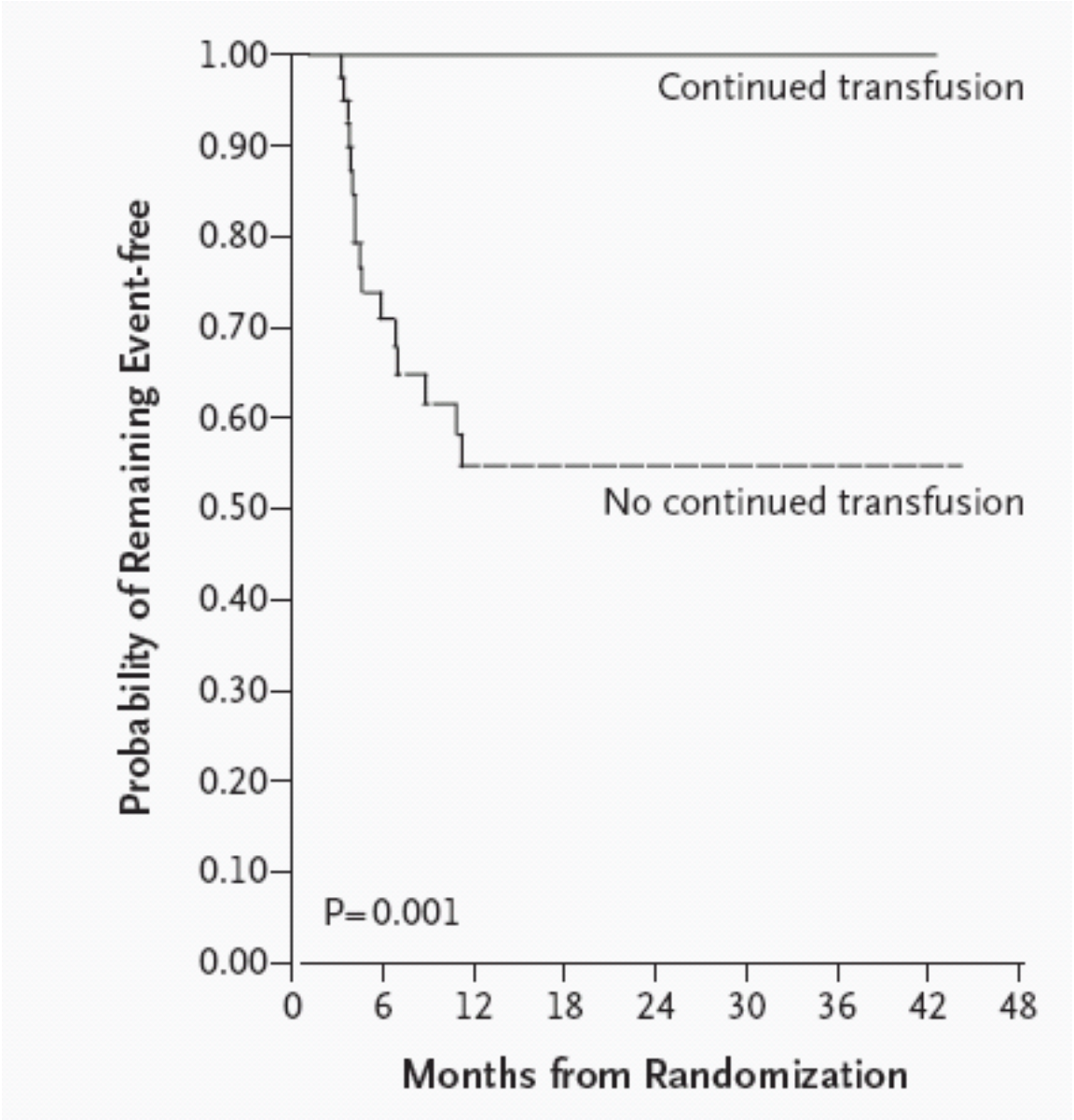
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
Probability of Remaining Event-free
Continued transfusion
No continued transfusion
P=0.001
0
6
12
18
24
30
36
42
48
Months from Randomization

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Impact of chronic transfusion on incidence of pain and acute chest syndrome during the Stroke Prevention Trial (STOP) in sickle-cell anemia

