Transfusion in Sickle Cell Disease
What the guidelines [are likely to] say

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Background to BCSH Guideline

Rationale

Current guidance in disparate publications
Concise evidence-based guideline needed
Essentials of transfusion practice in SCD and thalassaemia
Written with practitioners in low prevalence areas in mind
5,000 words long

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Transfusion in SCD

Strategies

- Episodically for acute complications
- Electively on long-term basis to prevent complications

Methods

- Simple or top up transfusion
- Exchange transfusion

Benefits versus Risks

Benefits

- May be life saving in acute situations
- Can reduce mortality and morbidity from post-op complications
- Effective in primary and secondary stroke prevention
- In selected patients, can ameliorate severe disease

Risks

- Greater risk of haemolytic transfusion reactions
  - Peculiar problems related to alloimmunisation
  - Increased rate of out of hours transfusion
  - Patients often present acutely to different hospitals
- Special requirements
- Iron overload
- Increased donor exposure

Aims of blood transfusion in SCD

- To correct anaemia and so improve the oxygen-carrying capacity of blood

- To treat or prevent complications by lowering the percentage of HbS relative to HbA

Indications for emergency transfusion

Established

- ACS with hypoxia
- Acute splenic sequestration
- Aplastic crisis
- Acute hepatic sequestration
- Acute ischaemic stroke
- Acute multi-organ failure

Not indicated/ Uncertain

- Uncomplicated vaso-occlusive crisis (N)
- Mild drop in Hb with no symptoms (N)
- Severe sepsis (U)
- Haemorrhagic stroke (U)

Indications for elective transfusion

Established

- Primary stroke prevention in children
- Secondary stroke prevention
- Pre-operatively
  - HbSS and HbSβ^{o} thalassaemia undergoing low and medium risk surgery

Possible

- Pregnancy
  - Not for uncomplicated pregnancy
  - Consider for variety of other clinical situations
- Repeated painful crises or acute chest syndrome
- Leg ulceration resistant to intensive local measures
- Pulmonary hypertension
- Chronic priapism refractory to medical treatment

