The effects of storage on blood products

Steven L. Spitalnik, M.D.

Laboratory of Transfusion Biology

Columbia University
College of Physicians and Surgeons

NewYork-Presbyterian
The University Hospitals of Columbia and Cornell

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The effects of storage on red blood cells

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The influence of donor genetics, diet, and environment on red blood cell storage quality

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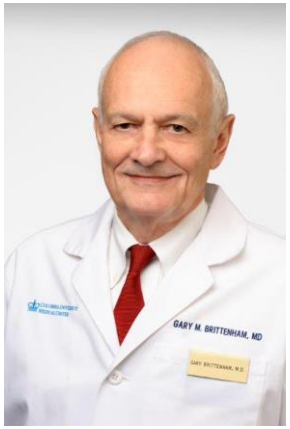
Potential Conflicts of Interest

Hemanext	Advisory Board
Tioma, Inc	Consultant
Team Conveyer Intellectual Prop.	Consultant
Ferrous Wheel Consultants	CEO
Worldwide Initiative For Rh Disease Eradication (WIRhE)	Executive Director

Laboratory of Transfusion Biology

Columbia University

I. Akpan



G. Brittenham

R. Francis

E. Hod

K. Hudson

D. Roh

S. Spitalnik

T. Thomas

S. Weisberg

Central Thesis

Blood products → Pharmaceuticals

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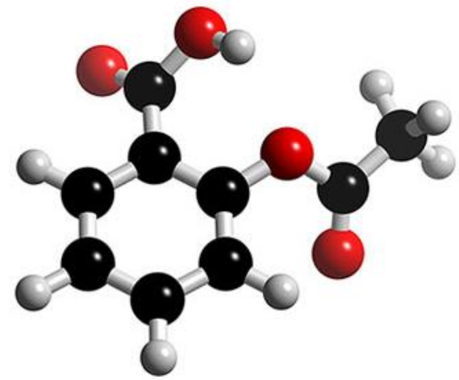
Blood products → Pharmaceuticals

Complex biological products → "Pure drugs"

Aspirin = Acetylsalicylic acid



Medical Model of a Pharmaceutical

Active ingredient(s)
Purity
Inactive ingredients: binders, fillers, etc.
Stability: shelf life, expiration date, storage conditions
Dosages
Route of administration, Bioavailability
Pharmacokinetics/Pharmacodynamics
Indications
Clinical effectiveness
Adverse outcomes

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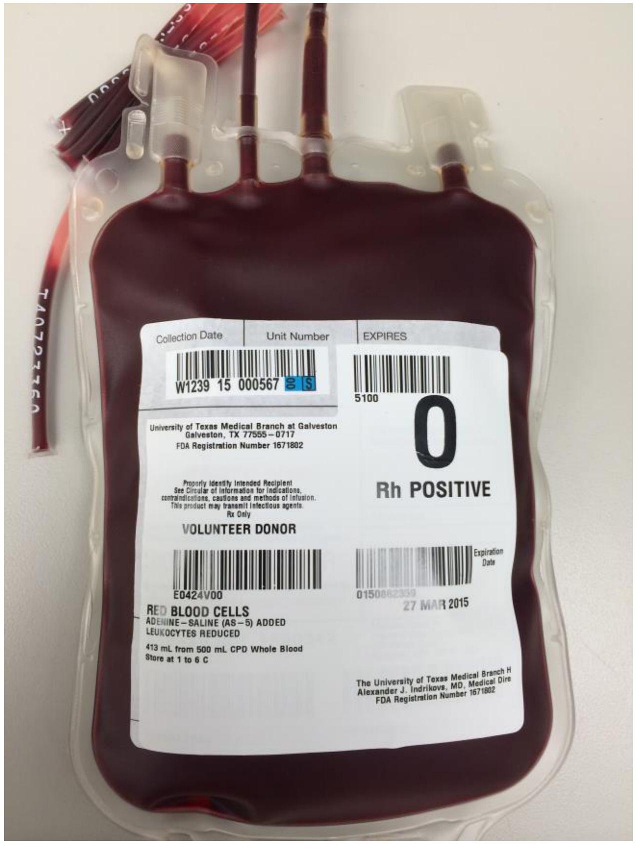
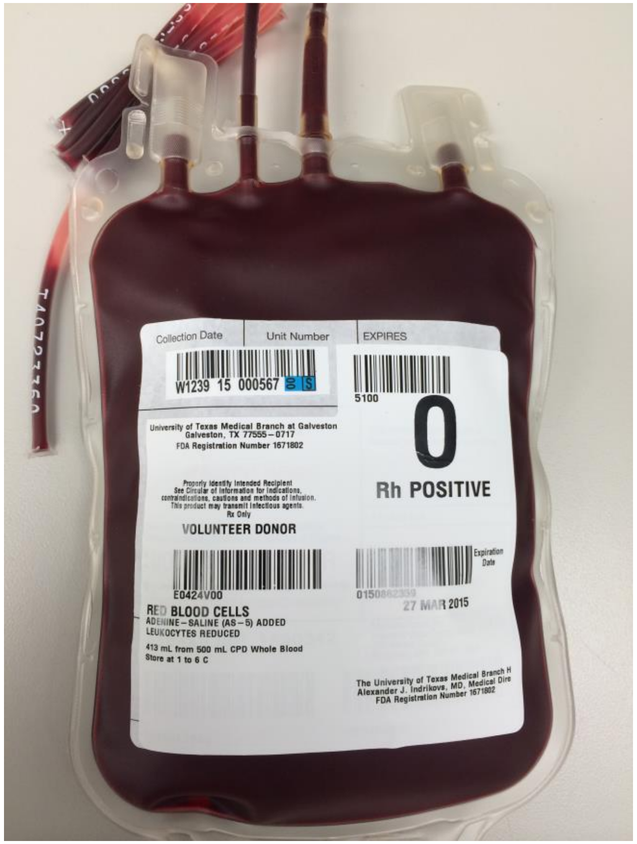
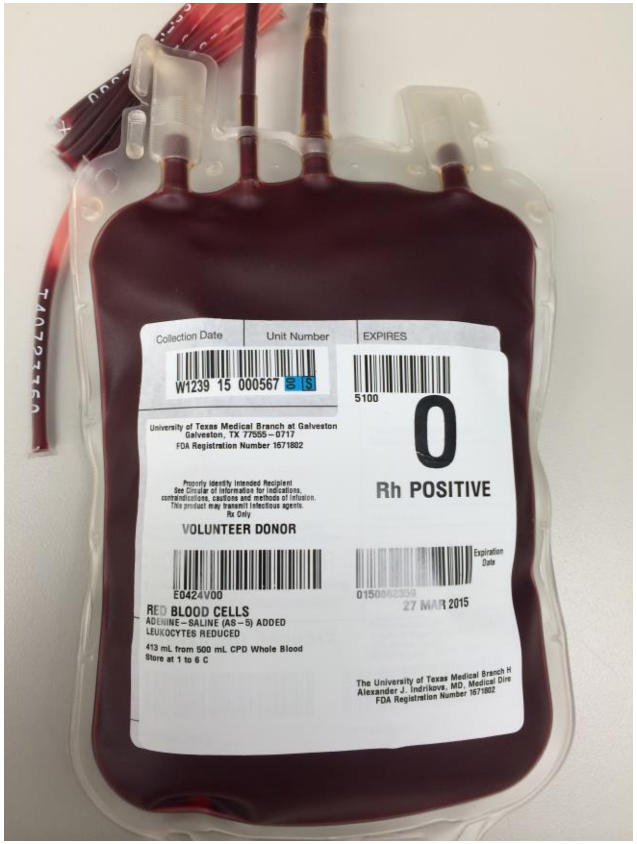


Complex biological products → "Pure drugs"



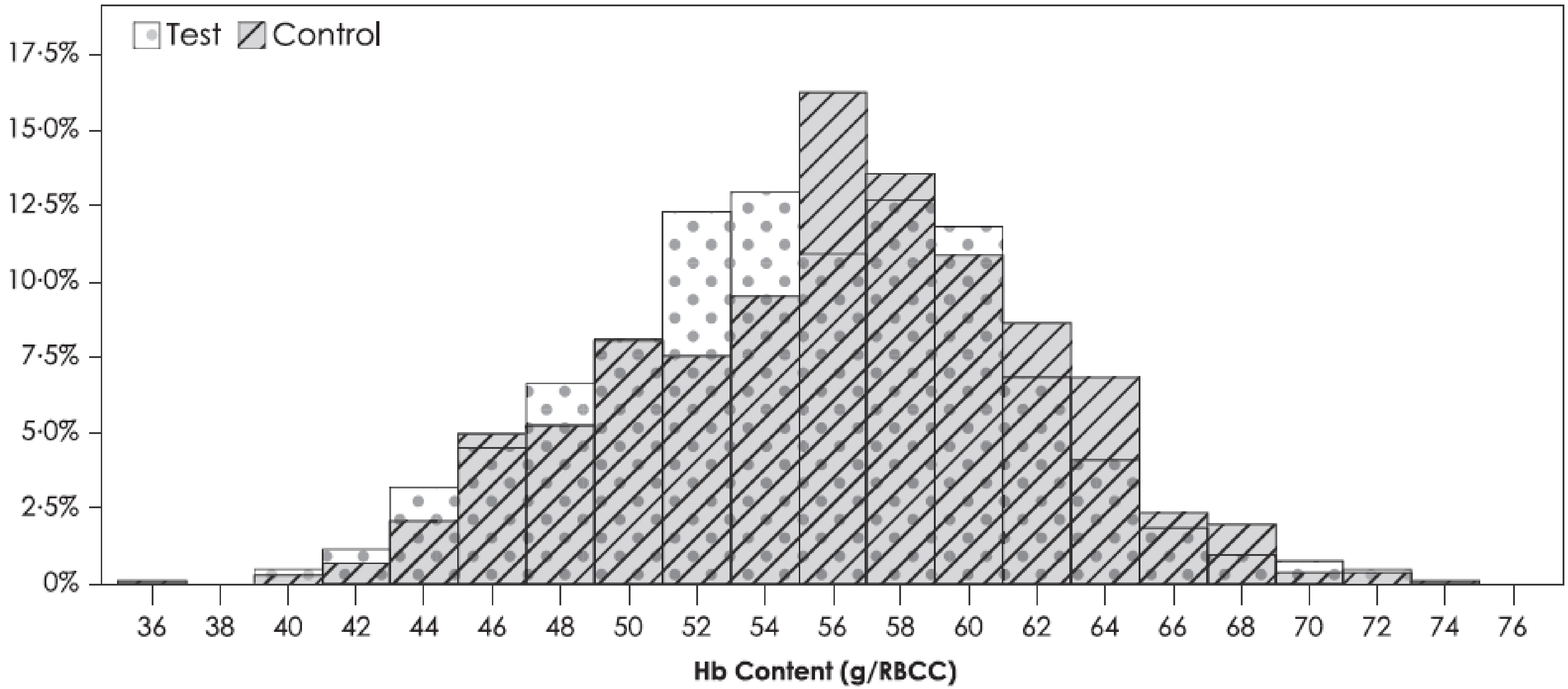
Blood "Pharm-ing"?

Complex biological products → "Pure drugs"



What about better starting material?

Complex biological products → “Pure drugs”



Aydinok et al. Brit. J. Haematol. 186:625-636, 2019

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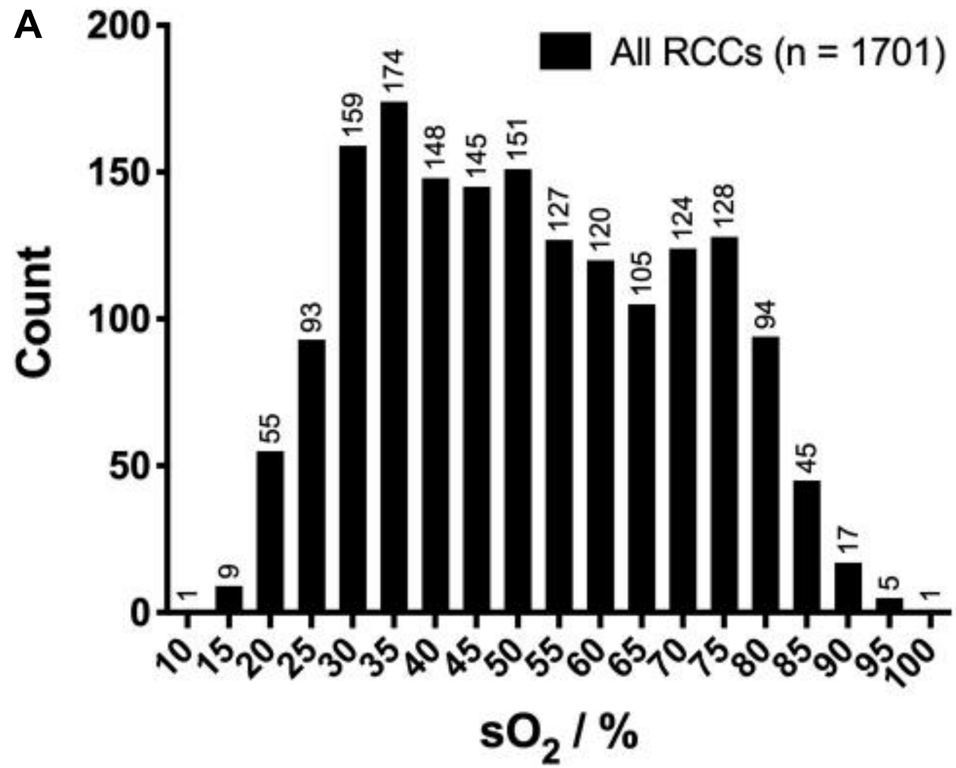

Bardyn et al. Front. Physiol. 11:616457, 2020

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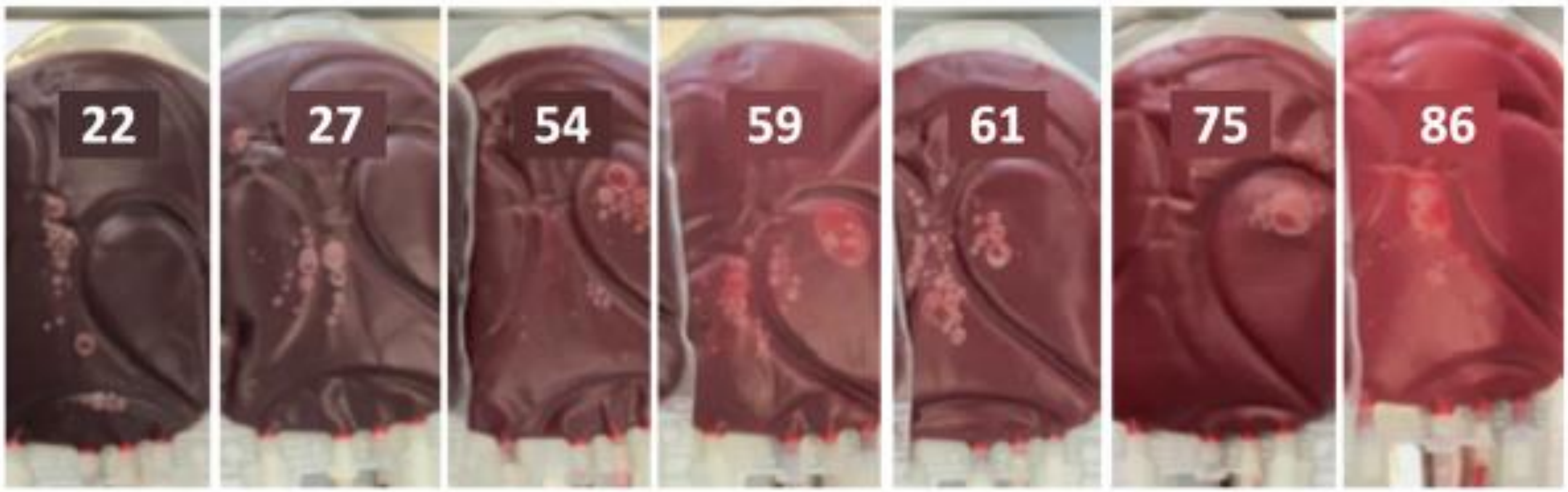

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What about better starting material?

What do we know about refrigerator-stored RBCs?

