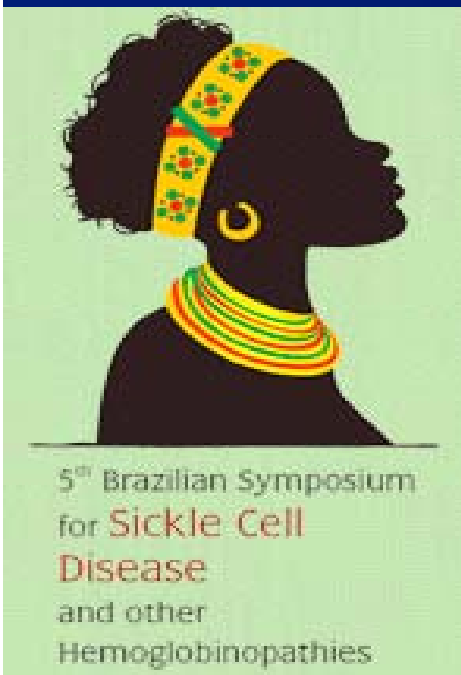


Erythrocytapheresis (RBC Exchange Transfusion) to Prevent Iron Overload in Patients with Sickle Cell Disease

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Haewon C. Kim, M.D.

Children's Hospital of Philadelphia
Univ. of Pennsylvania Sch. of Med.
Philadelphia, PA. USA



Erythrocytapheresis RBC Exchange Transfusion (Ex-Tx)

Objectives

- Describe **Goals** of Ex-Tx
- Define **Indications** for Ex-Tx
- Discuss **Benefits vs Risks** of Ex-Tx



Sickle Cell Disease

Clinical Manifestations

- ❖ Vaso-occlusive events
- ❖ Acute anemias
- ❖ Infections
- ❖ Chronic organ damage



Methods of RBC Transfusion

Acute vs. Chronic

- Simple Transfusion (S-Tx)
- Exchange Transfusion (Ex-Tx)



Goals of Transfusion (Tx) in SCD

1. ↑ O₂ delivery to tissues

Severe Acute Anemia

- Transient red cell aplasia
- Splenic sequestration
- Hyperhemolysis

Acute: S-Tx

2. ↓ Hb S conc.

Vasoocclusive Events

ACS, CVA, Eye Cx, VOC pain

Acute or Chronic
S-Tx or Ex-Tx

3. Both 1 & 2

4. Preparation for Surgery when Hb > 10 g/dL

Ex-Tx



RBC Exchange Transfusion (Erythrocytapheresis)

Goals

Remove patient's abnormal RBCs by exchanging them with normal RBCs



Comparison of S-Tx with Ex-Tx

	S-Tx		Ex-Tx
↑ Hb level	++++	>	NA
↓ Hb S level	++	<	++++
↑ Volume overload	++++	>	0
↑ Duration	++++	>	++



RBC Exchange Tx (Erythrocytapheresis)

Advantages

- ◆ Rapid **↑ Hct** level without volume overload
- ◆ Rapid **↓ Hb S** level without substantially **↑ Hct** level
- ◆ **↓** Duration of procedure



RBC Exchange Transfusion

- ❖ Manual
- ❖ Automated
(Erythrocytapheresis)



Therapeutic Apheresis

Guidelines for Indication on the Basis of Evidence

by

American Society for Apheresis (ASFA)

American Assoc. of Blood bank (AABB)



Therapeutic Apheresis

Indication Categories

- I Standard and acceptable as a primary therapy or a first-line adjunct therapy usually on the basis of randomized controlled trials
- II Sufficient evidence to suggest efficacy; acceptable therapy on an adjunctive basis
- III Insufficient evidence for efficacy and weighing cost/benefit or risk/benefit; may be of benefit when conventional therapy failed or as as an IRB-approved research protocol
- IV Lack of therapeutic benefit in controlled trials



Sickle Cell Disease

Indications for Erythrocytapheresis

Category I

Life and Organ Threatening Complications

- Acute chest syndrome
- Acute stroke
- Multiorgan failure

(by ASFA, 2007)



Category I

Life and Organ Threatening Cx in SCD

Emergency Erythrocytapheresis

Goal of Ex-Tx

- Post-Ex Hct: $30\% \pm 3\%$ ($\leq 36\%$)
- Post-Ex Hb S: $< 30\%$
- Isovolemia

Procedure Guidelines

- FCR: 25-30% (if no Tx for past 3 mo)
(desired Hb S/Current Hb S x 100)
- Post-Ex Hct: 30%
- Fluid balance: 100%
- No divert waste & rinseback