Transfusion practice in SCD

- Transfusing the acutely ill patient

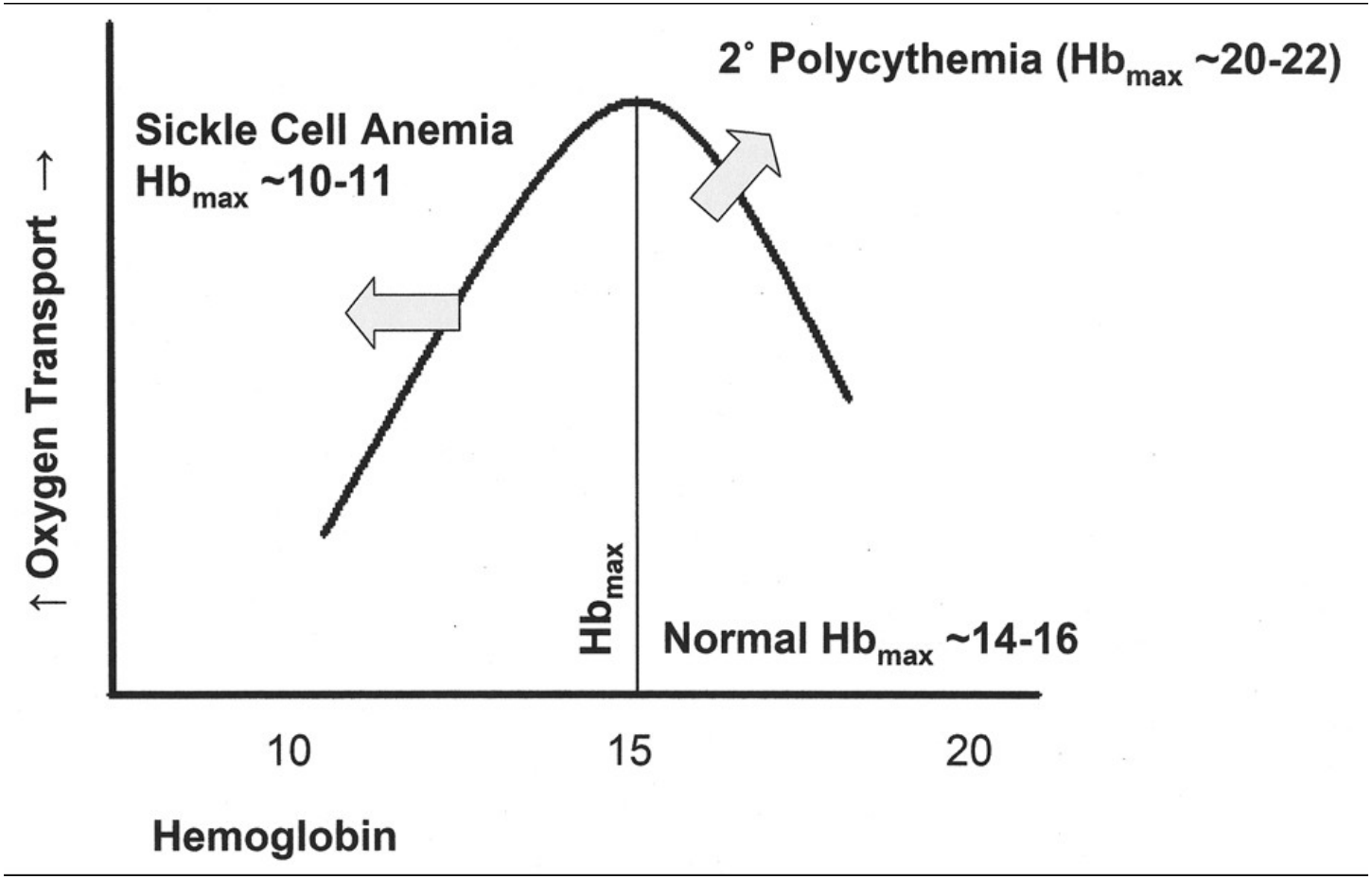
- Chronic blood transfusion

  - Make blood available in timely manner
  - Minimise risk – alloimmunisation, HTRs
  - Specify blood is for sickle patient

Transfusion practice in SCD

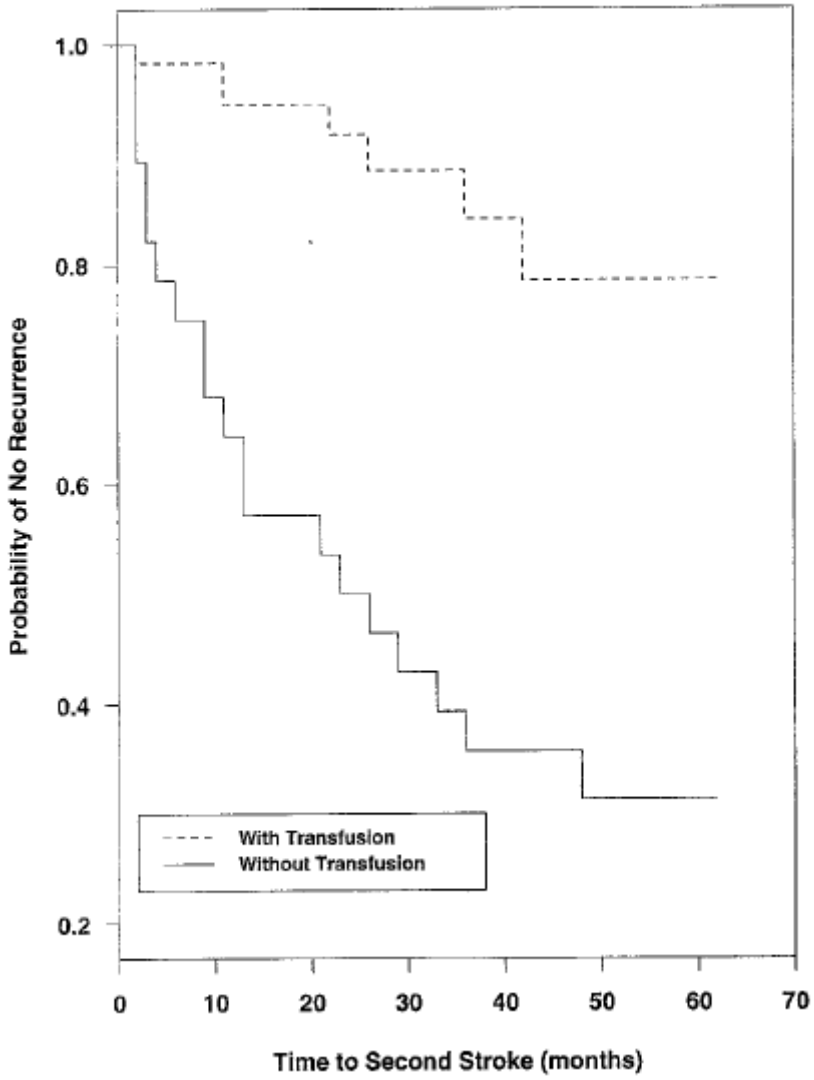
- Target Hb and HbS concentrations
- Volumes for complete exchange
- Manual exchange protocol