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As storage time increases (FDA criteria):

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Increasing hemolysis *ex vivo* (<1.0%)

Infuse free hemoglobin, etc.

What do we know about refrigerator-stored RBCs?

As storage time increases (FDA criteria):

Increasing hemolysis *ex vivo* (<1.0%)
- **Infuse free hemoglobin, etc.**

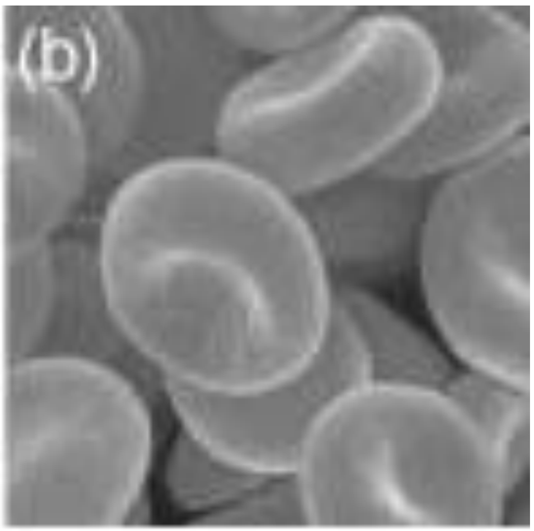
Decreasing 24-hr post-transfusion recovery *in vivo* (~≥75%)
- **Less than optimal dose**

What happens to the RBCs during refrigerated storage?

The “RBC storage lesion”

- ↓ 2,3-DPG, GSH, ATP
- ↓ Nitric oxide
- ↑ Protein oxidation
- ↑ Membrane- & cytoskeletal-associated hemoglobin
- ↑ Membrane lipid peroxidation
- ↑ Lysophosphatidylcholine species
- ↑ Vesiculation and membrane loss
- ↓ Deformability
- ↑ Phosphatidylserine exposure
- ↓ CD47

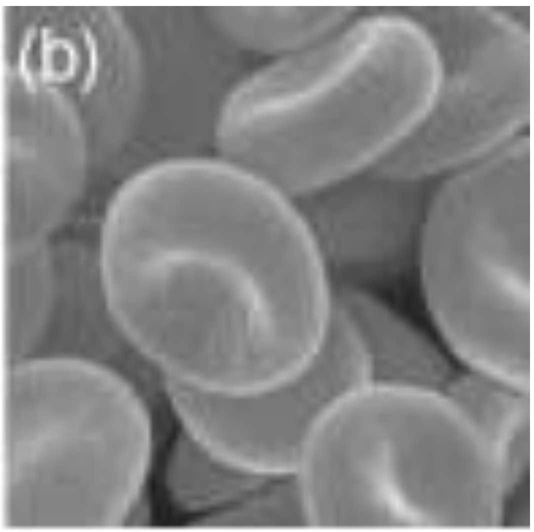
The "RBC storage lesion"



Day 0

Blasi, D'Alessandro, et al. Transfusion Medicine 22:90-96, 2012

The “RBC storage lesion”



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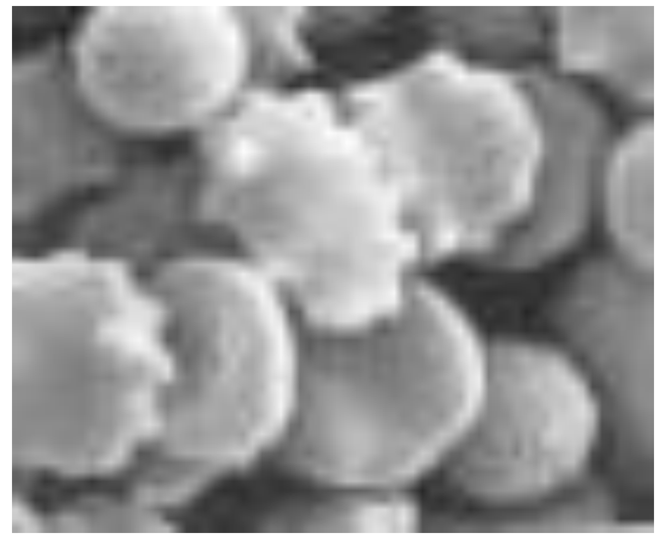

Day 42

Blasi, D’Alessandro, et al. Transfusion Medicine 22:90-96, 2012

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- ↑ Phosphatidylserine exposure
- ↓ CD47

The “RBC storage lesion”
Final common pathway?

Metabolic dysfunction & oxidative stress ➔

↓ Deformability

↑ “Eat me” signals (phosphatidylserine)

↓ “Don’t eat me” signals (CD47)

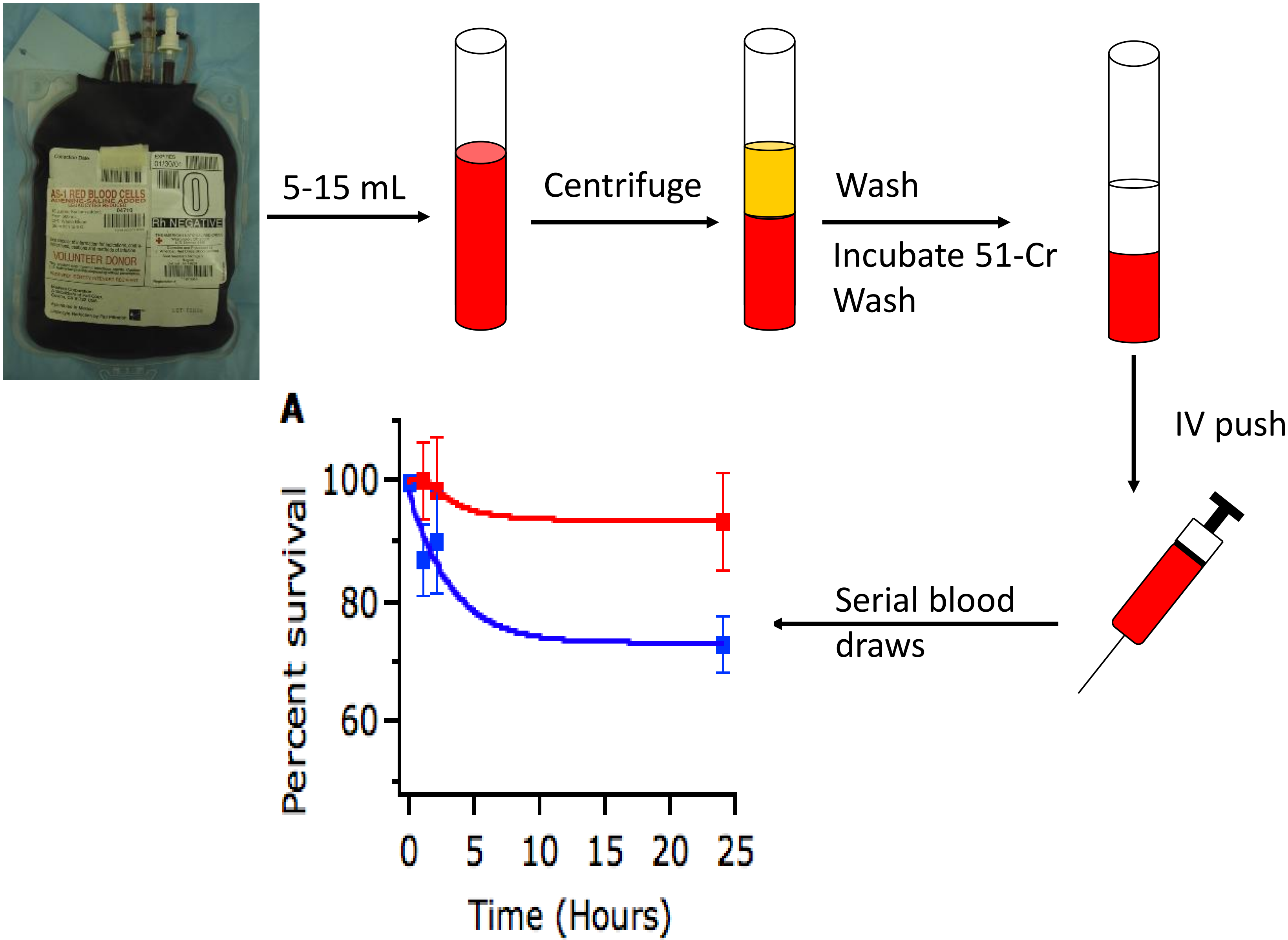
↑ Hemolysis *in vitro*

↑ RBC clearance *in vivo*

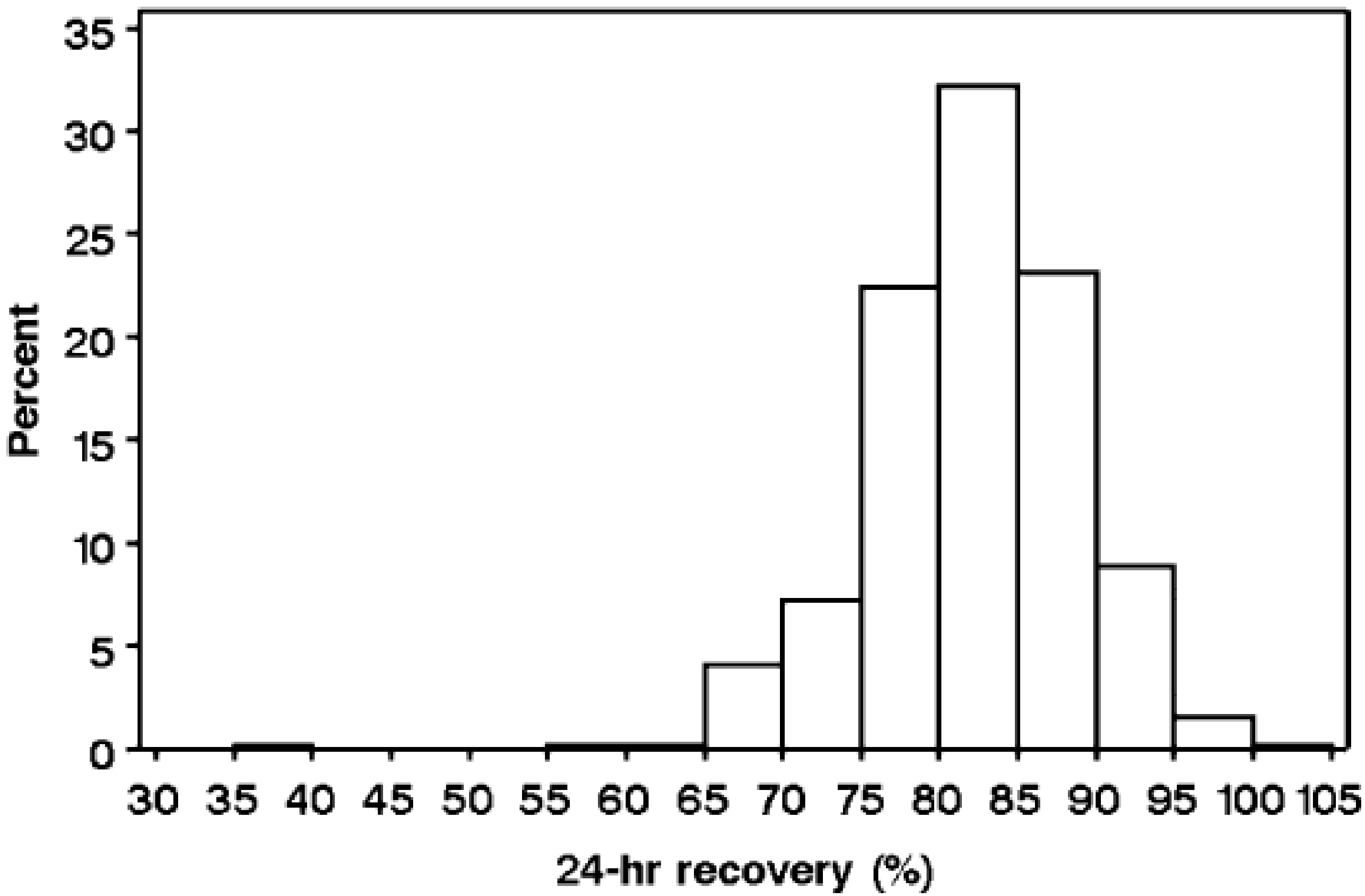
Intravascular and extravascular hemolysis

RBC Clearance Variability

RBC Recovery Study



24-hr RBC recovery in 641 healthy volunteers



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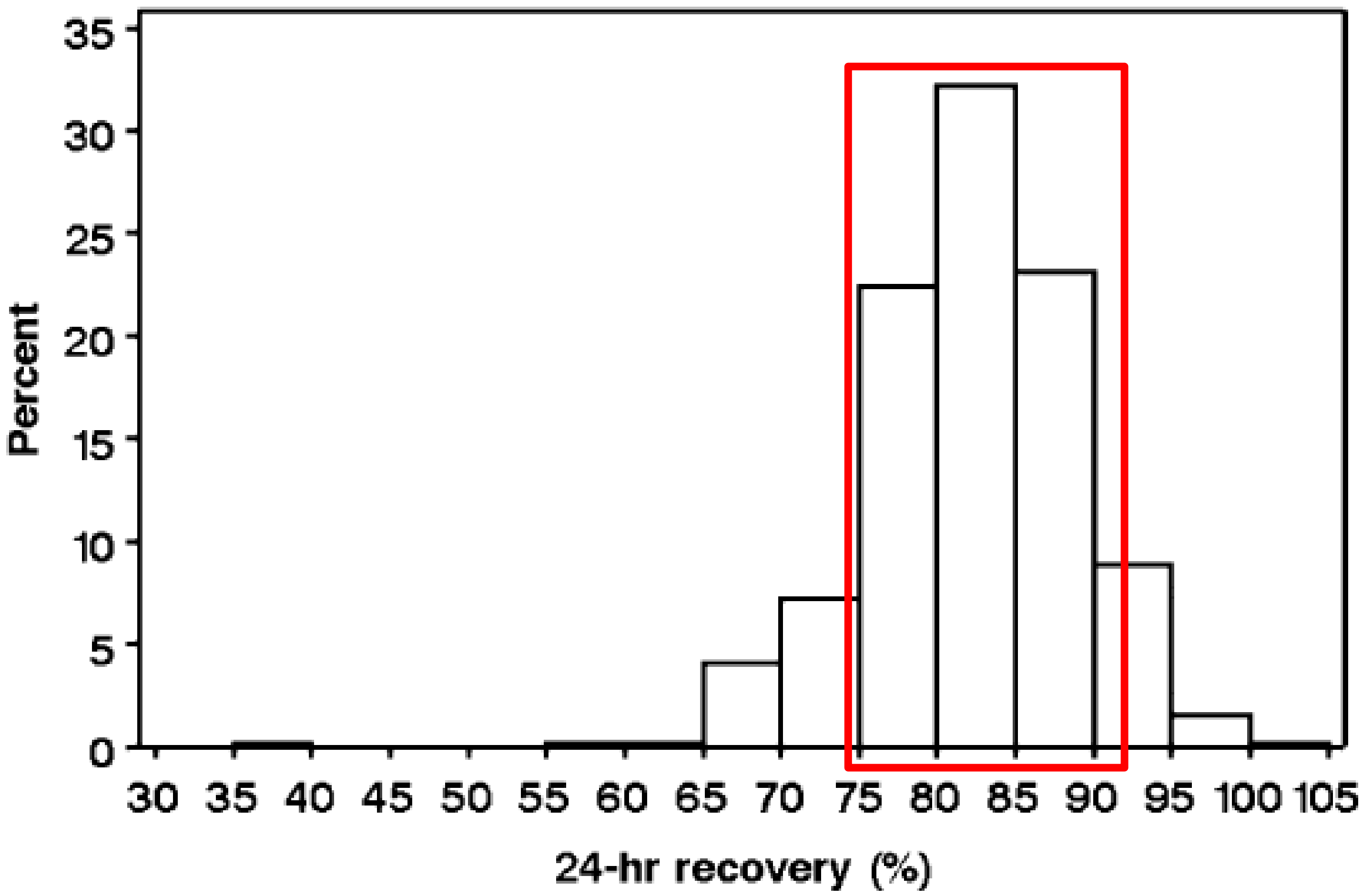