Category II

Erythrocytapheresis

- Stroke prophylaxis
- Prevention of transfusion-acquired iron overload

(by ASFA 2007)



Indications for RBC Ex-Tx (Erythrocytapheresis)

RBC Disorders

Hereditary (Intrinsic)

- Sickle cell disease
- Unstable hemoglobin with high O₂ affinity
- G6PD deficiency
- Thalassemia

Acquired (Extrinsic)

- Infected RBCs:
Malaria, Babesiosis
- Incompatible RBC Tx:



Sickle Cell Disease

Indications for Long-term Tx

↓ Vaso-occlusion by ↓ Hb S level

- ***Prevention of recurrent stroke or first (primary) stroke***
- Chronic debilitating painful crises
- Chronic lung disease with arterial hypoxemia



Complications of Chronic Transfusions

- ❖ Transfusion-transmitted Infections
- ❖ Alloimmunization
- ❖ Transfusional Iron Overload



Sickle Cell Disease and Stroke

Optimal Duration of Tx ?

No of Pts with CVA	Duration of Tx (yr)	Target HbS (%)	Recurrence Rate	Author
35	0	100	67%	Powers
10	1-2	<20	70%	Wilimas
10	5-12	<30	50%	Wang
23	0.7-9.2	<30	<10%	Russell
15	1.2-10.8	<50	0%*	Cohen
14	4.5-13.7	<30	0%	Miller

**2 pts had fatal CNS hemorrhage when their Hb S \leq 30%.*



Stroke Prevention Trial in Sickle Cell Anemia (STOP)

STOP I

Transfusion reduced the risk of a ***primary stroke by over 90%*** in those with abnormal TCD

No Tx: 11/67 (16%); with Tx: 1/63 (1.6%)

STOP II

- Discontinuation of transfusion after 30 mo:
2 CVAs & 14 abnormal TCDs in 41 pts
- *Continued transfusion: 2 CVAs in 38 pts*



Stroke Prevention in SCD

- No known “safe” time to discontinue transfusions in primary (first time) and secondary (recurrent) stroke prevention
- *Continue transfusion indefinitely*