Scott T. Miller, MD, Elizabeth Wright, PhD, Miguel Abboud, MD, Brian Berman, MD, Bea Files, MD, Charles D. Scher, MD, Lori Styles, MD, and Robert J. Adams, MD, for the STOP Investigators

	Transfusion	Standard care	Poisson R
Intent to treat			
N	63	66	
Patient-years	104.96	97.88	
No. patients with ACS	4	14	
Total ACS events	5	15	
ACS events/100 patient-years	4.8	15.3	0.0027
No. patients with pain	11	13	
Total pain events	17	27	
Pain events/100 patient-years	16.2	27.6	0.13
Compliant patients			
N	59	65	
Patient-years	92.78	95.84	
No. patients with ACS	2	14	
Total ACS events	2	15	
ACS events/100 patient-years	2.2	15.7	0.0001
No. patients with pain events	6	12	
Total pain events	9	26	
Pain events/100 patient-years	9.7	27.1	0.014

ACS, Acute chest syndrome.

(J Pediatr 2001;139:785–9)

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RISKS OF TRANSFUSION

1. The formation of red cell allo-antibodies
2. Hyperhemolysis
3. Hyperviscosity
4. Iron overload

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studie	n pat		Allo ab (% pt)		Auto ab	Match strategy
		tot	1	> 1		
Ameen (2003)	190 (thal)	30	13	17	11	ABO-D
Moreira (1996)	85	13	8	5		ABO-D
Vichinsky (1990)	107	30	14	16		ABO-D
Murao (2005)	828	10	6	4		ABO-B
Aygun (2002)	140	37	10	27	9	ABO-D/CEK
Castro (2002)	351	29				ABO-D
Singer (2000)	64 (thal)	22			25	ABO-D
Rosse (1990)	1814	19	9	10		ABO-D
Overall		**24**	**10**	**14**	**15**	

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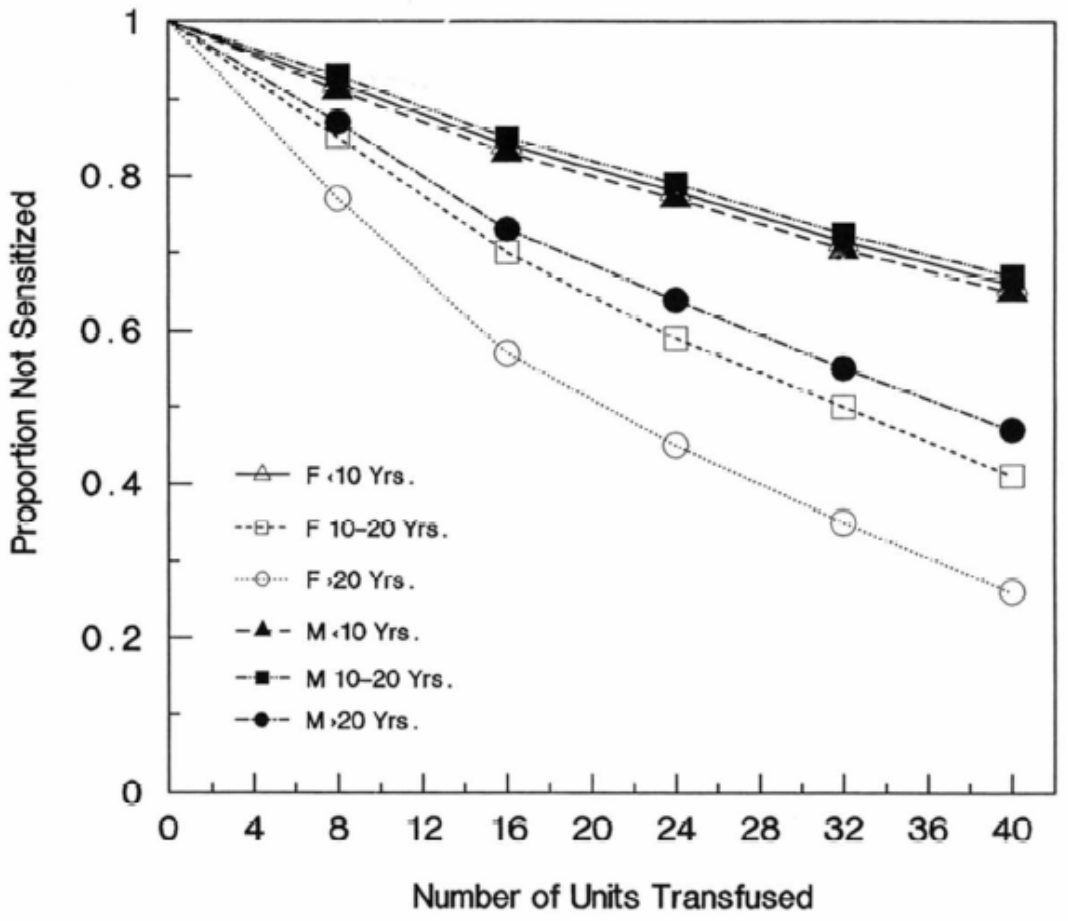