Oxygen transport versus haemoglobin in SCD



Swerdlow, Hematology 2006

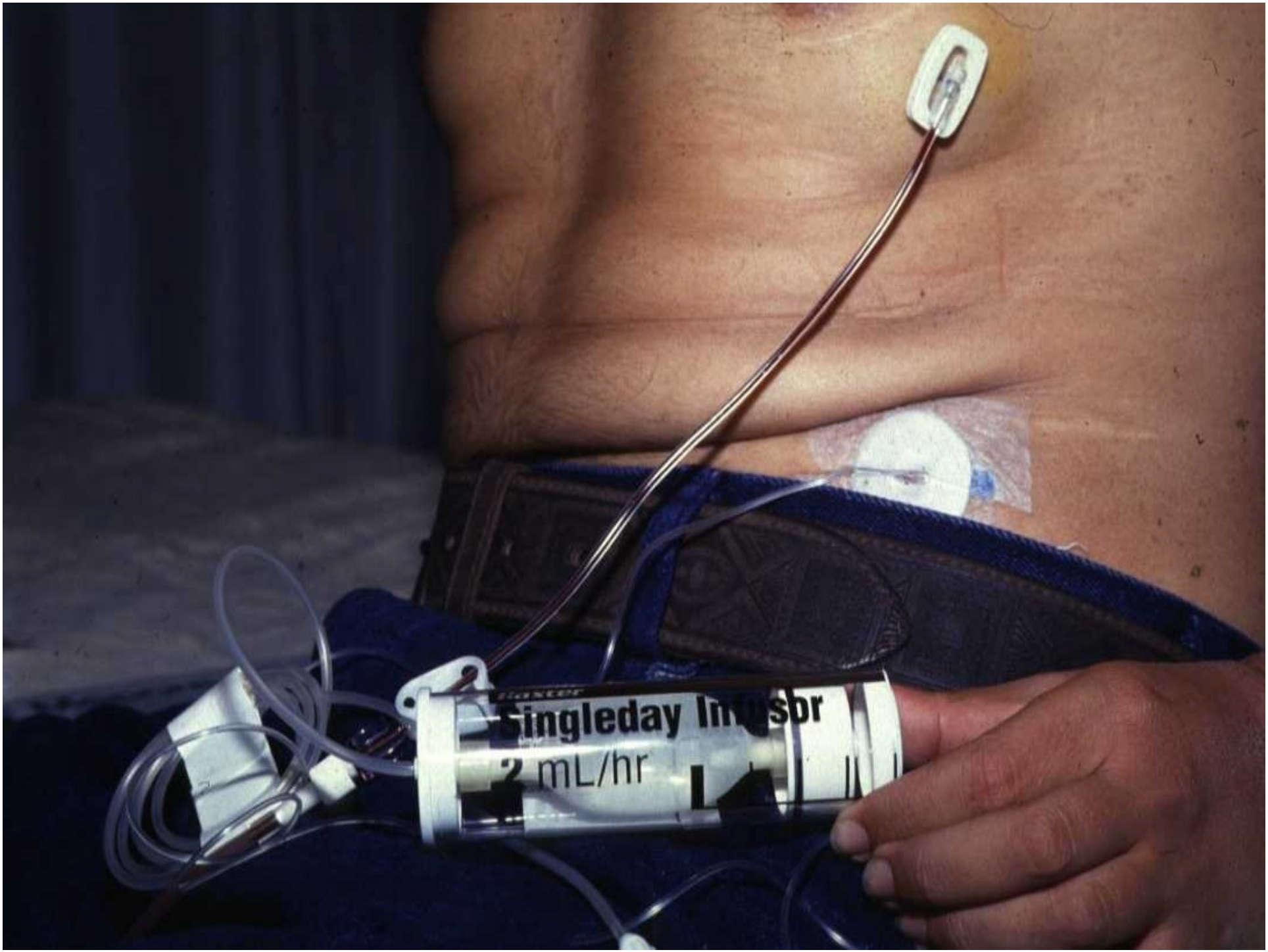
Stroke recurrence in SCD patients on chronic transfusions