Goal of Tx: Hb S <30%

S-Tx: 10-15 ml RBC/kg, q 3-4 wks

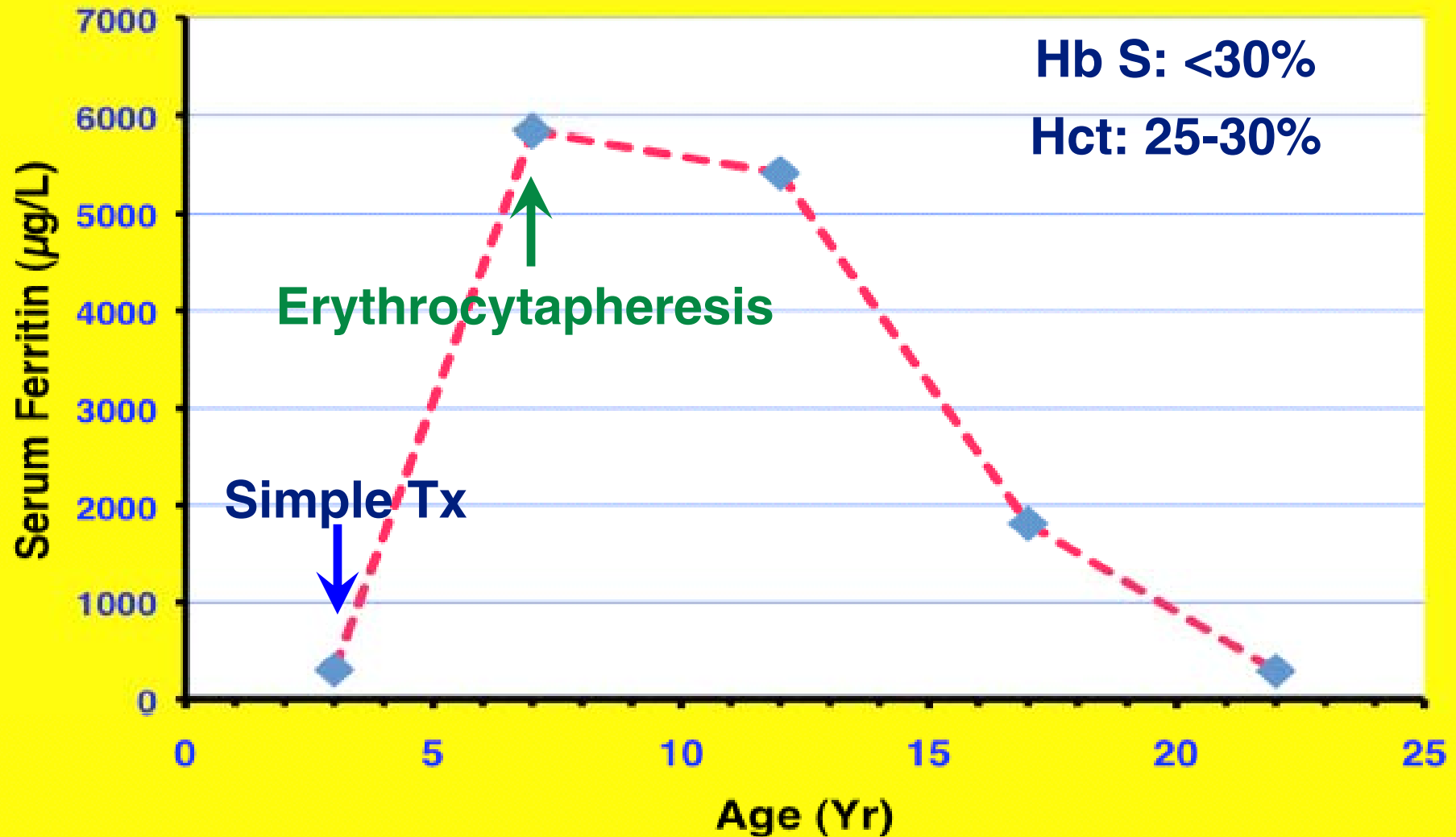


Case MS: 7 yo boy with sickle cell anemia S/P stroke at 2 yr 9 mo

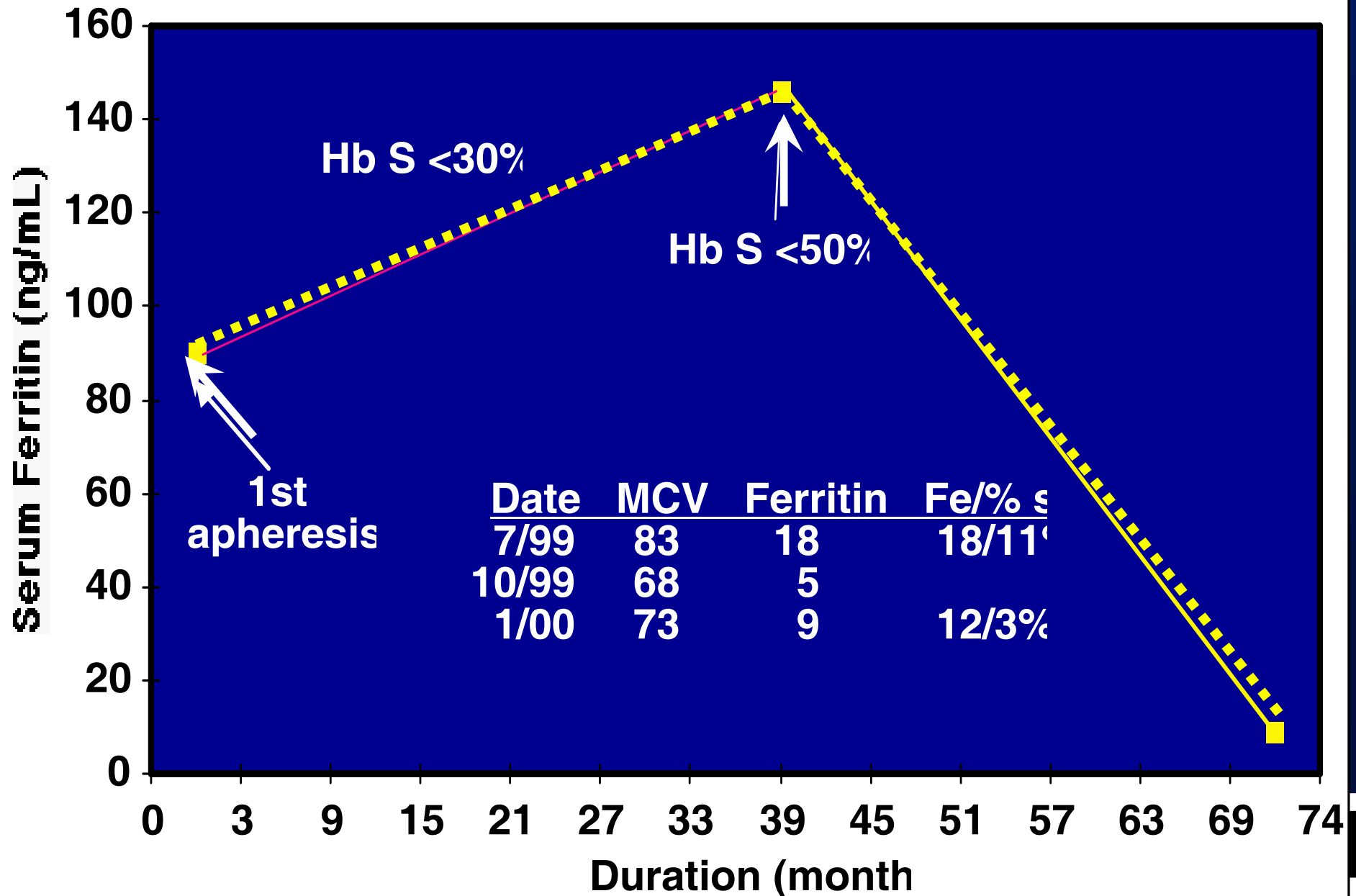
- ❖ **at 2.7 yo:** Hct: 22%
Serum ferritin: 302 $\mu\text{g/L}$
- ❖ **S-Tx:** Target Hb S <30%
10-15 mL RBC/kg, every 3-4 wks
- ❖ **at 7 yo:** Serum ferritin: 5,846 $\mu\text{g/L}$
Referred for erythrocytapheresis