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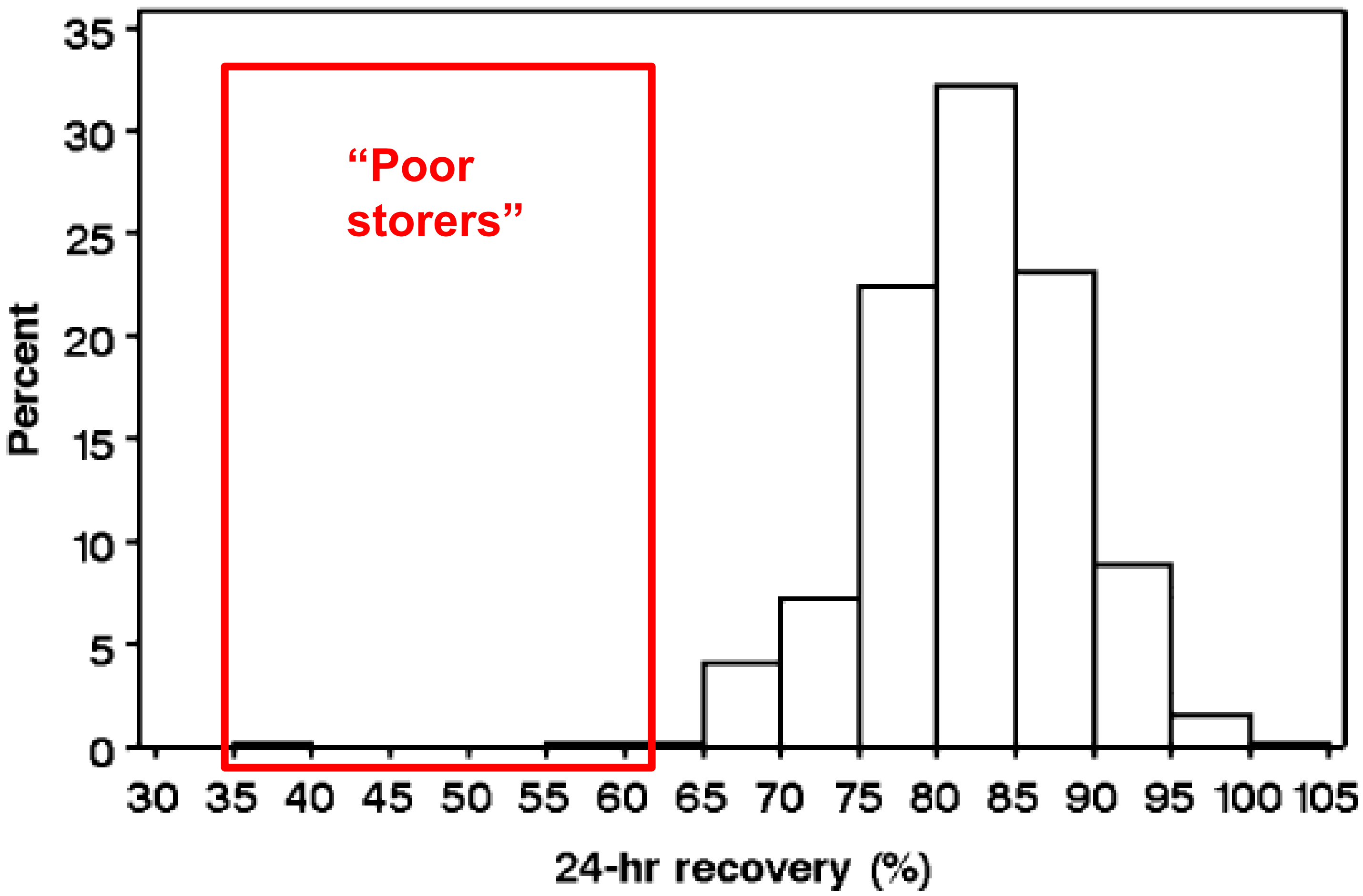

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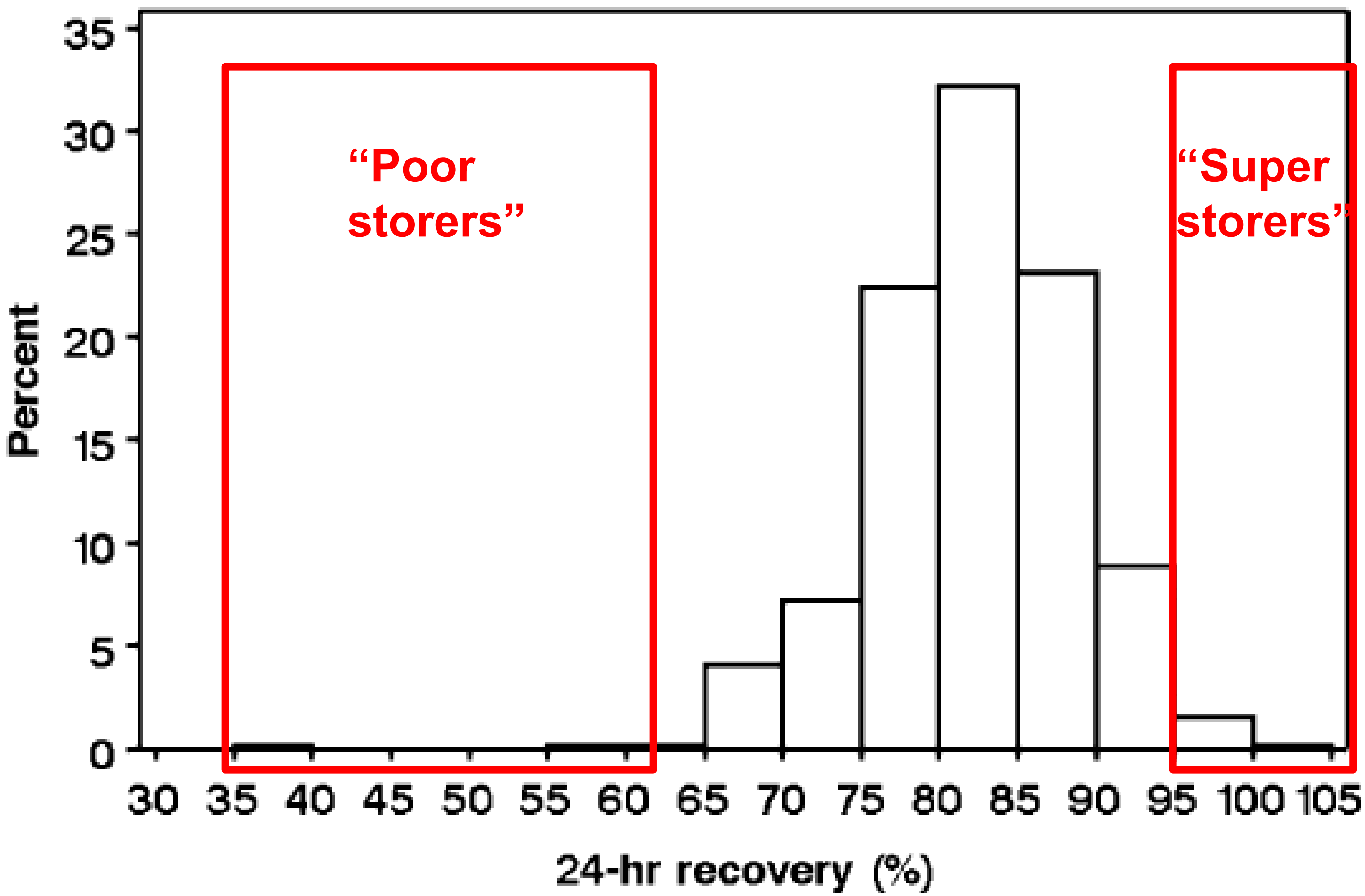

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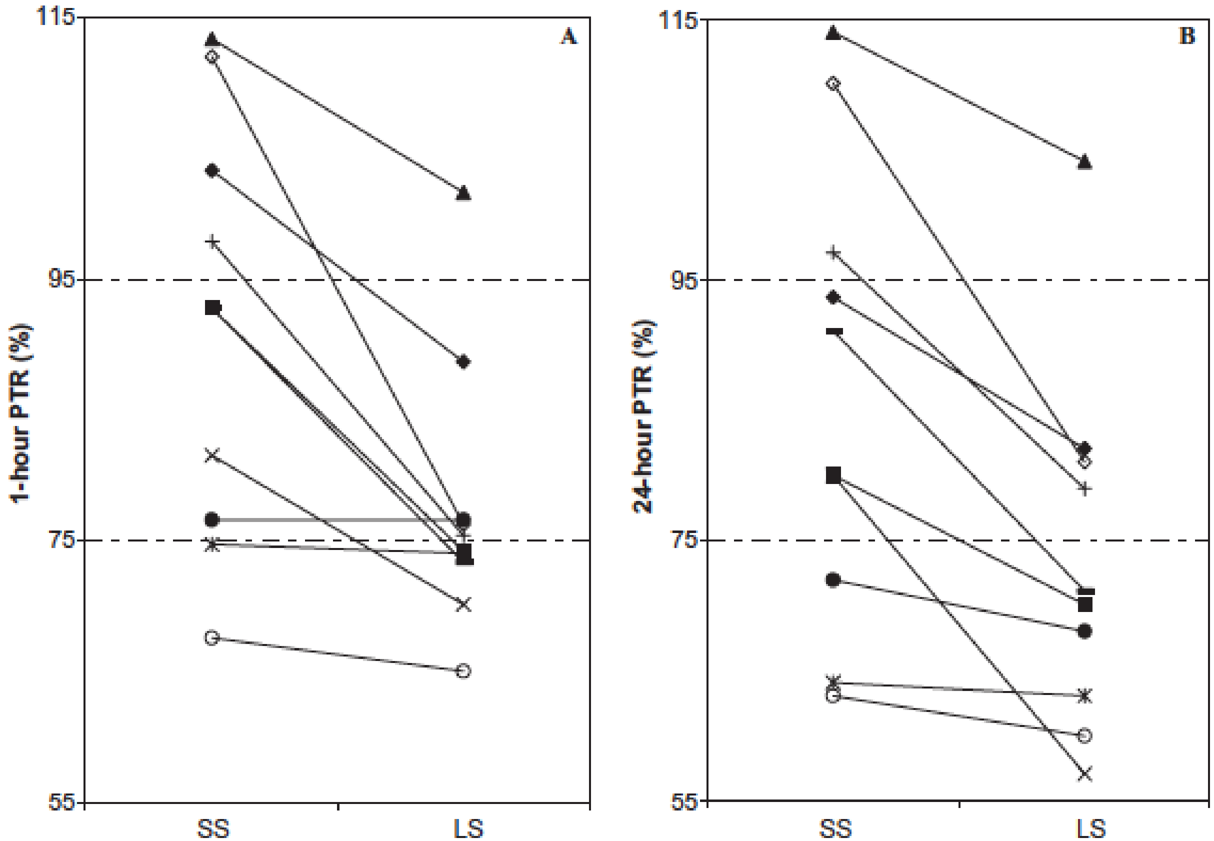

Fig. 1. Individual 1-hour PTR (A) and 24-hour PTR (B) of SS and LS RBCs. SS and LS RBCs that have been transfused into the same patient are connected to each other. Each symbol represents a patient.

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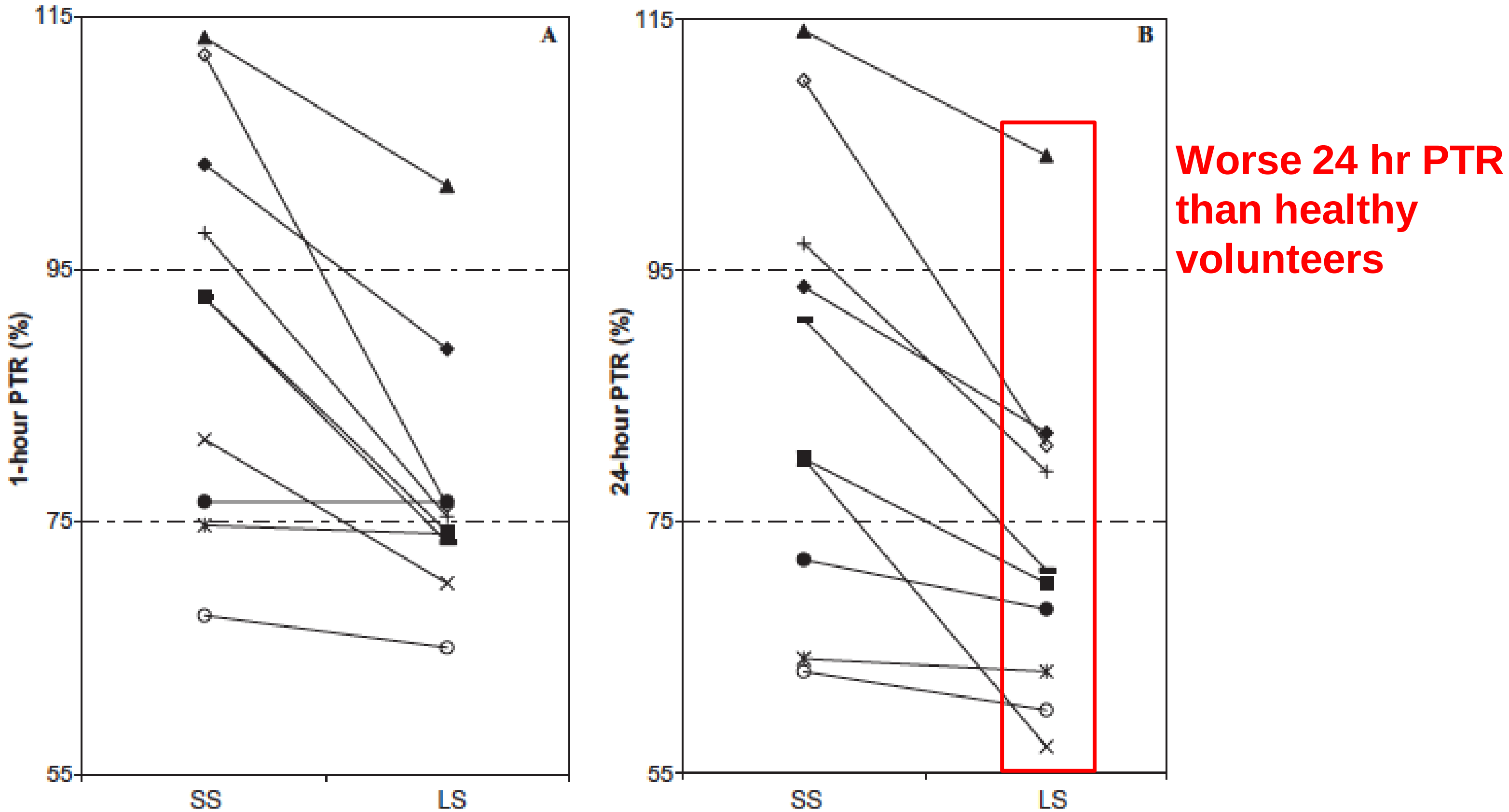

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We know remarkably little about recipient influences on this effect

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RBC recovery is worse in patients than in healthy volunteers

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TRANSFUSION MEDICINE

Effect of donor, component, and recipient characteristics on hemoglobin increments following red blood cell transfusion

Nareg H. Roubinian,[1-3] Colleen Plimier,[1] Jennifer P. Woo,[4] Catherine Lee,[1] Roberta Bruhn,[2,3] Vincent X. Liu,[1] Gabriel J. Escobar,[1] Steven H. Kleinman,[5] Darrell J. Triulzi,[6] Edward L. Murphy,[3,2] and Michael P. Busch[2,3]

Roubinian et al. Blood 134:1003-13, 2019

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Adverse consequences of RBC transfusion

Infectious
Immunological
Volume related
Other ("old" RBCs?)

Is “old” blood bad?

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Infection?
Inflammation?
Thrombosis?
Mortality?

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Infection?
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Thrombosis?
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Not going to talk about these now

Is “old” blood bad?

Infection?
Inflammation?
Thrombosis?
Mortality?

Not going to talk about these now
We can discuss these later, if you would like

Is "old" blood bad?