Rosse (1990)

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(Hyper)hemolysis

Definition: hemolysis 6-10 days 1 week after RBC transfusion, associated with pain and profound anemia. Incidence: 1-4%.

Signs: Pain, fever and hemogloninuria most prominent.

Lab: ↓↓HbA and HbS; DAT+ 30%; new allo-Ab 30%; reticulopenia 60%!;

Complications/associations: ACS, CHF, ARF, pancreatitis; Mortality: 10-20% (?).

Therapy: corticosteroids, IVIG, epo

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Journal of Pediatric Hematology/Oncology, Vol. 24, No. 4, May 2002

Longitudinal Changes in Ferritin During Chronic Transfusion: A Report From the Stroke Prevention Trial in Sickle Cell Anemia (STOP)

Beatrice Files, M.D., Don Brambilla, Ph.D., Abdullah Kutlar, M.D., Scott Miller, M.D., Elliott Vichinsky, M.D., Winfred Wang, M.D., Suzanne Granger, M.S., and Robert J. Adams, M.S., M.D.

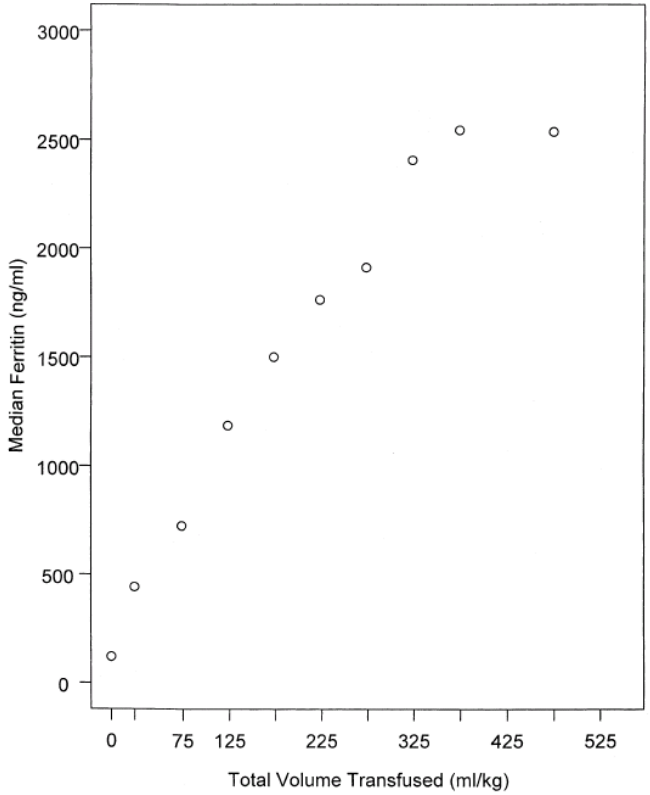
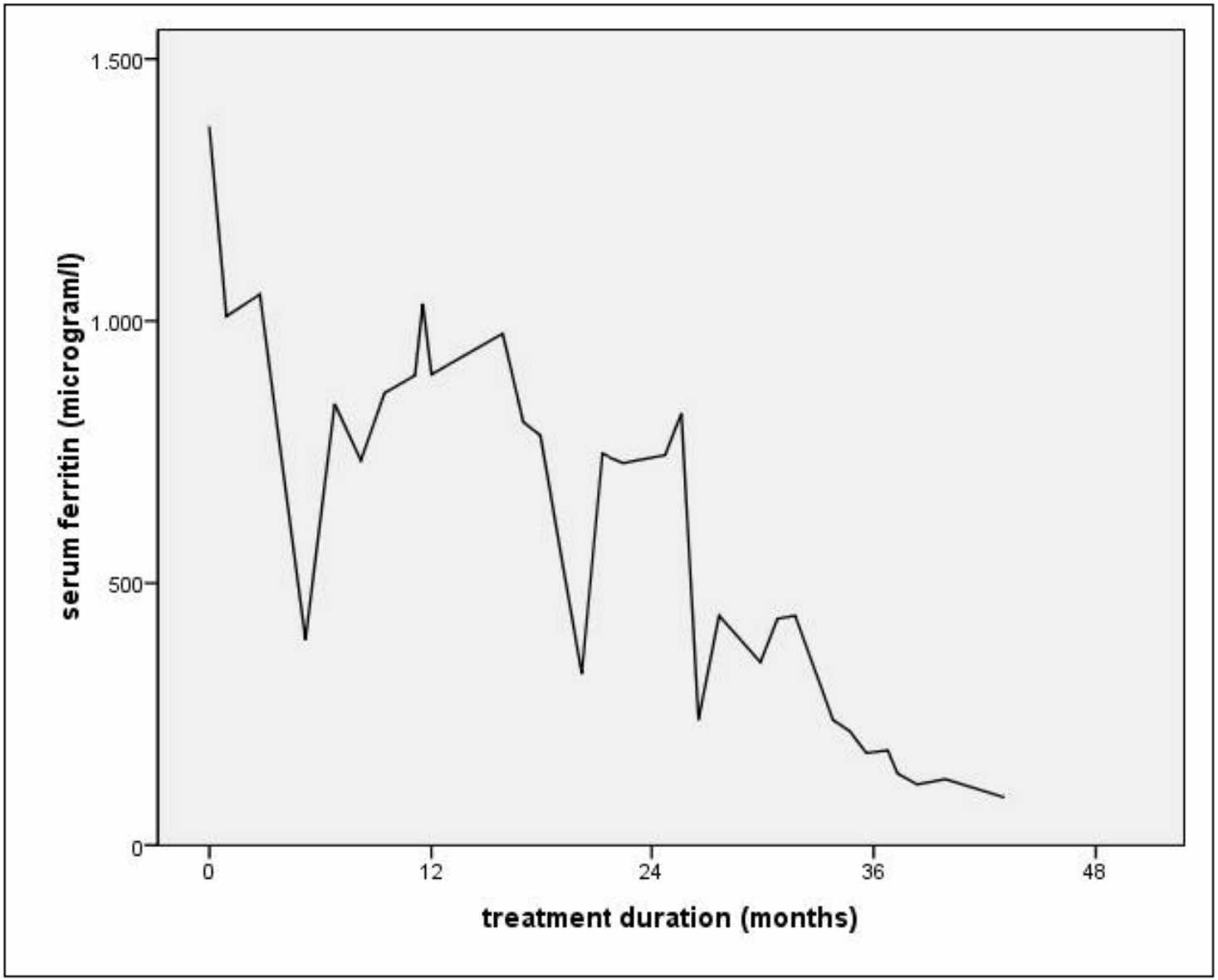


FIG. 2. Each point represents the median of serum ferritin at cumulative transfusion volume per kg for the 10 patients who reached the highest total transfusion volume. Plots occur at 50-mL/kg intervals


1.500
1.000
500
0
serum ferritin (microgram/l)
0
12
24
36
48
treatment duration (months)