Effect of Long-term Transfusions on Serum Ferritin Levels



Effect of Erythrocytapheresis on Serum Ferritin Level: Absence of Iron Chelation



Erythrocytapheresis in Reducing Iron Overload

Rationale

With exchange transfusion, RBCs from patients are **removed** while donor RBCs are being **given**, resulting in ***fewer RBCs to contribute iron to the body*** in comparison with simple transfusion.



PEDIATRIC RBC-Ex

Can procedure be performed safely?

Children \neq Small Adult



Complications of Apheresis in Children

	Aph Proc	Patients
Total No.	1632	186
Adverse effects	55%	82%

Adults: 4.3% - 28% 40%

B. Michon, et al. Transfusion.2007;47:1837



Pediatric Erythrocytapheresis

Can procedure be performed safely?

Special Considerations for Safety

I. Psychological considerations

- N S

P

II. Vascular access

III. Technical considerations

- Equipment

- Patient



Pediatric Erythrocytapheresis

Vascular Access

Draw:

- ◆ Peripheral vein (\geq 18 G needle)
- ◆ Central Venous Catheter-Double lumen:
MedComp, Hickman. etc
- ◆ Ports (Vortex)

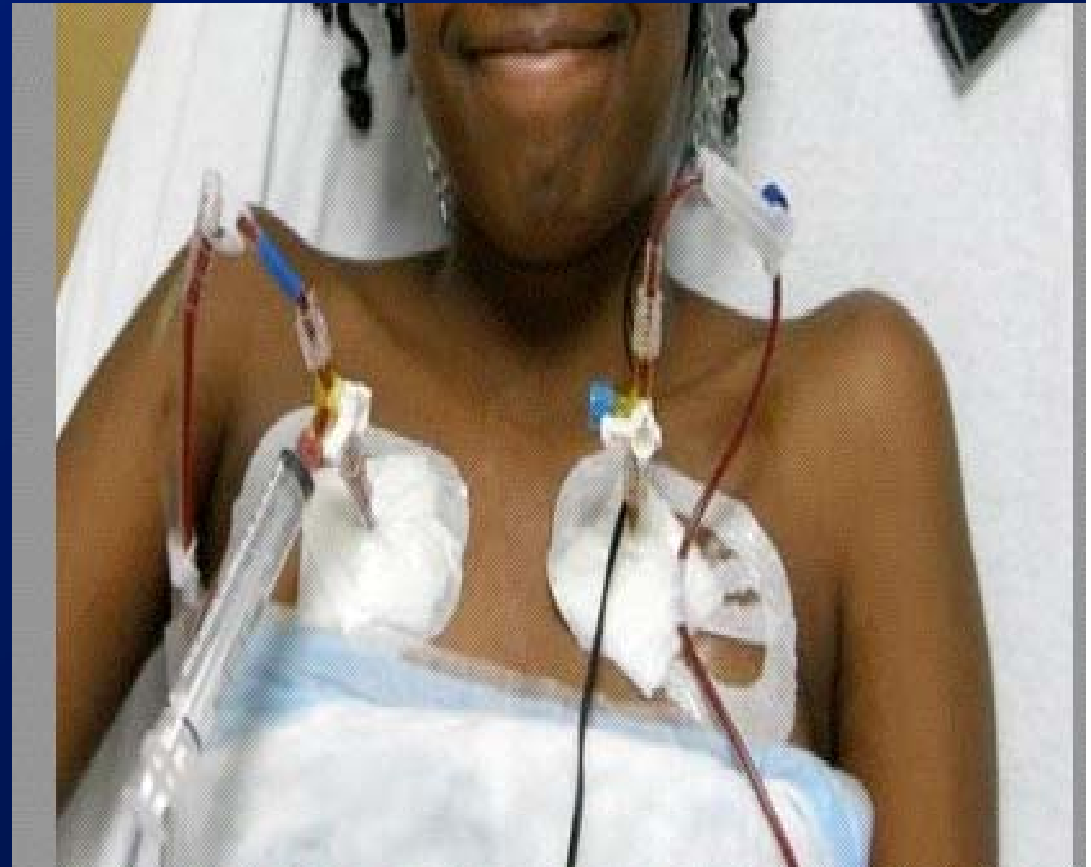
Return:

- ◆ Peripheral vein (\geq 22 G needle)
- ◆ Central Venous Catheter:
Broviac, Infusaport, etc
- ◆ PICC





Draw: Vortex Port
Return: Infusaport



Technical Considerations: RBC-Ex

A. Extracorporeal volume (ECV) Shift

Spectra Proc.	Diverted NSS	Rinseback	Intra-proc.	Post-Proc.
RBC-Ex	-100	+345	-100	+245

13 yo boy, 50 kg, Hct = 30%

TBV: $75 \text{ ml/kg} \times 50 = 3500$

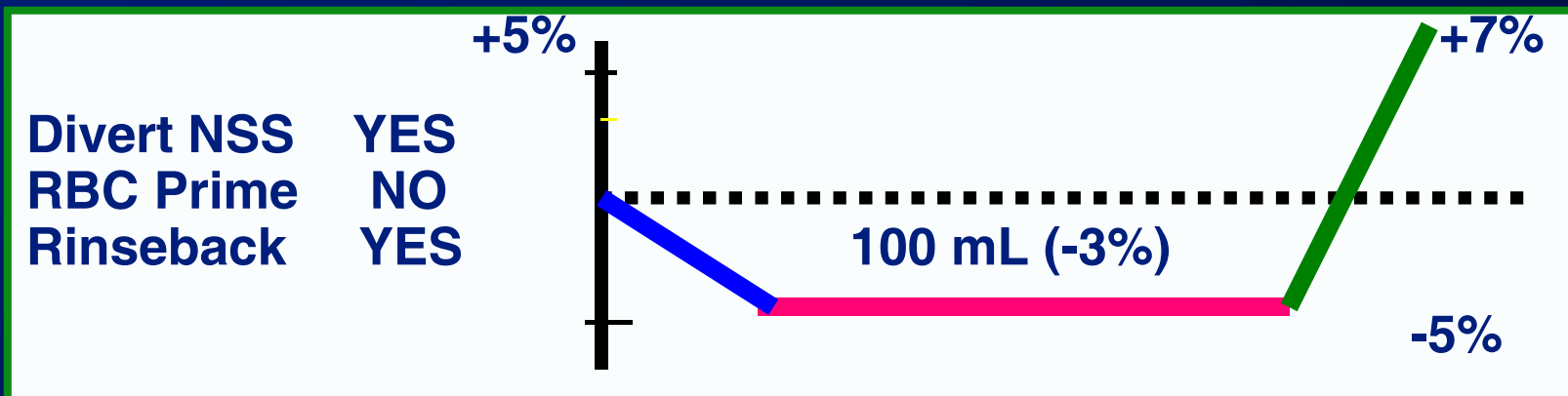
PV: $3500 \times 0.7 = 2450$

RCV: $3500 - 2450 = 1050$

Standard RBC-Ex

Intra-vol shift: $-100/3500 \times 100 = -3\%$

Post-vol shift: $245/3500 \times 100 = +7\%$



Pediatric RBC-Ex

A. Extracorporeal volume (ECV) Shift

Spectra Proc.	Diverted NSS	Rinseback	Intra-proc.	Post-Proc.
RBC-Ex	-100	+345	-100	+245