↑ **RBC refrigerated storage time**

↓

↑ **RBC storage lesion *in vitro***

↓

↓ **RBC recovery *in vivo***

Is “old” blood bad?

Why is transfusion of less than a full “dose” OK?

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Transfused RBCs that don’t circulate cannot provide their “pharmaceutical” function (e.g., O_2 delivery)

Is “old” blood bad?

Why is transfusion of less than a full “dose” OK?

Transfused RBCs that don’t circulate cannot provide their “pharmaceutical” function (e.g., O_2 delivery)

What other drug do we give whose potency decreases over time? And that’s OK?

Not just RBC quality

Not just RBC quality

Activity of recipient's mononuclear phagocyte system

(1) Quality of transfused donor RBCs

and

(2) activity of recipient mononuclear phagocyte system

determine post-transfusion recovery and RBC lifespan *in vivo*

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and

(2) activity of recipient mononuclear phagocyte system

determine post-transfusion recovery and RBC lifespan *in vivo*

When do RBCs “go bad”?

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The Journal of Clinical Investigation CLINICAL MEDICINE

Prolonged red cell storage before transfusion increases extravascular hemolysis

Francesca Rapido,[1,2] Gary M. Brittenham,[3,4] Sheila Bandyopadhyay,[1] Francesca La Carpia,[1] Camilla L'Acqua,[1] Donald J. McMahon,[4] Abdelhadi Rebbaa,[1] Boguslaw S. Wojczyk,[1] Jane Netterwald,[1] Hangli Wang,[1] Joseph Schwartz,[1] Andrew Eisenberger,[4] Mark Soffing,[5] Randy Yeh,[5] Chaitanya Divgi,[5] Yelena Z. Ginzburg,[6] Beth H. Shaz,[6] Sujit Sheth,[7] Richard O. Francis,[1] Steven L. Spitalnik,[1] and Eldad A. Hod[1]

Journal of Clinical Investigation 127:375-382, 2017

E. Hod

60 healthy volunteers enrolled

52 completed study

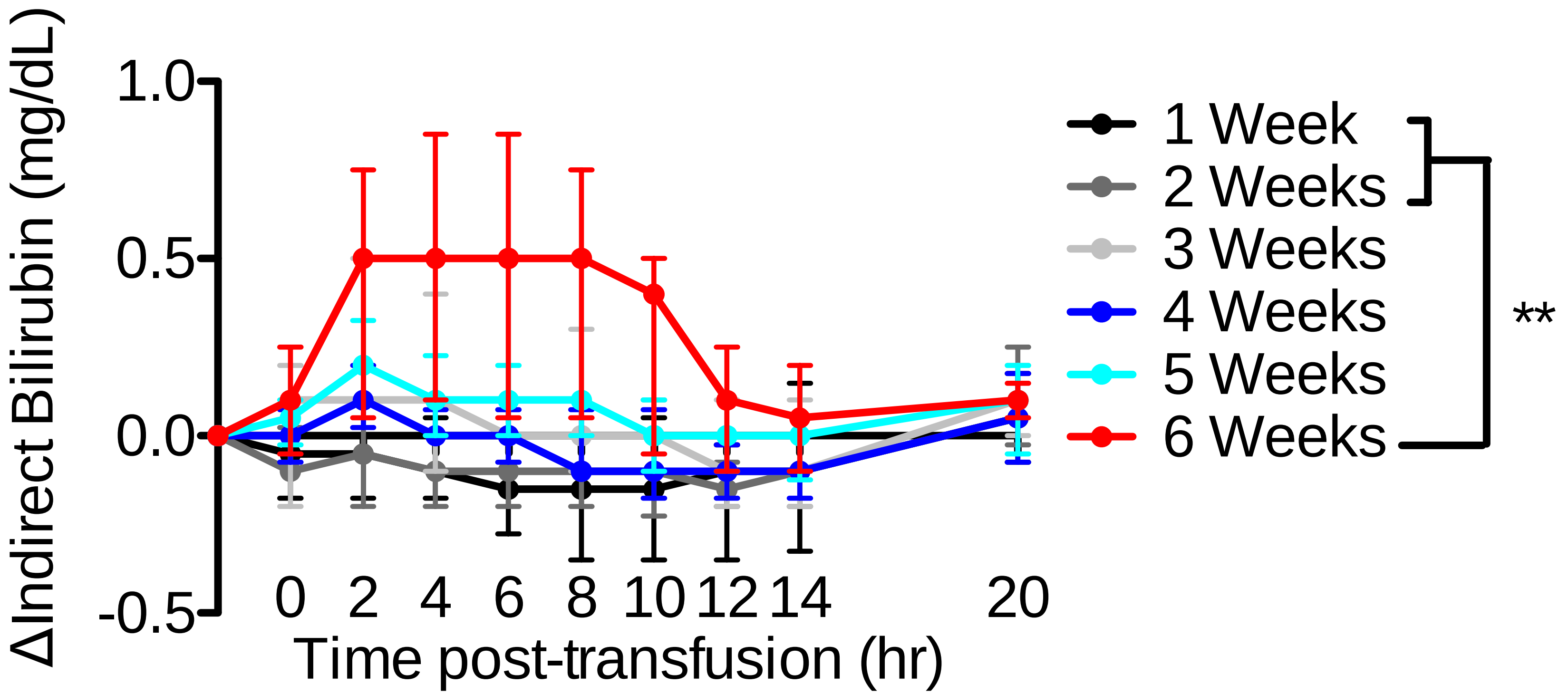
Randomized to 1, 2, 3, 4, 5, 6 weeks of storage

Donation at NYBC; leukoreduced; AS-3

Transfused with entire unit

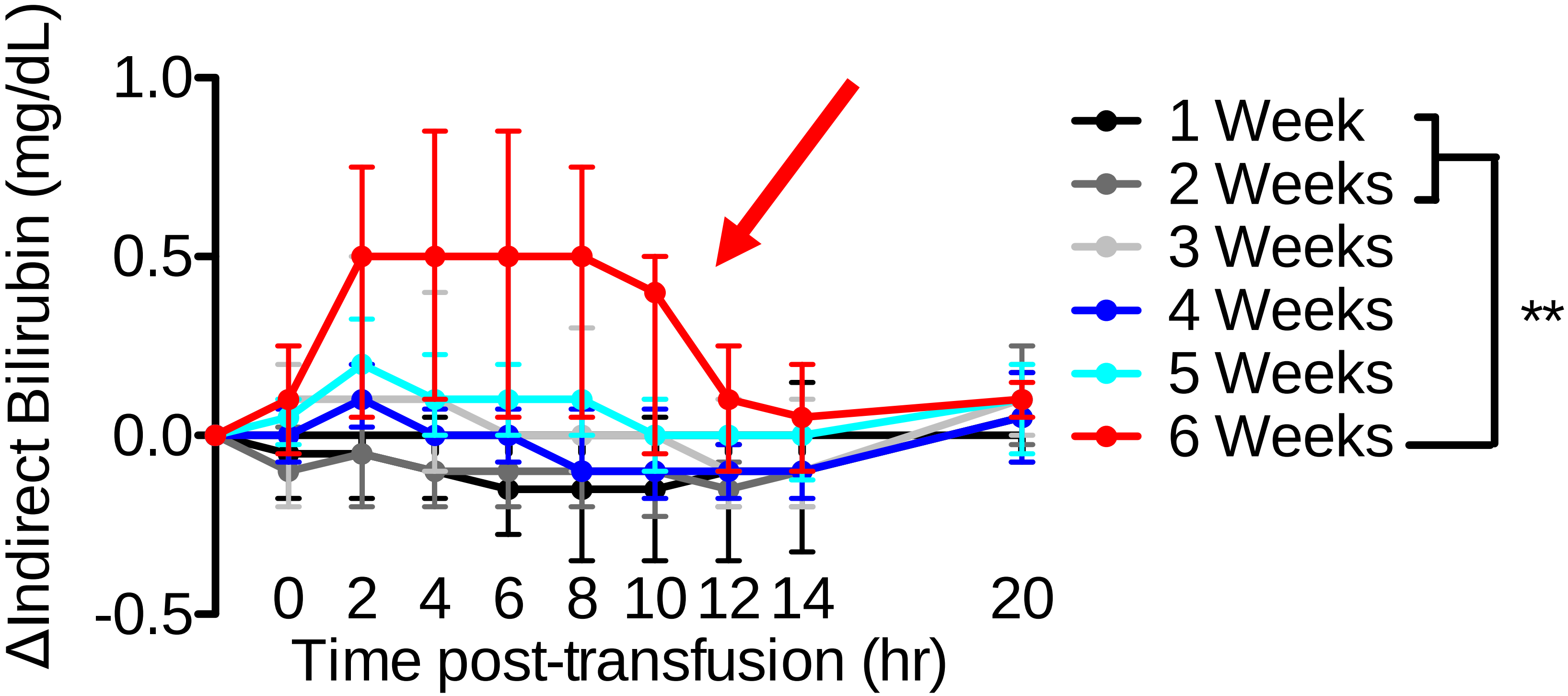
^{51}Cr-labeled post-transfusion recovery

When do RBCs “go bad”?



When do RBCs "go bad"?

6 Weeks



Transferrin Saturation (Tf_{sat})

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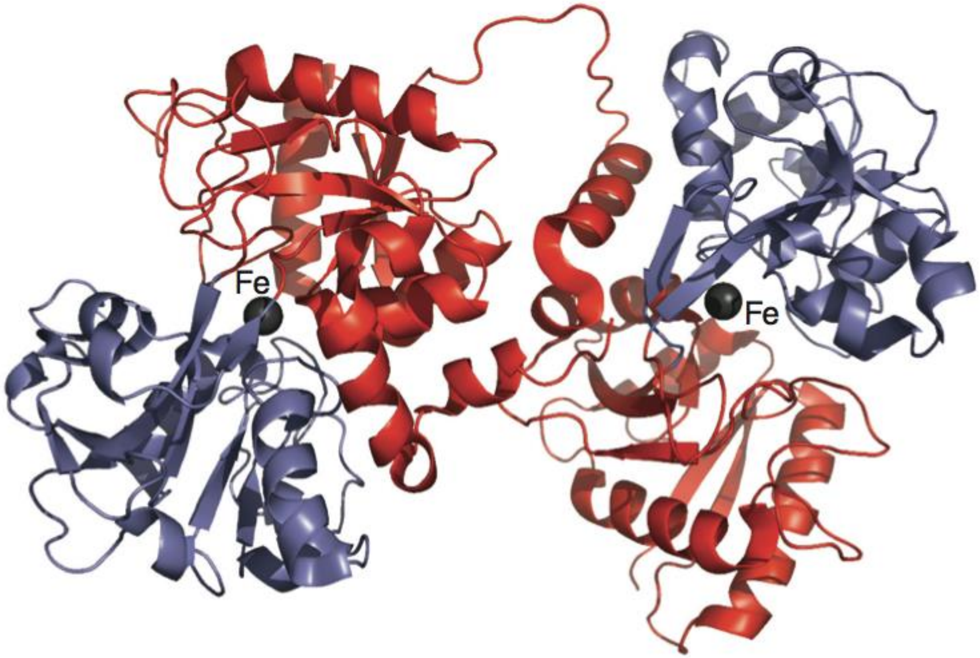

http://www.chemtube3d.com/solidstate/BC-26-13.htm

Apo-Tf: no iron bound
Holo-Tf: 2 iron atoms bound
Tf_{sat} = 20% → 80% of iron-binding sites available
Tf_{sat} = 75-80% → NTBI appears

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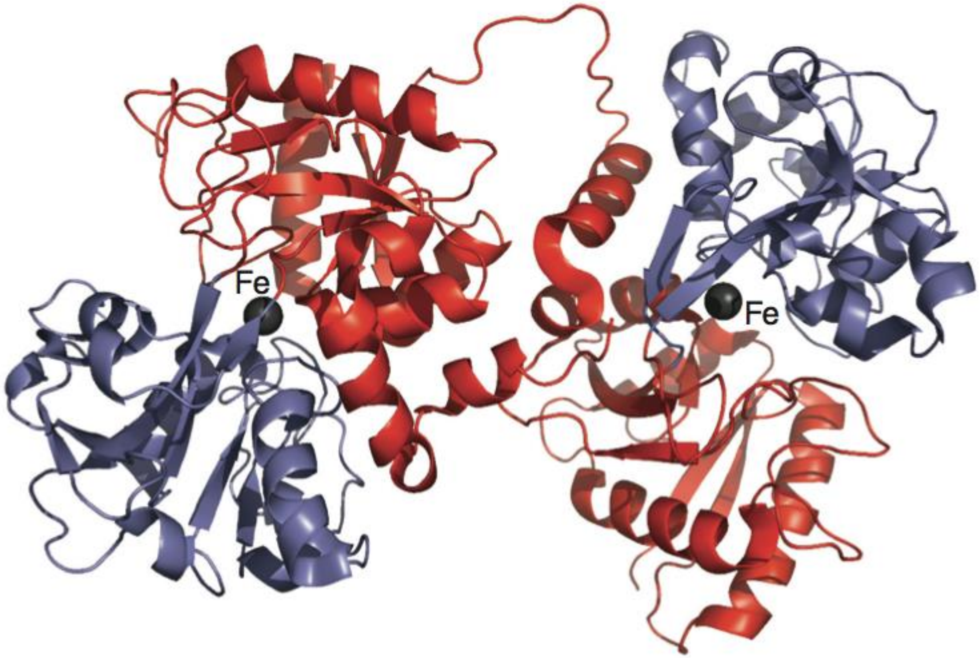

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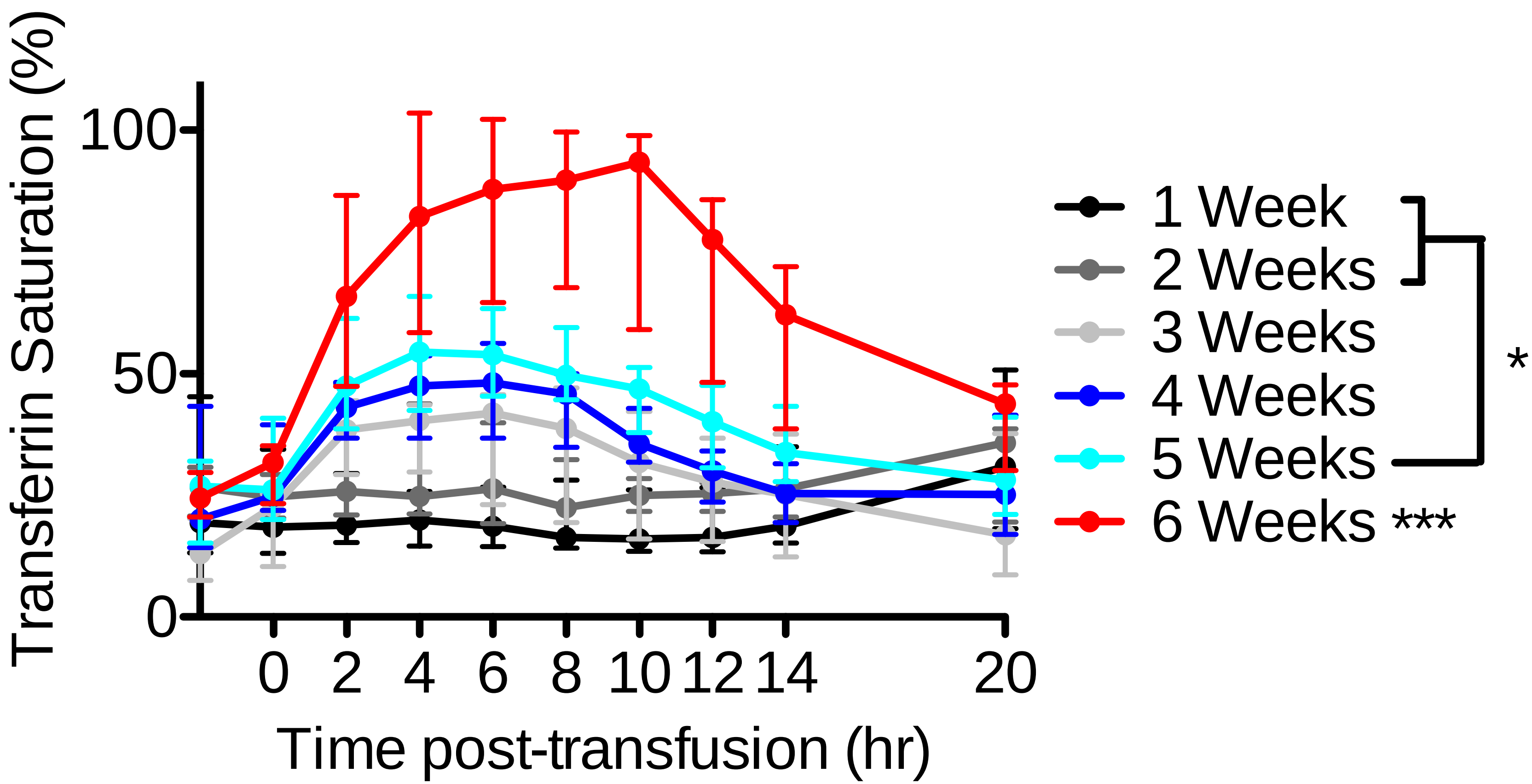