*Pegelow et al, J.Pediatr, 1995, **126**:896-899*

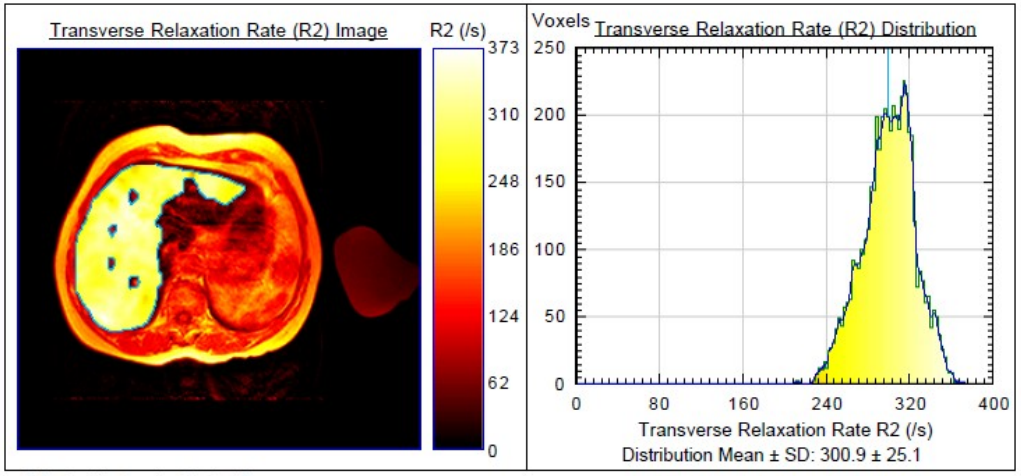
Exchange transfusion or top up?

- Hyperviscosity
- Venous access
- Maintaining iron balance
- Alloimmunisation
- Clinical indication
- Clinical status of the patient


singleday In sbr
mL/hr

Average Liver Iron Concentration	**> 43.0 mg/g dry tissue**	(NR: 0.17-1.8)
	> 769 mmol/kg dry tissue	(NR: 3-33)

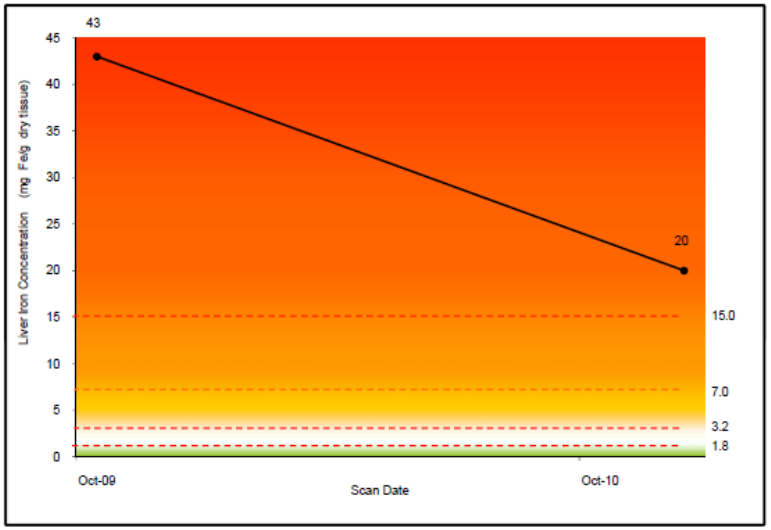
Normal range (NR) is taken from Bassett et. al., Hepatology 1986; 6: 24-29.