1 yo infant, 10 kg, Hct:30%

TBV: $70 \text{ ml/kg} \times 10 = 700$

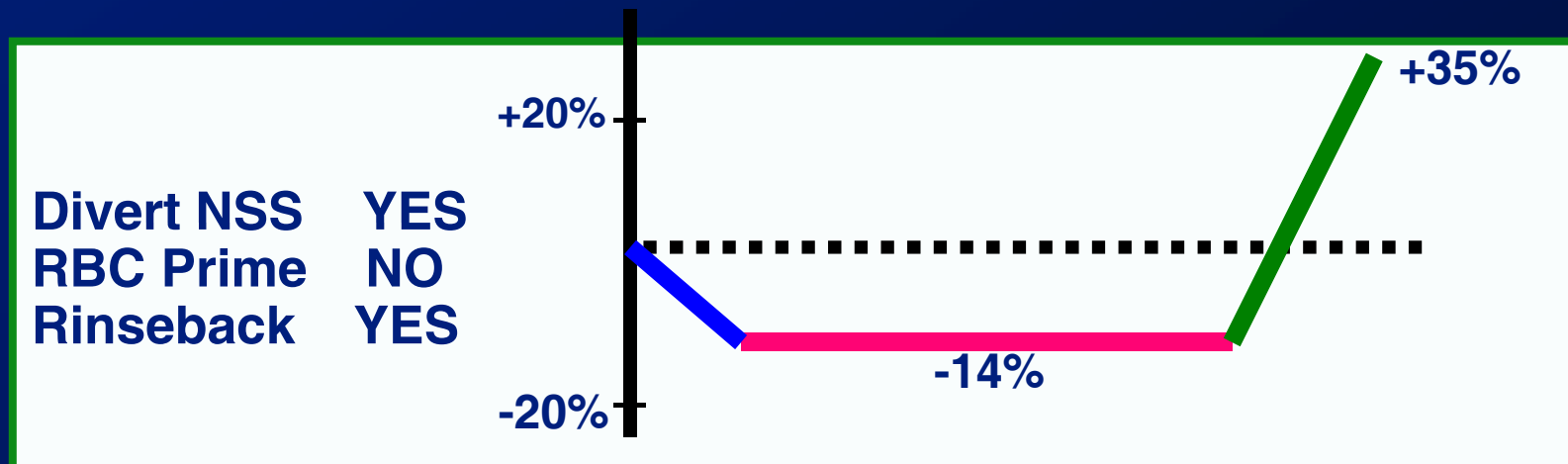
PV: $700 \times 0.7 = 490$

RCV: $700 - 490 = 210$

Standard RBC-Ex

Intra-vol shift: $-100/700 \times 100 = -14\%$

Post-vol shift: $245/700 \times 100 = +35\%$



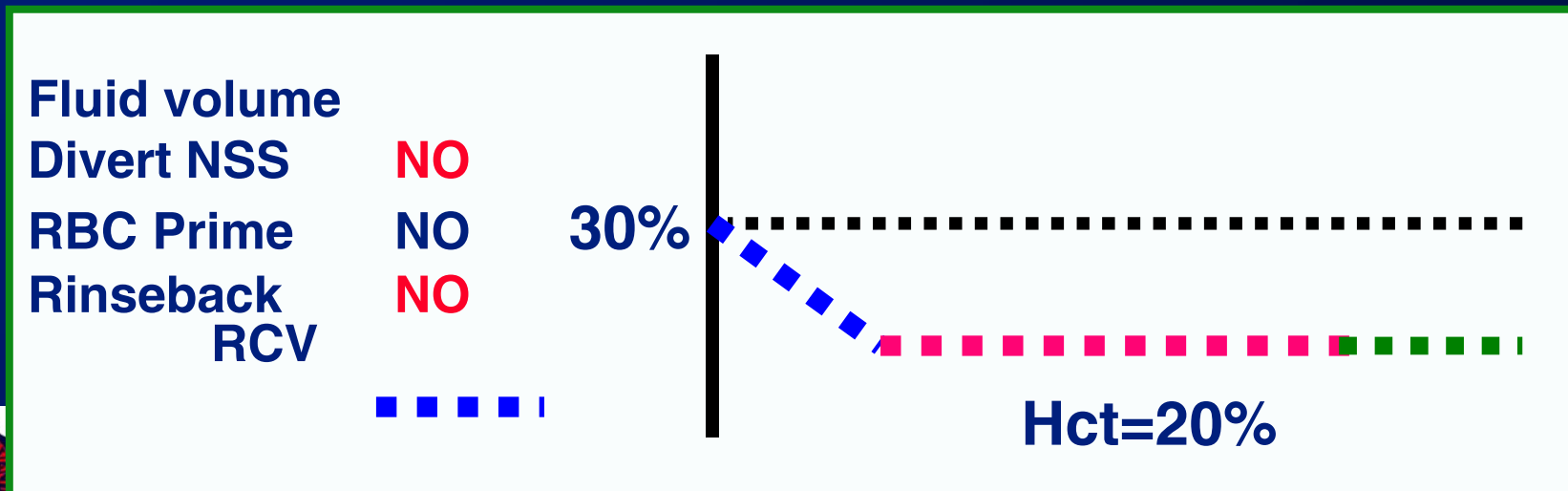
Pediatric RBC-Ex

B. Red Cell Volume (RCV) Shift

Spectra Proc.	During Run	Rinseback	Residual volume	Intra-proc	Post-proc
RBC-Ex	-68	+53	-15	-68	-15

10 kg infant, Hct = 30%
TBV: 70 ml/kg x 10 = 700
PV: 700 x 0.7 = 490
RCV: 700 - 490 = 210

Standard RBC-Ex
Intra-RCV shift: -68/210 x100 = -32%
Intra-& post-proc Hct: 20%



Pediatric RBC-Ex

B. Red Cell Volume (RCV) Shift

10 kg infant, Hct = 30%

TBV = 700 ml RCV = 210 ml

#2 Modified RBC-Ex
No Divert & Rinseback
 Volume shift: 0%
 Intra- & post-Hct: 20%



#3 Modified RBC-Ex
Blood prime: YES
 How much RBC to order?
 $70/0.6 = 117$ ml of RBC

Fluid volume █
 Divert NSS NO (**YES**)
 RBC Prime **YES**
 Rinseback NO
 RCV ■ ■ ■ ■ |





Guidelines for Long-Term Erythrocytapheresis in SCD with Stroke

	< first 3 yr	> 3 yr
Target Hb S (%)	< 30	< 50*
Post-Hb S (%)	12 - 15	20 - 25
Post-Hct (%)	27 - 36	27 - 36

* *Patient must be clinically and neurologically stable before raising the target Hb S to <50% from <30%.*



Erythrocytapheresis

Sickle Cell Disease with Stroke

Laboratory Studies

Patient

- Pre- & Post-: **CBC**
- Pre- & Post-: **Hb S**
- Serum ferritin: **quarterly**
- Viral serology: **annually**
e.g., HBsAg, anti-HCV,
anti-HIV

Replacement RBC and Waste Bag:

- **Volume**
- **Spun Hct**



Erythrocytapheresis

Calculation of net RBC Load/kg/proc

❖ Total RBC volume replaced (A)

= Total donor RBCs vol x average Hct
of donor RBCs

❖ Total RBC volume removed (B)

= Waste vol x Spun Hct of waste bag
+ residual volume left in machine (70 mL)

❖ Net RBC load (mL of RBC) /Kg/proc

= (A - B) /Kg of body wt.



Long-term Erythrocytapheresis

Disadvantages

- Problem with venous access
- * *Increased blood requirements*
- * *Increased no. of donor exposure*
- Increased cost for the proc. (?)
- Universally not available



Erythrocytapheresis

Isovolemic Hemodilution

Phase I: RBC Depletion

Removal of RBC and replacement by an equal volume of 0.9% NaCl until desired Hct is reached.

Pre-Hct **Intra-Hct**
30% **→** **24%**

Phase II: RBC exchange

Without terminating phase I of procedure, phase II is carried out according to the standard exchange procedure.