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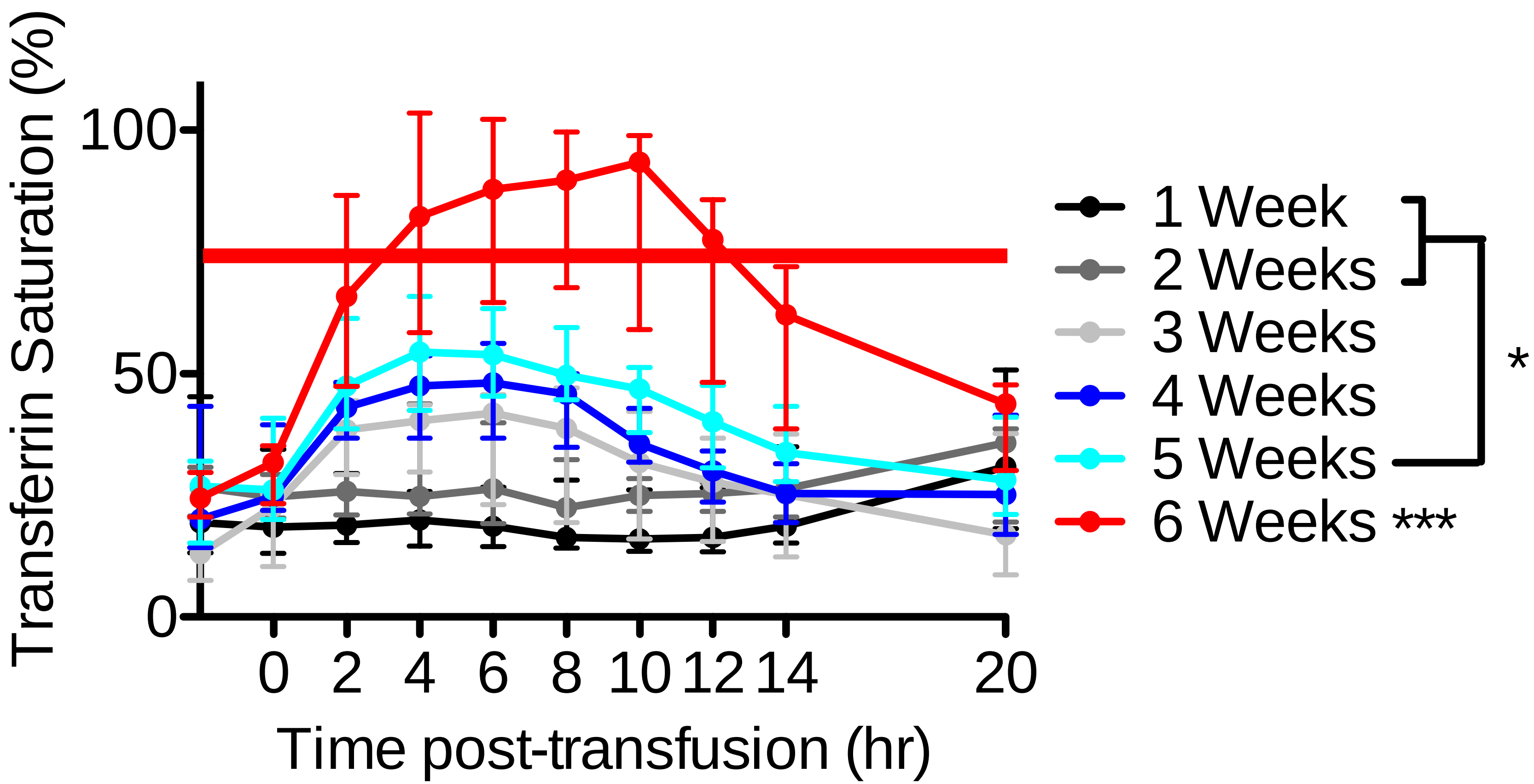

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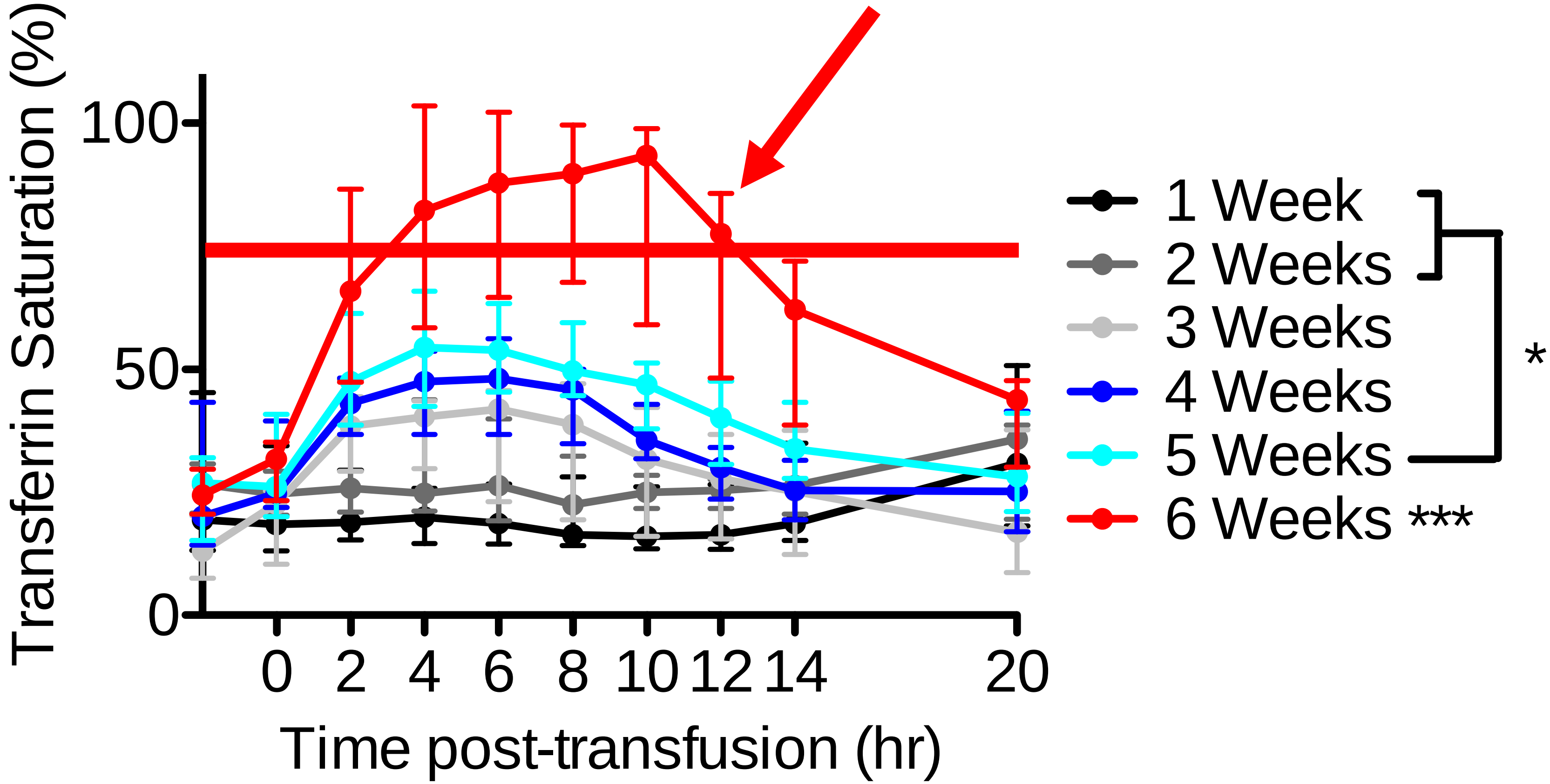

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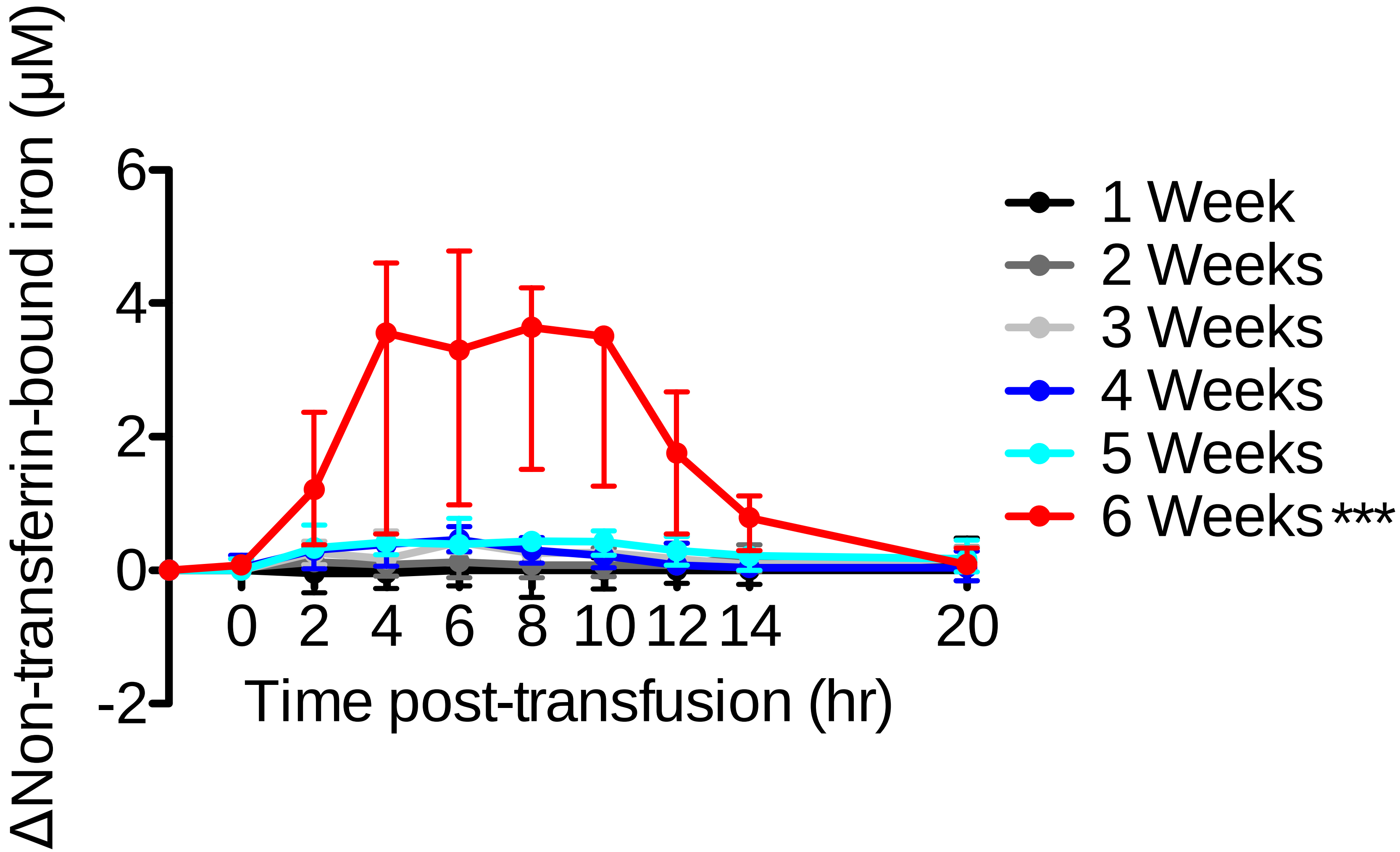

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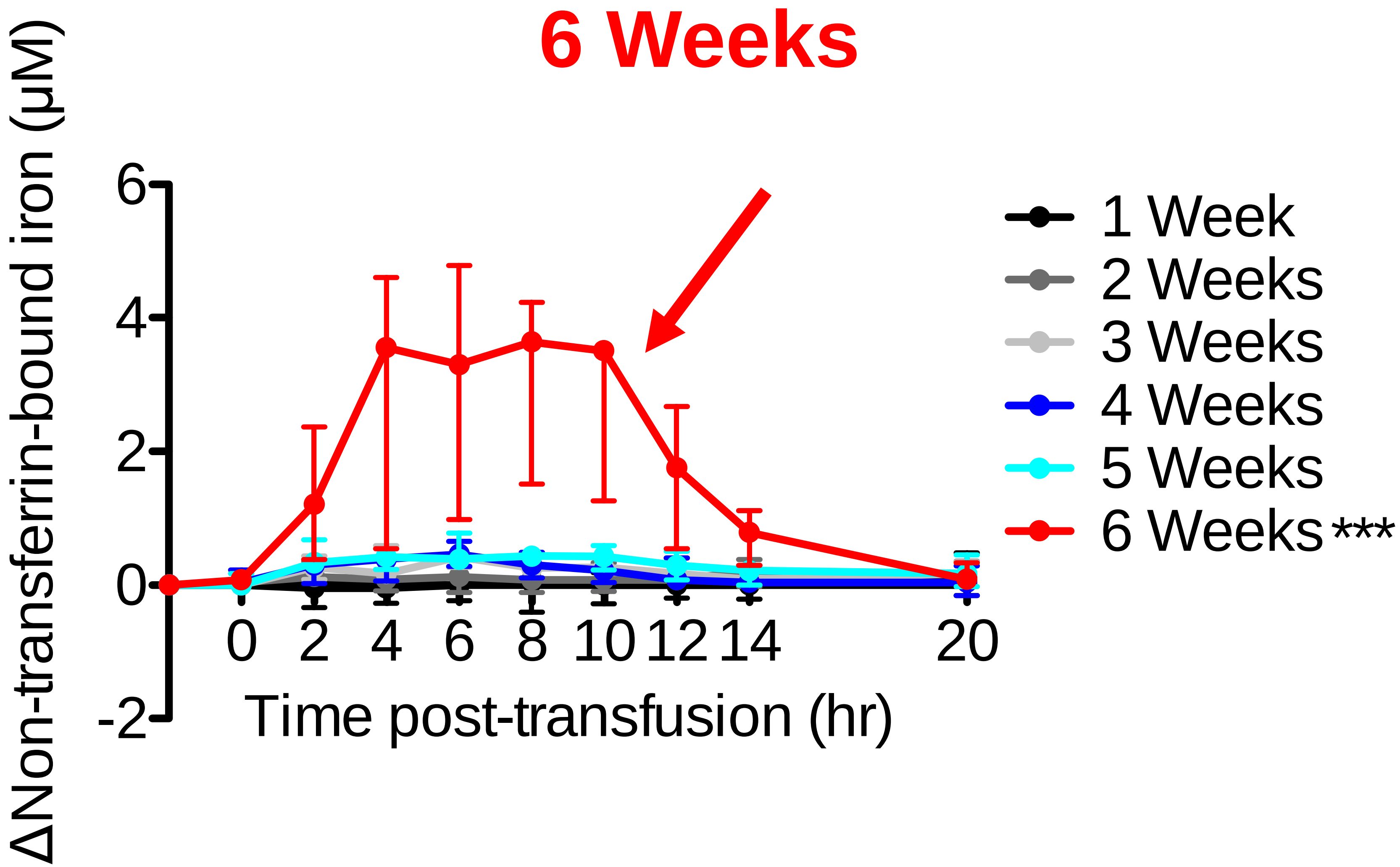