LIC Historic Values

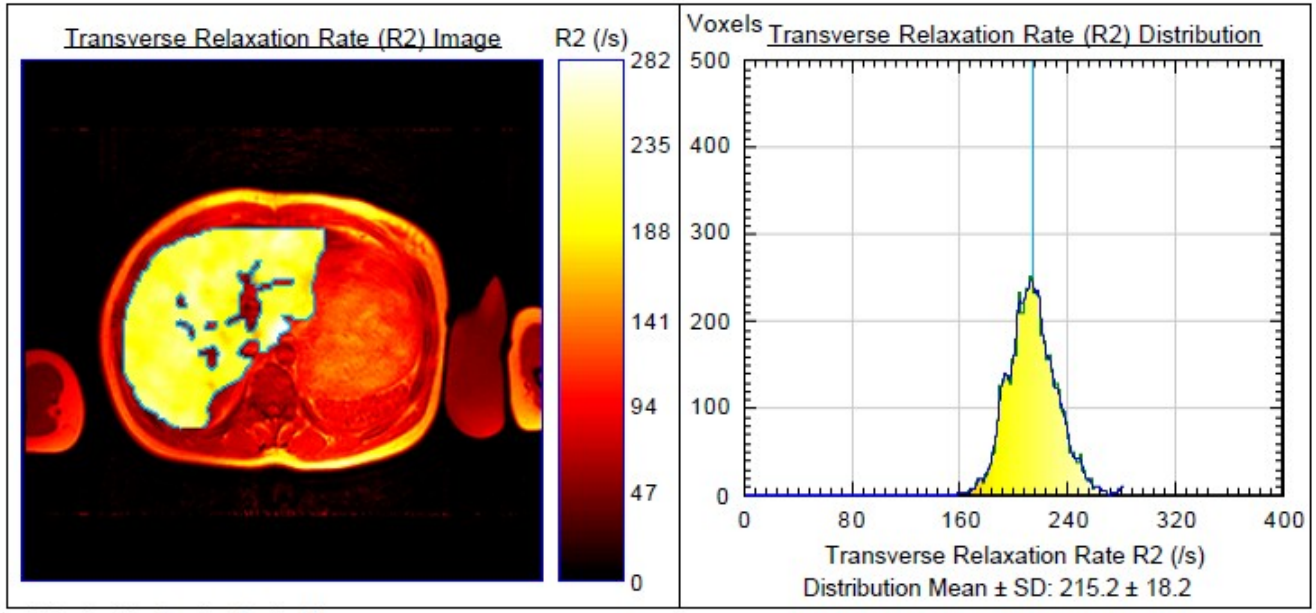
Scan Date	LIC mg Fe/g dw
07 Oct 2009	>43
13 Dec 2010	20.0

LIC Historic Plot



Average Liver Iron Concentration	**24.2 mg/g dry tissue**	(NR: 0.17-1.8)
	434 mmol/kg dry tissue	(NR: 3-33)