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HYPERVISCOSITY

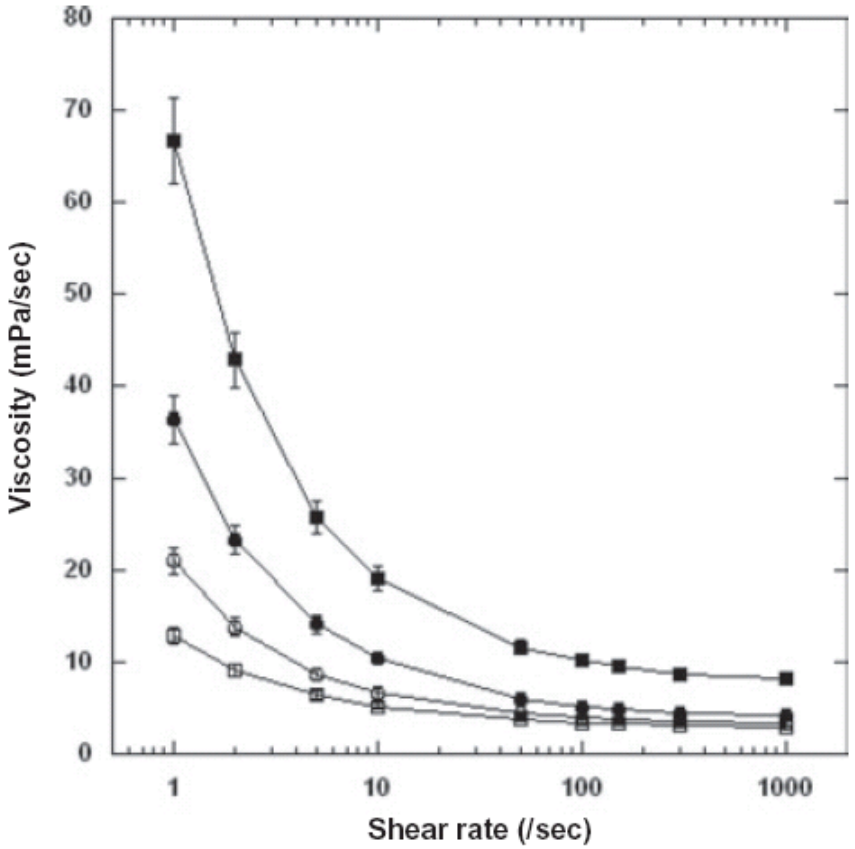

Fig. 3. Blood viscosity-shear rate relations for deoxygenated 100 percent SS RBCs suspended in autologous plasma at 0.20 (□), 0.25 (○), 0.30 (●), and 0.40 Hct (■). Data are mean ± SD; n = 7.

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EXCHANGE VS “TOP-UP”

TOP-UP

- ✓ Easy
- ✓ Rarely necessary
- ✓ Risk of hypervoscisity
- ✓ Risk of Iron overload

RBC EXCHANGE

- ✓ Less easy
- ✓ Adequate for isocritic decreasing HbS%
- ✓ No of reduced risk of hyperviscosity or iron overload

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GENERAL REMARKS

- ✓ Goals for RBC(x): Ht 30% and HbS < 30%
- ✓ RBCs should be matched for: ABO-D-CEK
- ✓ In case of parvo B19 IgG negativity: “Parvo-safe”

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Samenvatting indicaties voor transfusie bij SCD

Acute indicaties		
Milt sequestratie als Hb < 3.3 en/of circulatoir falen	*Enkelvoudige transfusie*	*D*
Acute chest syndroom met (dreigend) respiratoir falen	*Wisseltransfusie*	*C*
Acuut CVA	*Wisseltransfusie*	*D*
Multiorgaanfalen	*Wisseltransfusie*	*D*
Priapisme	*Geen indicatie*	*D*
Vaso-occlusieve crisis	*Geen indicatie*	*D*
Preoperatieve voorbereiding	*(Wissel)transfusie*	*C*
Zwangerschap; meerlingzwangerschap of belaste VG	*(Wissel)transfusie*	*A2*
Chronische indicaties		
Preventie recidief CVA	*(Wissel)transfusie*	*C*
Primaire CVA preventie, afwijkend TCD onderzoek	*(Wissel)transfusie*	*A2*
Stille herseninfarcten	*Geen indicatie*	*D*
Recidiverende vaso-occlusieve crisis niet reagerend op HU	*(Wissel)transfusie*	*C*
Recidiverend ACS	*(Wissel)transfusie*	*C*

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