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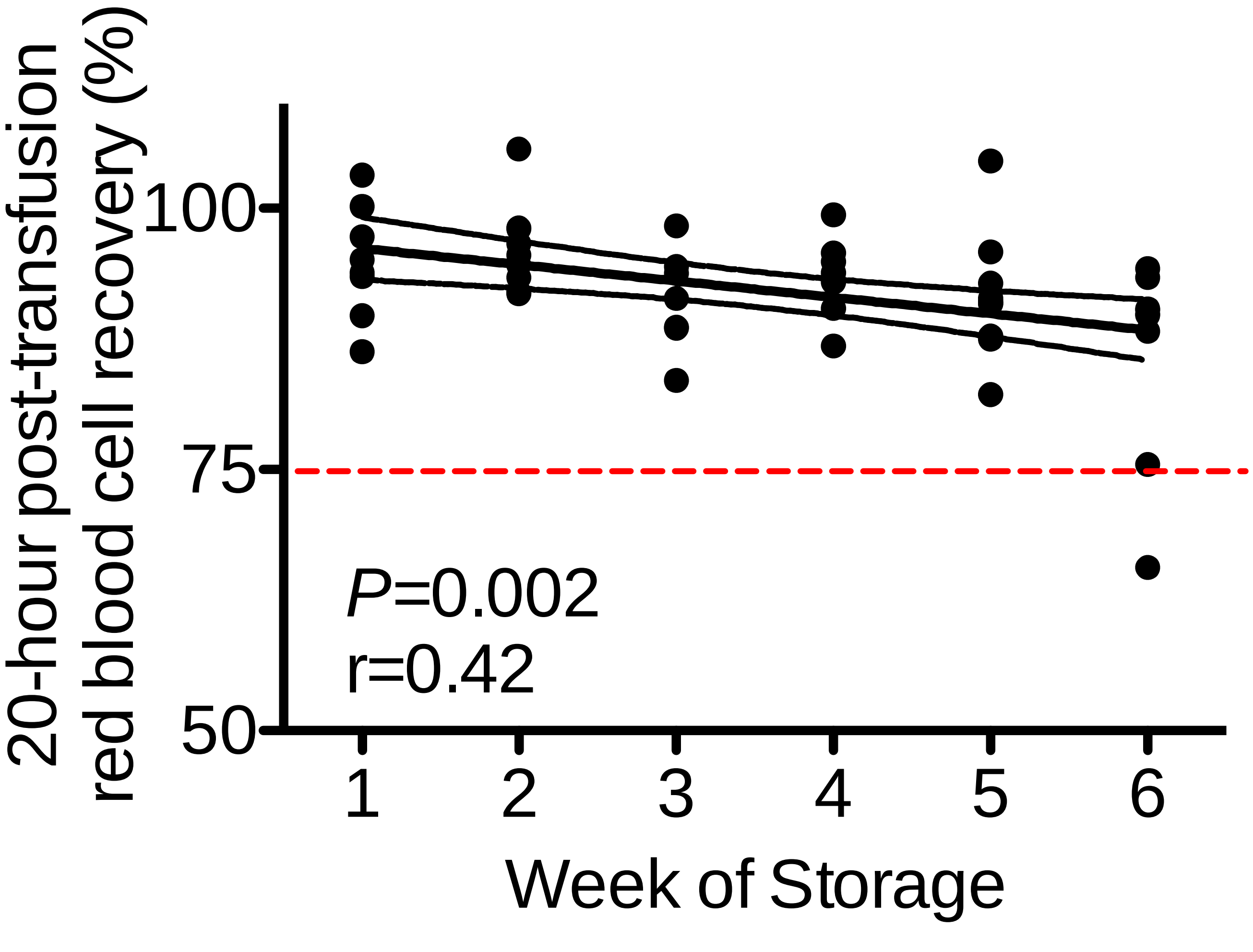

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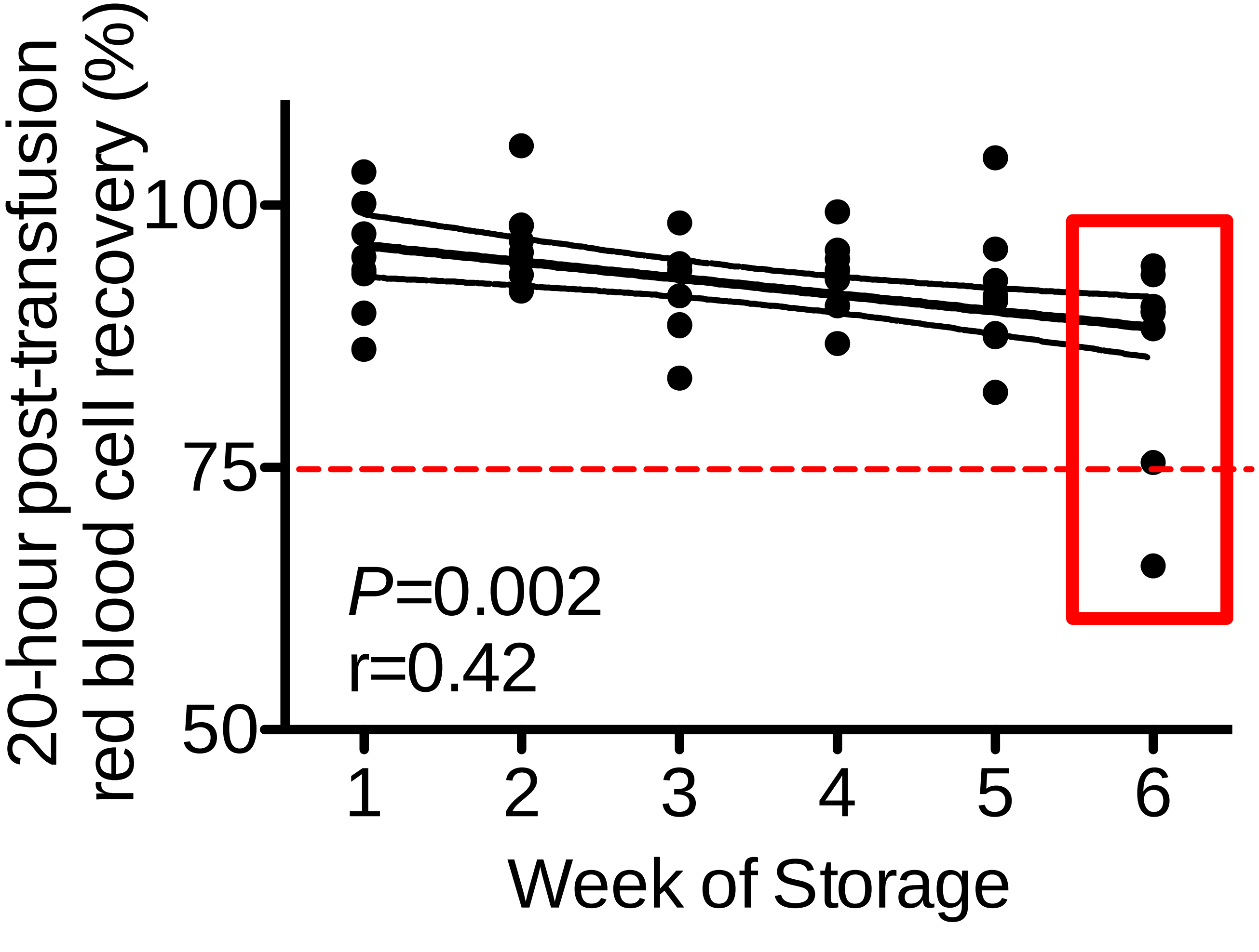

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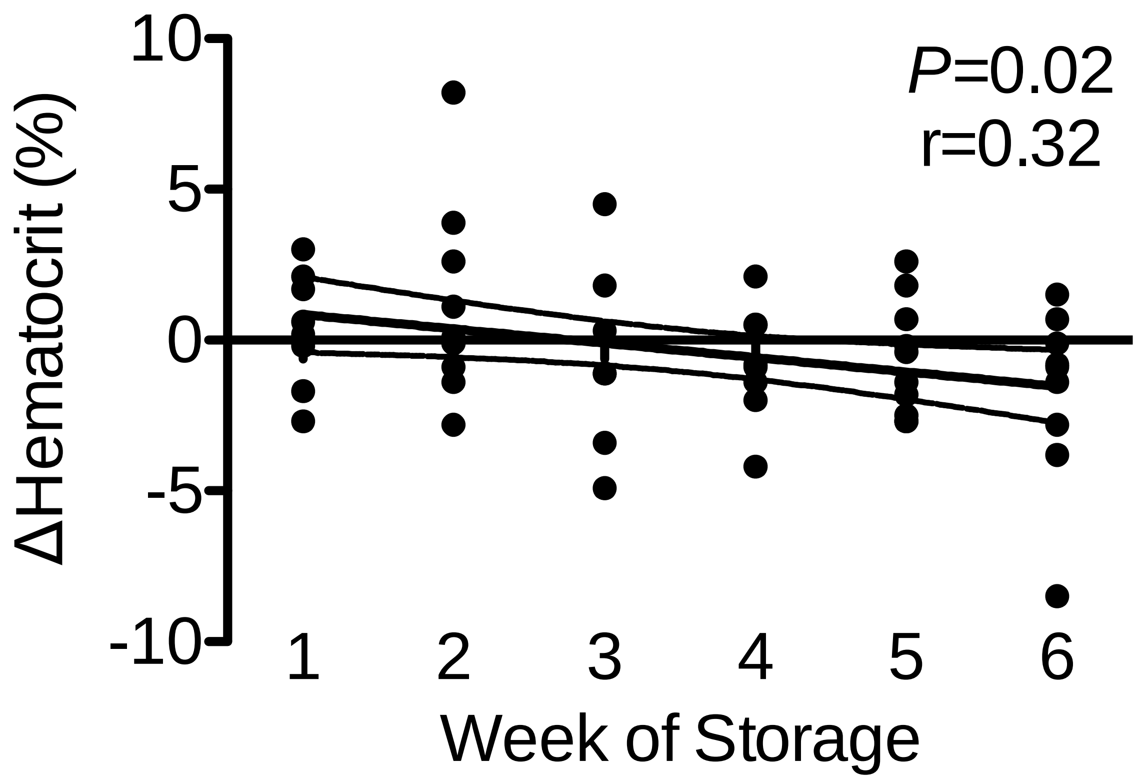

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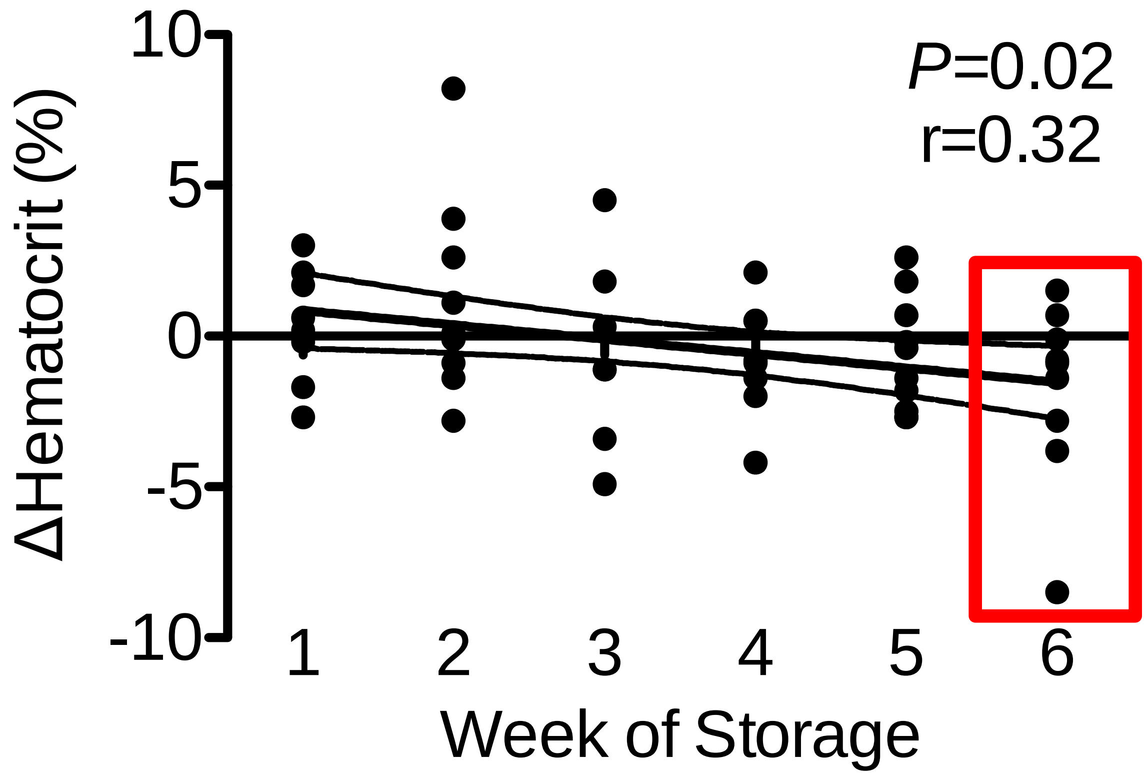
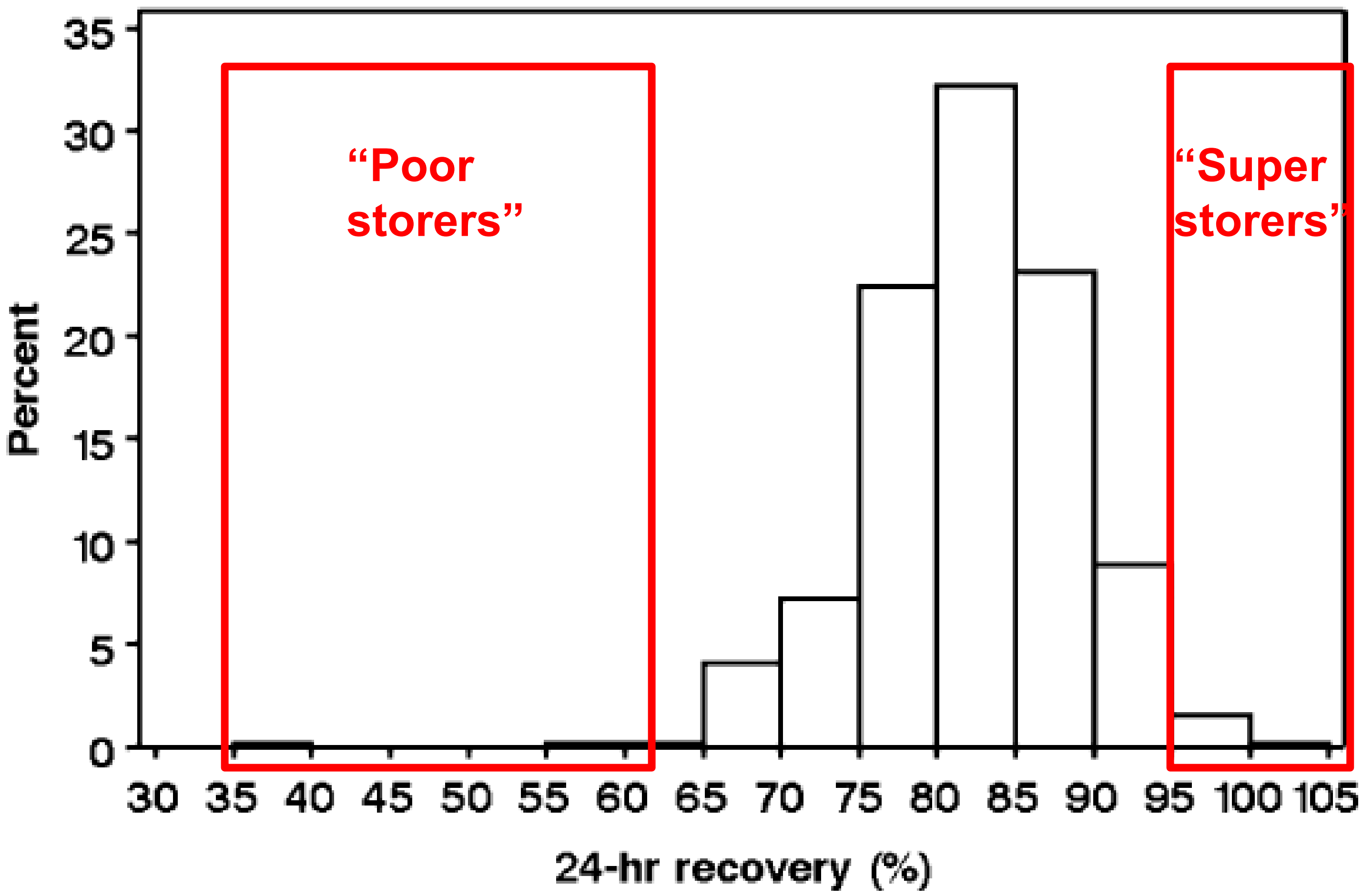


What influences variation in post-transfusion recovery?