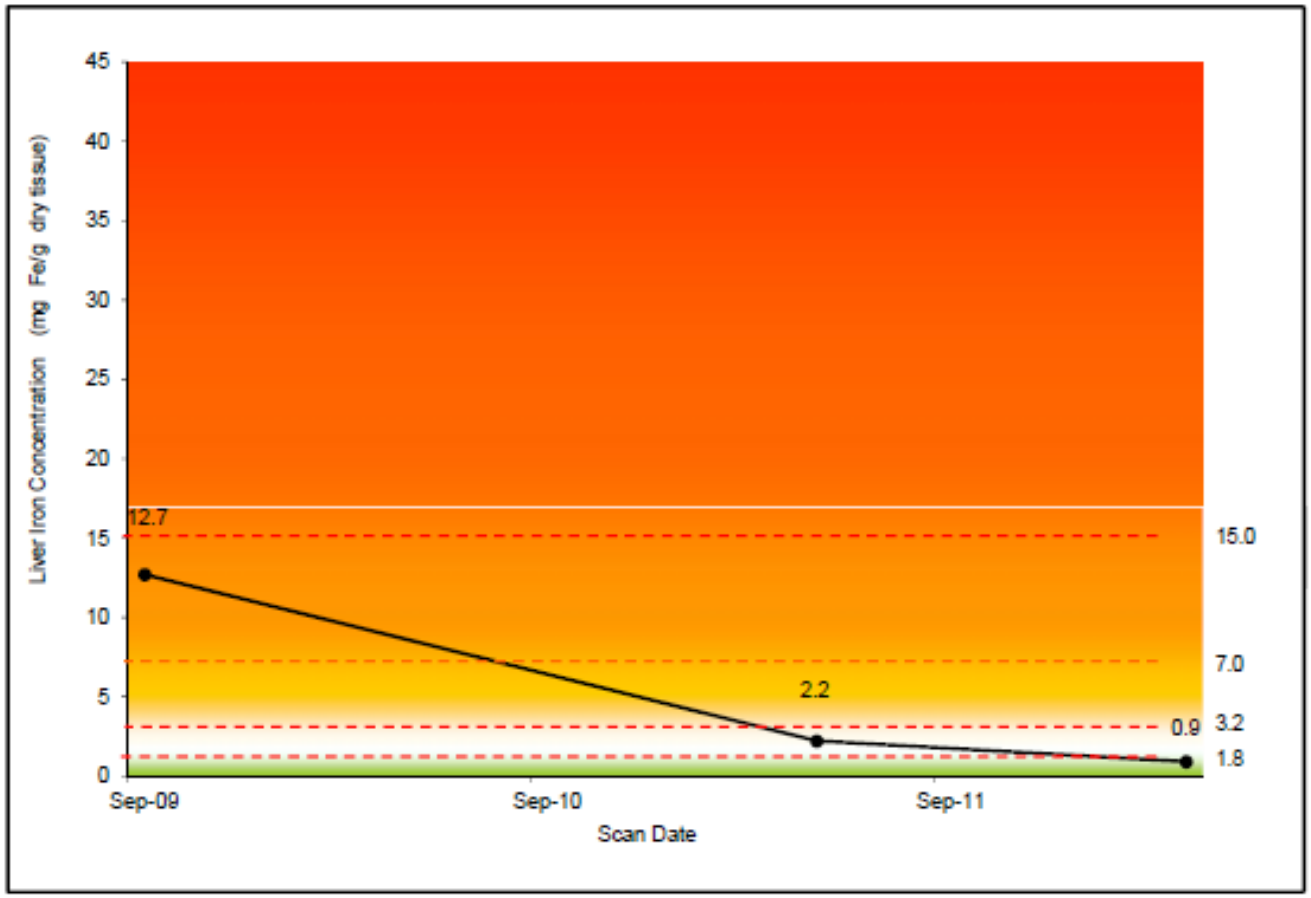
Normal range (NR) is taken from Bassett et. al., Hepatology 1986; 6: 24-29.



LIC Historic Values

Scan Date	LIC mg Fe/g dw
07 Sep 2009	12.7
11 May 2011	2.2
18 Apr 2012	0.9

LIC Historic Plot



Top up v Exchange

Top up

- Technically easier
- Fewer resources required
- Reduced donor exposure

- Faster rate of iron accumulation
- Difficult to achieve HbS <30% without increasing blood viscosity

Exchange

- Slower rate of iron accumulation
- Better control of desired HbS
- Reduced risk of hyperviscosity

- Vascular access problems
- Complications associated with long lines
- More resources
- Increased donor exposure

Manual v Automated Exchange

Manual

- Relatively less equipment
- Can be done at bedside
- Partial exchange (30% of blood volume can be achieved quickly
- Rapid reversal of ACS with partial exchange
- Can maintain HbS<30% if done every 4 weeks
- Different units have different protocols