Intra-Hct (24%) → Post-Hct (30%)



Erythrocytapheresis

Isovolemic Hemodilution

Goal: To reduce the replacement RBC vol and donor exposure

- ↓ circulating SS-cell load by RBC depletion prior to RBC exchange
- ↑ efficiency of exchange (↓ FCR → ↓ Hb S)
- Uses less donor RBC



Transfusion Support in Sickle Cell Patients

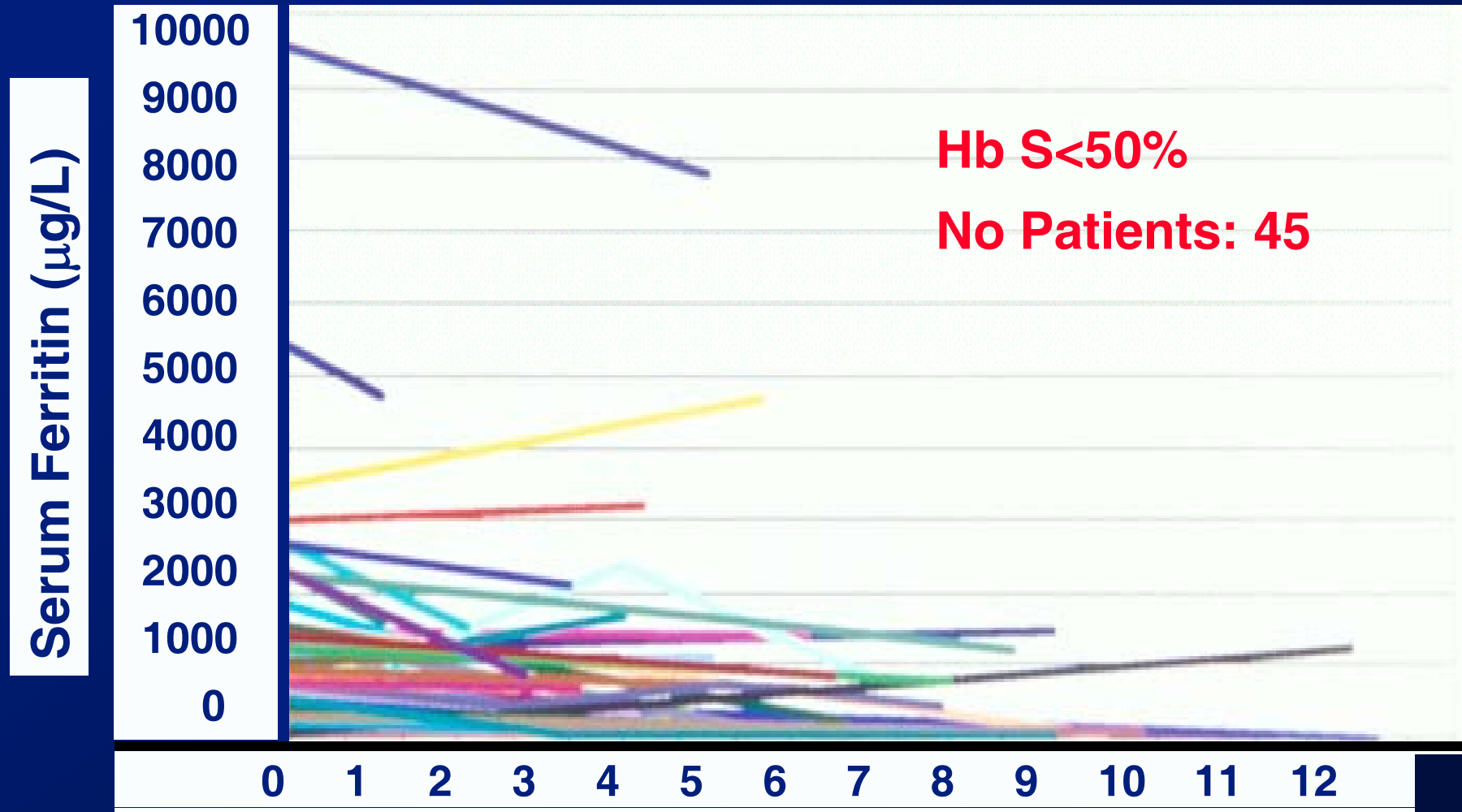


RBC Product for Sickle Cell Patients

- ❖ Transfusion Protocols differ across institutions
 - Hb S-negative RBC
 - Antigen matched for E, C, K and other antigens as appropriate
- ❖ Common African American Phenotype:
 - E-, C-, K-, Fy(a-), Jk(b-): 93% AA
 - Caucasians: 7% (*Walker RH, 1990*)
- ❖ Recruitment of African-American Donors



Effect of Long-term Erythrocytapheresis on Serum Ferritin Levels



Duration (yr) of Erythrocytapheresis



Long-term Erythrocytapheresis

Advantages

Prevents/reduces the transfusional iron accumulation while preventing primary & secondary stroke

- Delays onset of iron-induced organ damage
- Delays initiation of iron chelation therapy
- Prevents the need for iron chelation therapy



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