Genetics

24-hr RBC recovery in 641 healthy volunteers



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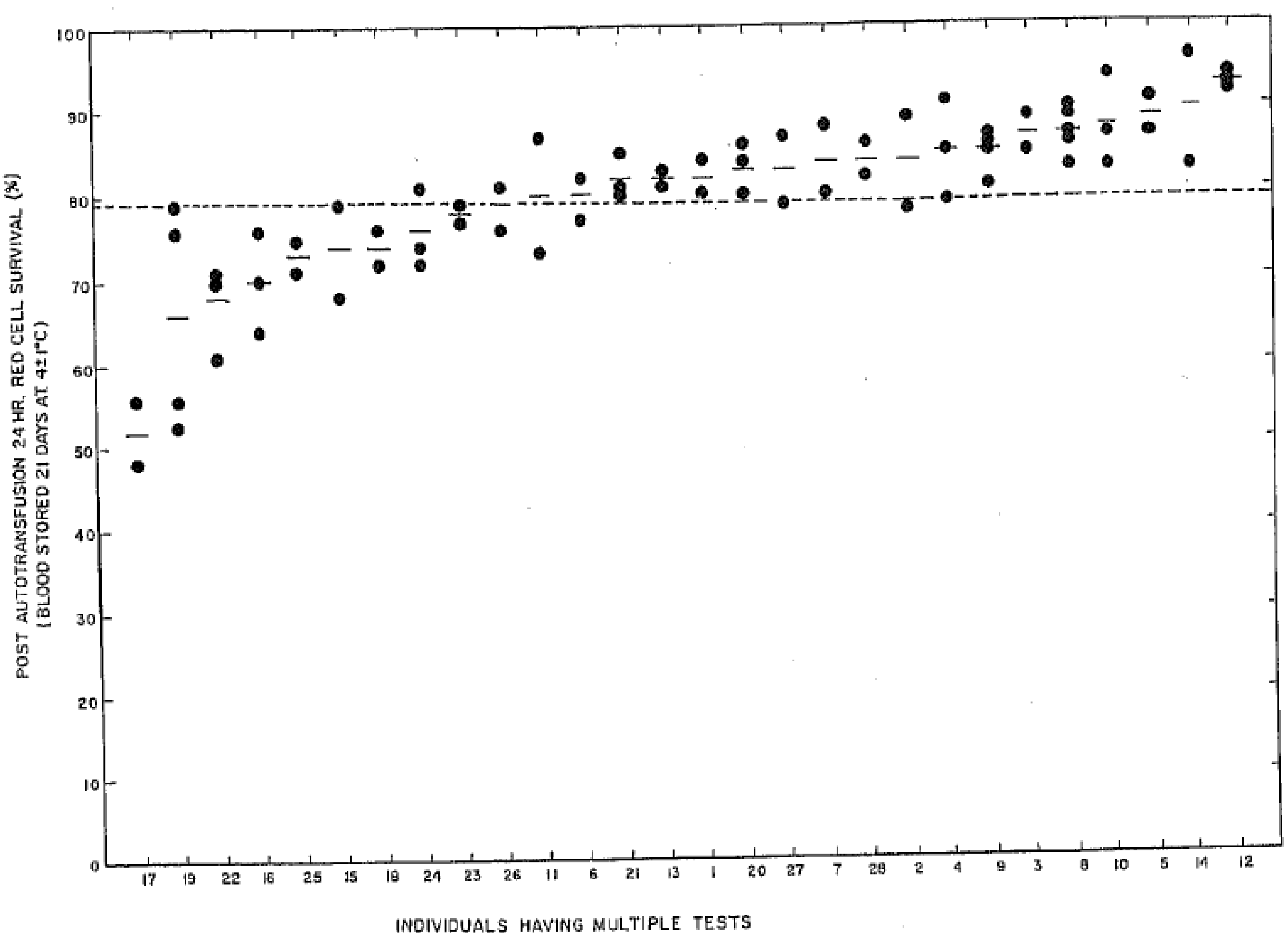
Repetitive 24-hr RBC recovery in 28 healthy volunteers



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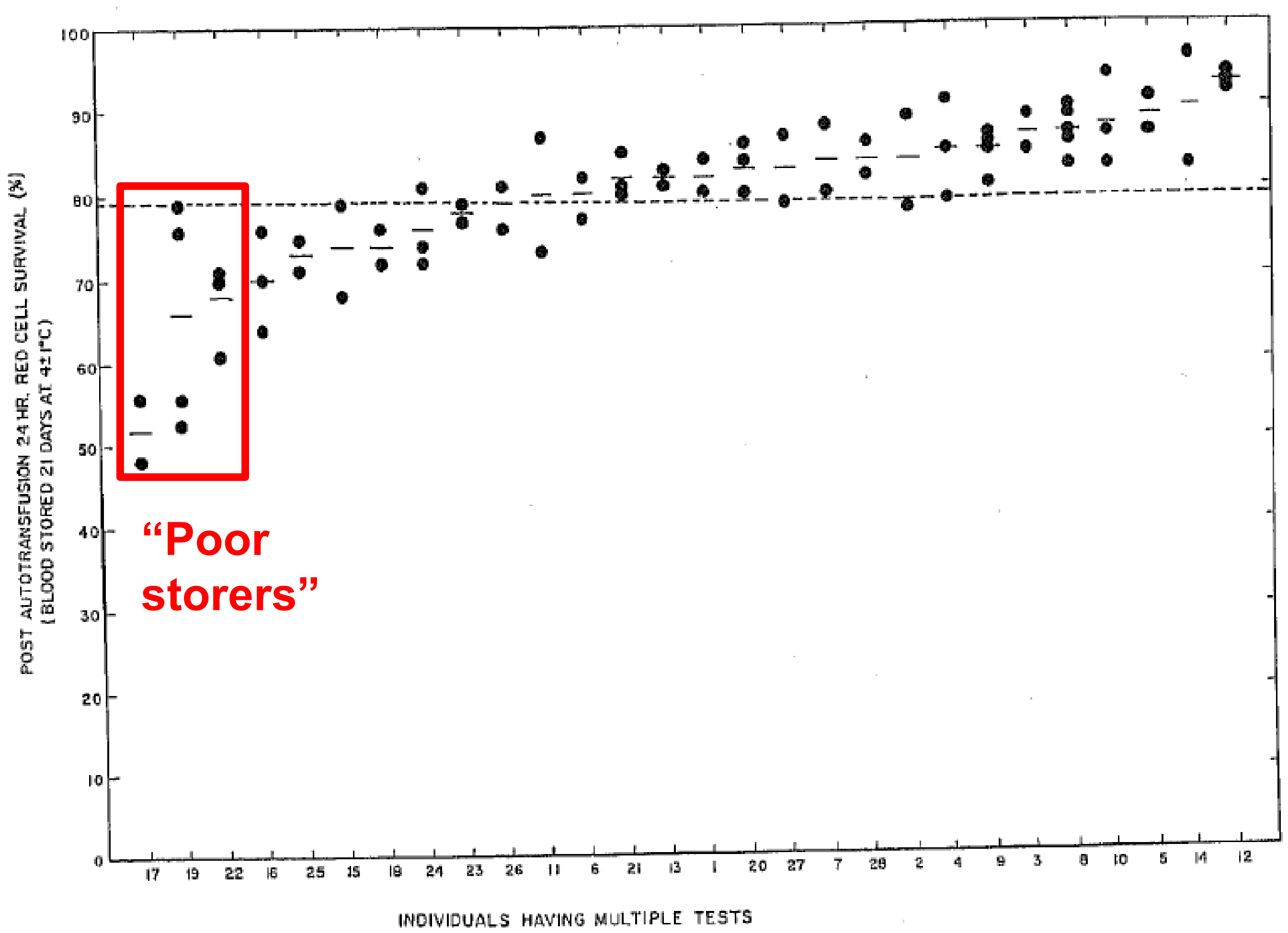

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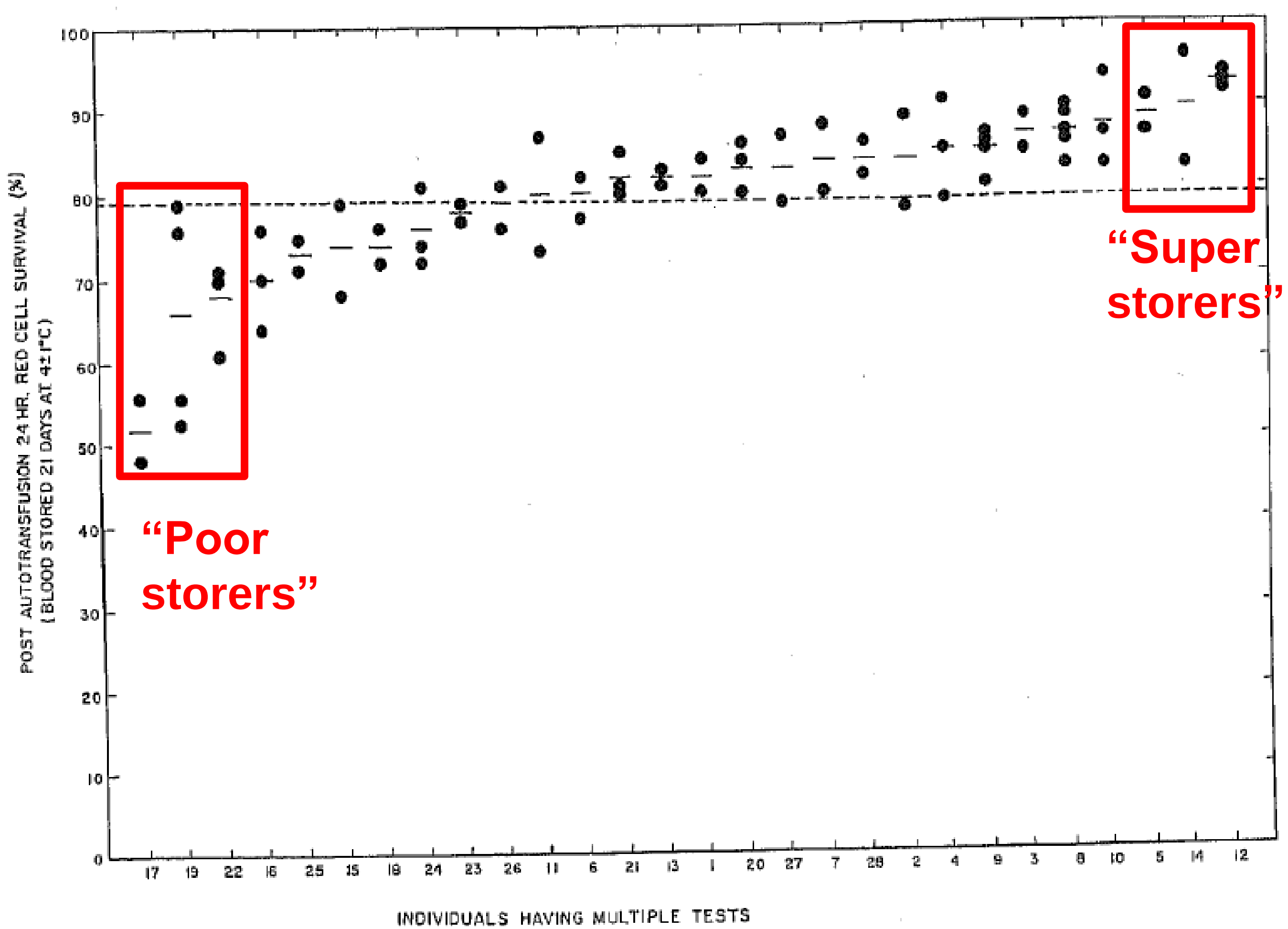

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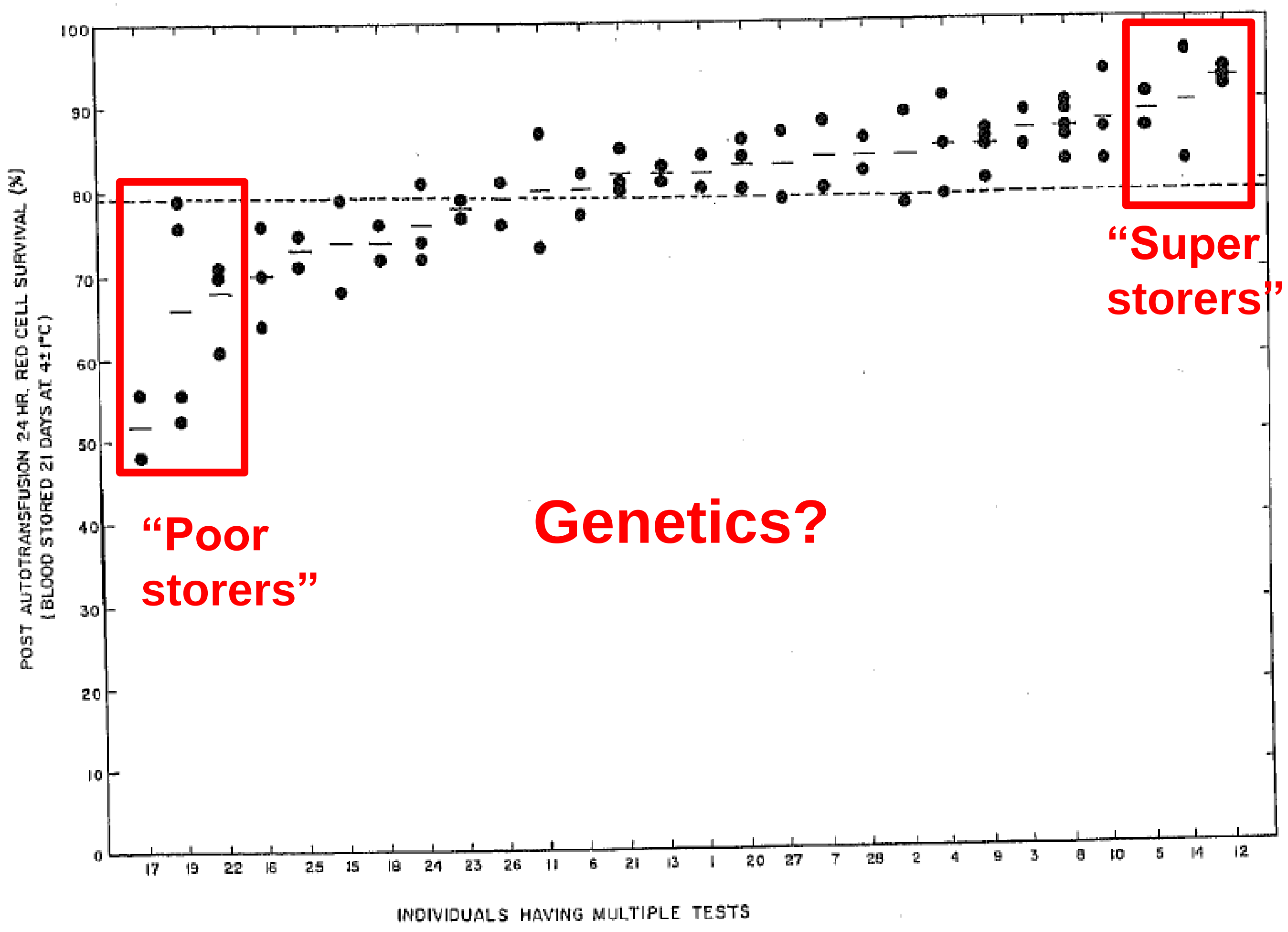