Automated

- Relatively quick procedure
- Can achieve HbS<30% within 2 hours
- Can be programmed to achieve final Hb, HbS and net fluid balance
- Hypocalcaemia and thrombocytopenia can occur
- Use limited in many parts of the country

Laboratory Aspects

Extended phenotype (or genotype) & compatibility testing

- Phenotype/genotype prior to transfusion
- Serological usually; molecular if recently transfused
- C c E e K k Jk^a Jk^b Fy^a Fy^b S s
- U typing if S-s-
- Fully automated systems for ABO grouping
- Antibody screening as standard
- Antibody identification if screen positive
- Antibody card if alloantibodies detected

Choice of blood product

- Match for Rh (D C c E e) and K as a minimum
- Select R0 blood for R0 individuals; use rr in emergency if R0 unavailable
- If antibodies, select blood that is negative for corresponding antigens
- HbS negative
- <14 days old; <7 days old for automated exchange if possible

Alloimmunisation in SCD

The serious problem of alloimmunisation

•Reported frequency 18-36% in sickle cell disease
•30% sickle v 5% non-sickle (Vichinsky, NEJM 1990)
•Likely an underestimate – 37% of antibodies undetectable (Rosse Blood 1990)
•K C E account for 66% of antibodies (Davies BJH, 1987; Vichinsky NEJM 1990)
•Higher rate of multiple alloantibodies (Rosse, Blood 1990)
•Increased rate of autoantibodies (Castellino, BJH 1999)

Factors implicated in alloimmunisation

- Phenotype differences between donors and recipients (Vichinsky, NEJM 1990)
- Greater number of transfusions (Rosse Blood 1990; Olujohungbe BJH 2001)
- Later start to transfusions (Spanos, Vox Sanguinis 1990)

Red cell phenotypes (%) patients and donors

	Caucasian	African
*C	70 (68)[+]	30 (28)
*E	30 (35)	19 (24)
*K	9 (9)	2 (2)
Jk^a	77 (77)	92 (91)
*Jk^b	74 (72)	49 (39)
S	55 (55)	31 (26)
s	89 (94)	97 (95)
**U	>99.9	99
*Fy^a	66 (67)	10 (15)
*Fy^b	83 (82)	23 (11)

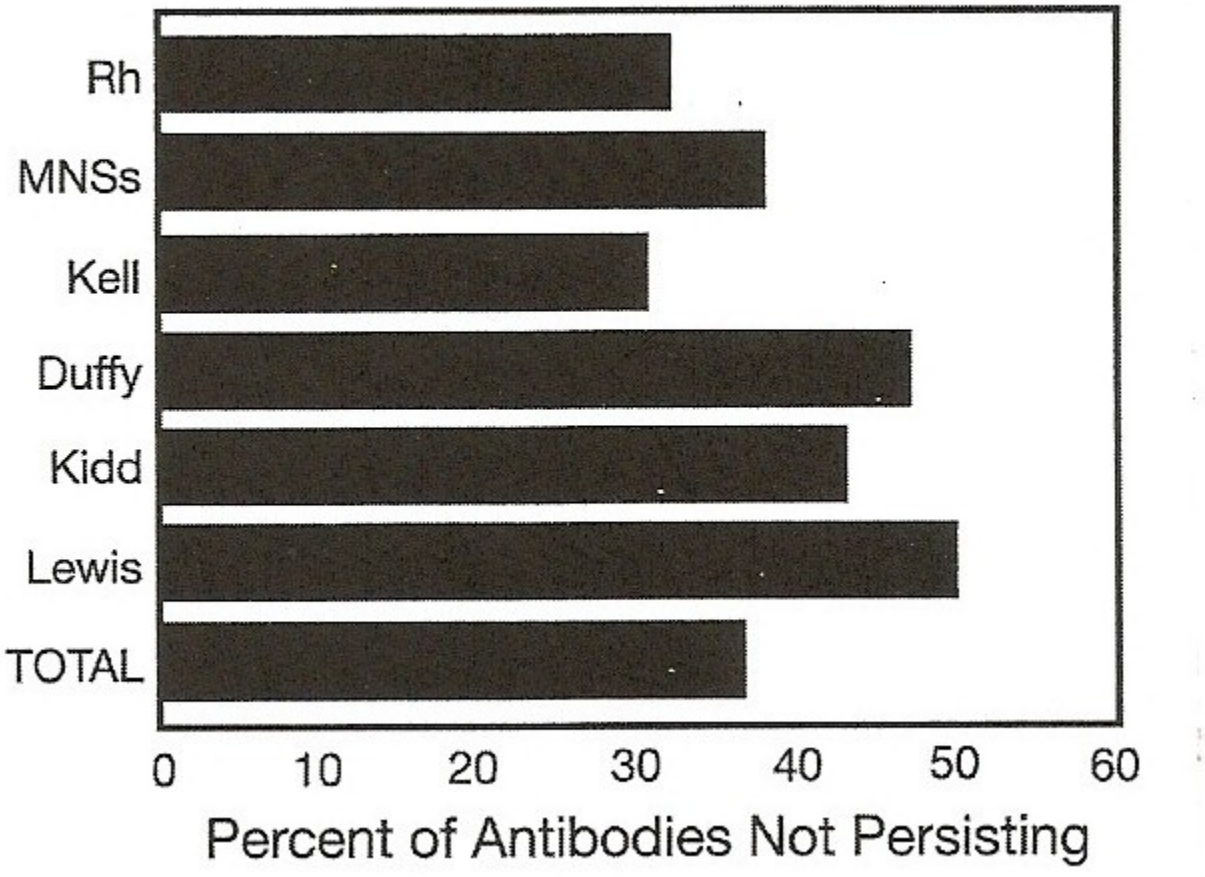
[+]*Vichinsky NEJM 1990; 322:1617-21*

Frequency of alloantibodies in transfused sickle cell patients

Specificity	Frequency (%)	Specificity	Frequency (%)
K	26	Le^a	4
E	24	M	4
C	16	Fy^b	3
Jk^b	10	e	2
Fy^a	6	Jk^a	2

*Vichinsky NEJM 1990; **322**:1617-21*

Disappearing alloantibodies in SCD



Vichinsky Semin Hematol, 2001

Minimising Alloimmunisation

Reduced use of transfusions

- Avoid transfusion unless absolutely necessary
- Incentive spirometry *(Bellet, NEJM 1995)*
- Hydroxyurea *(Charache, NEJM 1995)*

Give phenotype-matched blood

- Matching for K, C, E reduced alloimmunisation rate from 3% to 0.5% *(Vichinsky, Transfusion 2001)*
- 10x reduction if fully phenotyped (17 alloantigens) (*Ambruso, Transfusion 1987)*

Difficult to transfuse patients

Rare blood types

•Multiple alloantibodies – particular combinations may pose more difficulties
•Common phenotype in Blacks, rare in Caucasian donors (eg. Fy^{a-b-})
•Rare phenotype occurring exclusively in Blacks (S-s-U- and Js^{a+b-})

Hyperhaemolysis

- Technically not a rare blood group problem
- Problem of provoking or exacerbating life-threatening haemolysis
- Transfusion management during active haemolysis
  - Avoid transfusion if mild
  - Small volume top ups if severe, rapid haemolysis

Difficult to transfuse patients

Management

- Antibody and hyperhaemolysis cards
- Transfuse only with consultant authorisation
- Active involvement of NBS consultants
- Planning for elective transfusions eg. (pre-op)
  - Prevention of further alloimmunisations
  - Limiting blood loss at operations
  - Location of red cell units
- Planning for emergencies

National Transfusion Database for SCD

•No national database
- Extended phenotype results
- Alloimmunised patients
- Hyperhaemolysis patients

•No centralised system for phenotyping or antibody identification
- In-house
- National Blood Service

•A central database – hospital transfusion labs can very easily access patients' transfusion records
- Telephone hotline
- Directly by electronic means

Conclusions

- Transfusion is a major part of SCD management but has risks
- Risks can be minimised by attention to specific principles
- Guideline should help disseminate good practice
- A central database will facilitate transfusion management of sickle cell patients