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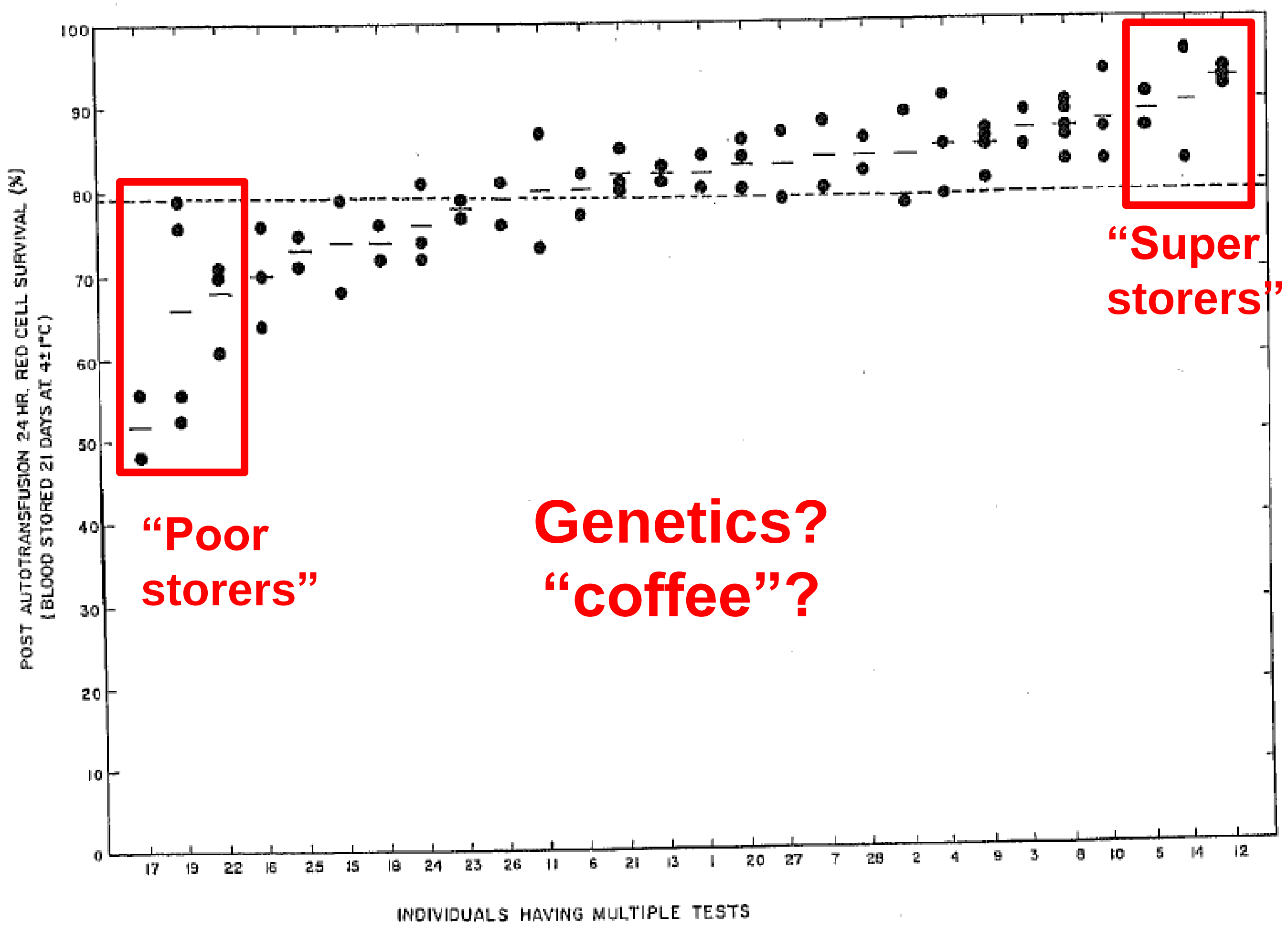

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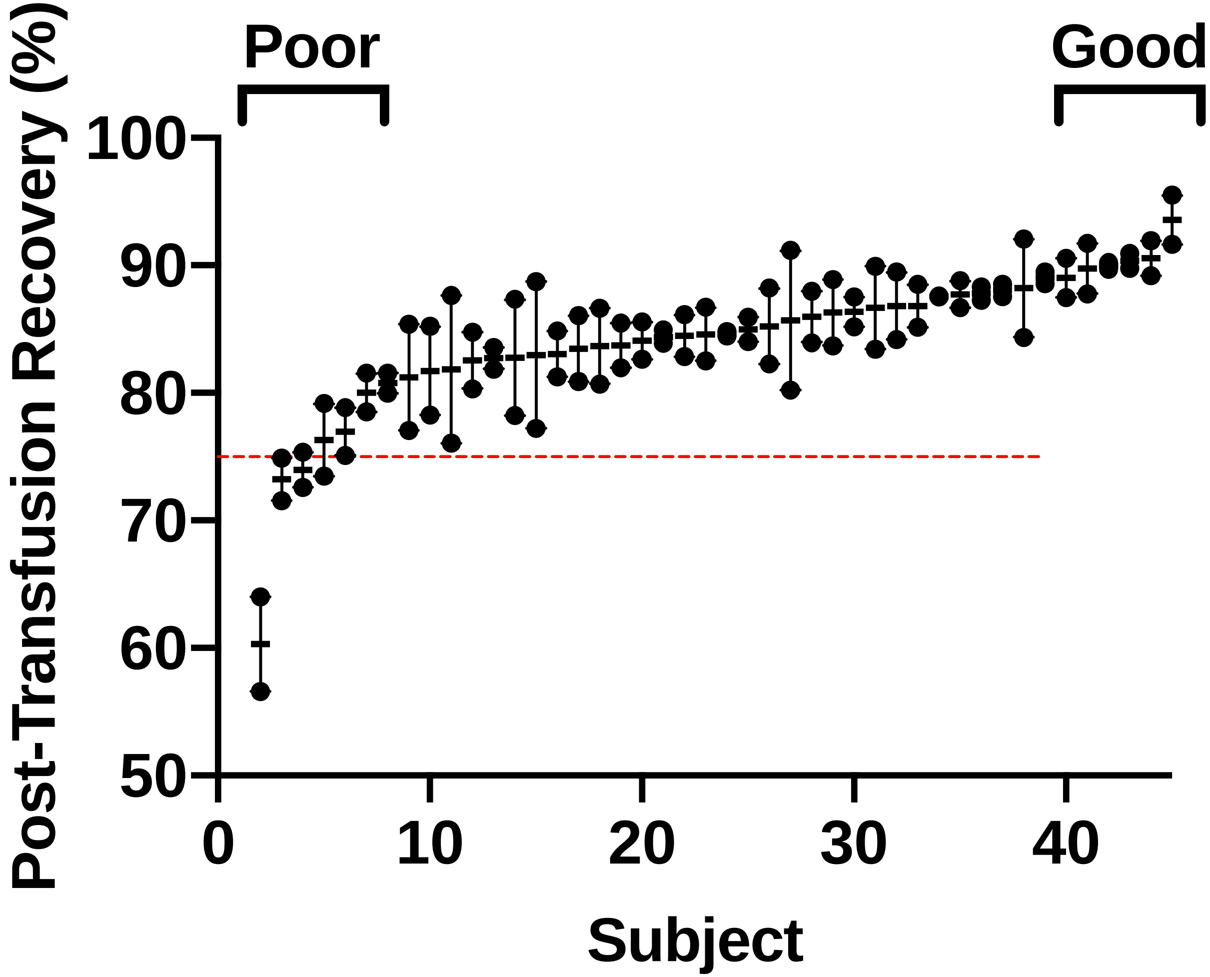

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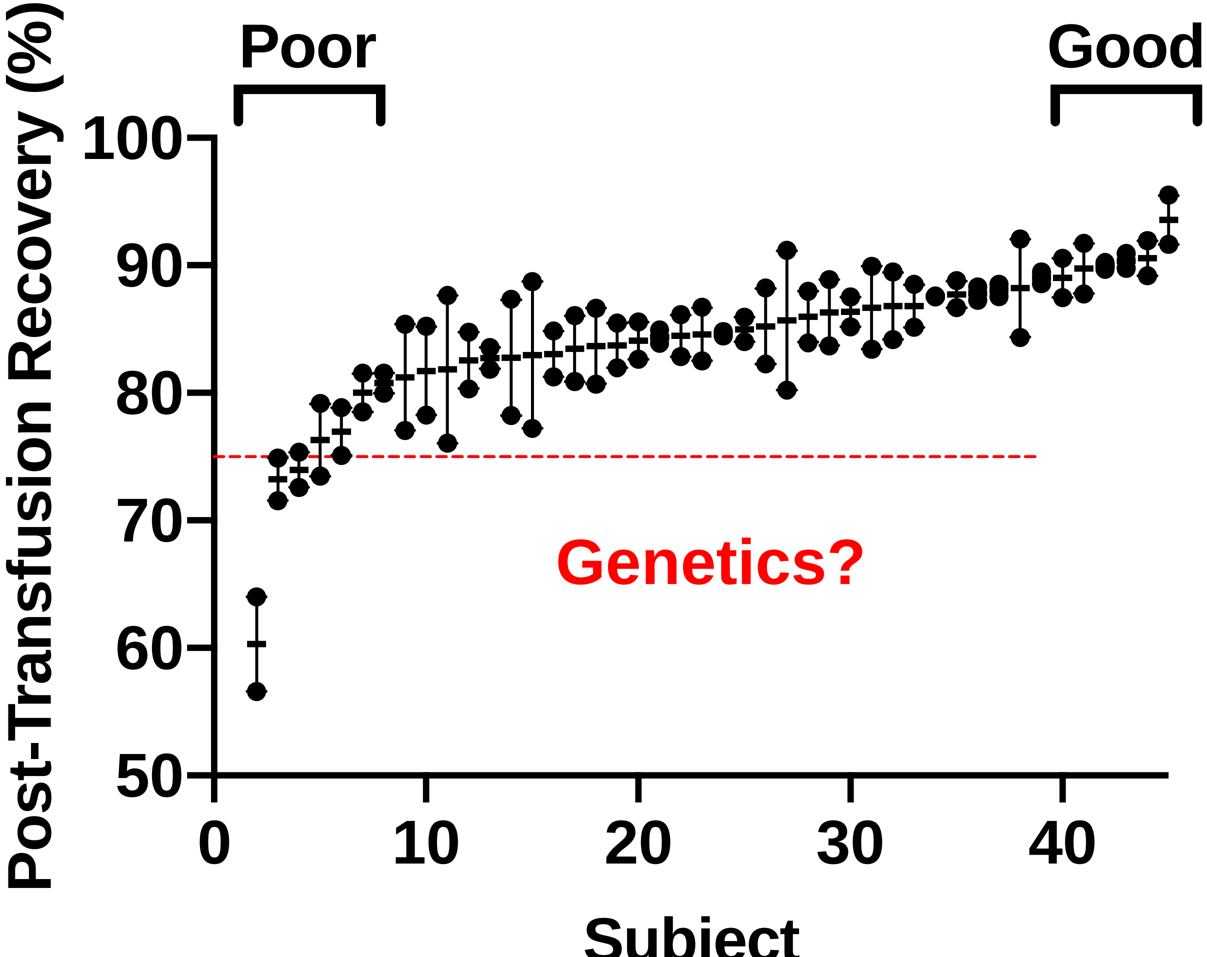
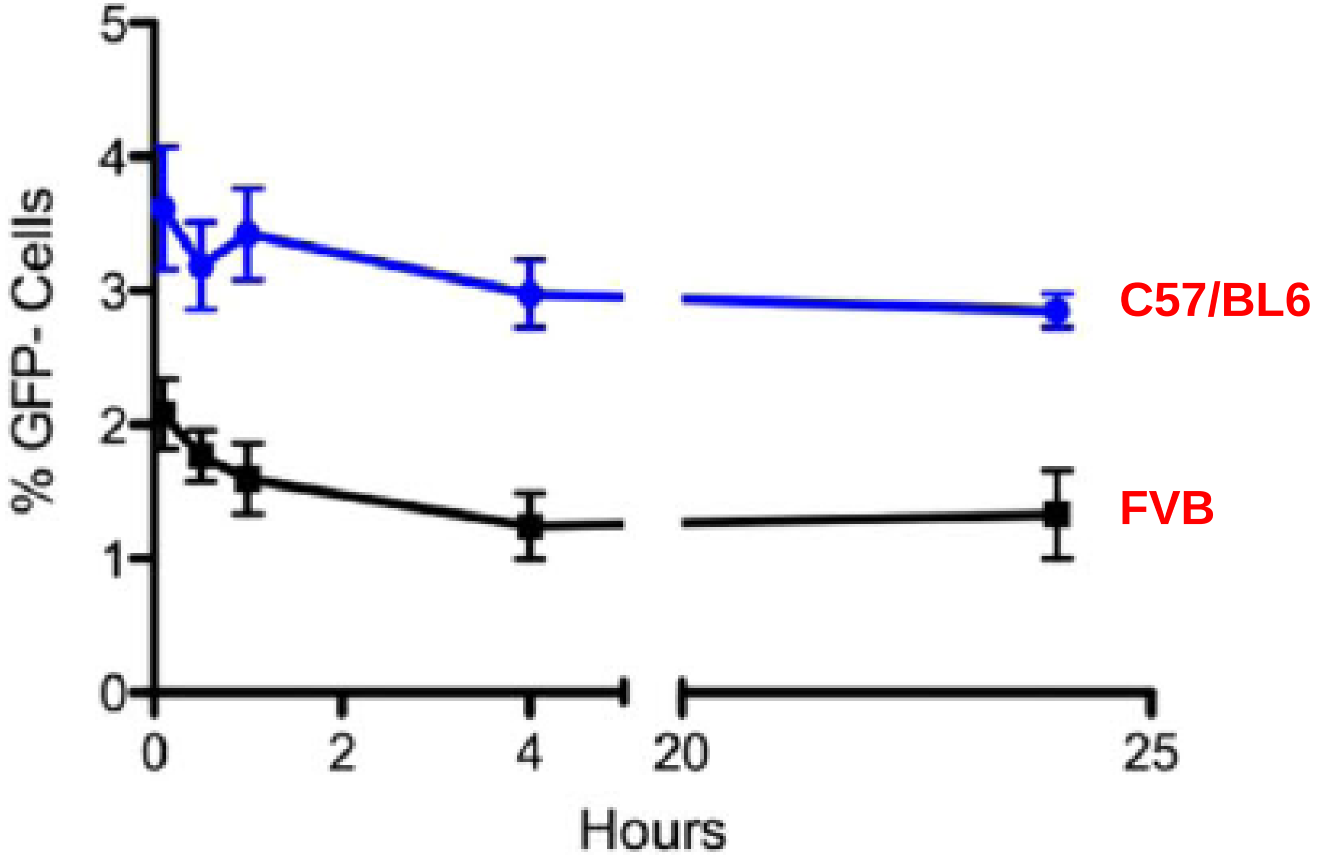


24-hr RBC recovery in inbred mouse strains



Zimring et al. Transfusion 54:137-148, 2014.

What specific genes could be involved in RBC storage quality?

General

Humans:

- Gender
- Race

Mice:

- Gender
- Strain

The “RBC storage lesion”
Final common pathway?

Metabolic dysfunction & oxidative stress ➔

↓ Deformability

↑ “Eat me” signals

↓ “Don’t eat me” signals

- ↑ Hemolysis *in vitro*
- ↑ RBC clearance *in vivo*
  - Intravascular and extravascular hemolysis

Inherited Hemolytic Anemias
Final common pathway

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Intravascular and extravascular hemolysis

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Final common pathway

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↑ Hemolysis *in vitro*

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Intravascular and extravascular hemolysis

G6PD-deficiency

Hemoglobin S, C, E, F, etc.

α- and β-thalassemias

Inherited Hemolytic Anemias
Final common pathway

Metabolic dysfunction & oxidative stress →

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↑ Hemolysis *in vitro*

↑ RBC clearance *in vivo*

Intravascular and extravascular hemolysis

G6PD-deficiency

Hemoglobin S, C, E, F, etc.

α- and β-thalassemias

What are the consequences (if any) of the clearance of stored RBCs?

RBC storage lesion *in vitro*

↓

Decreased RBC recovery *in vivo*

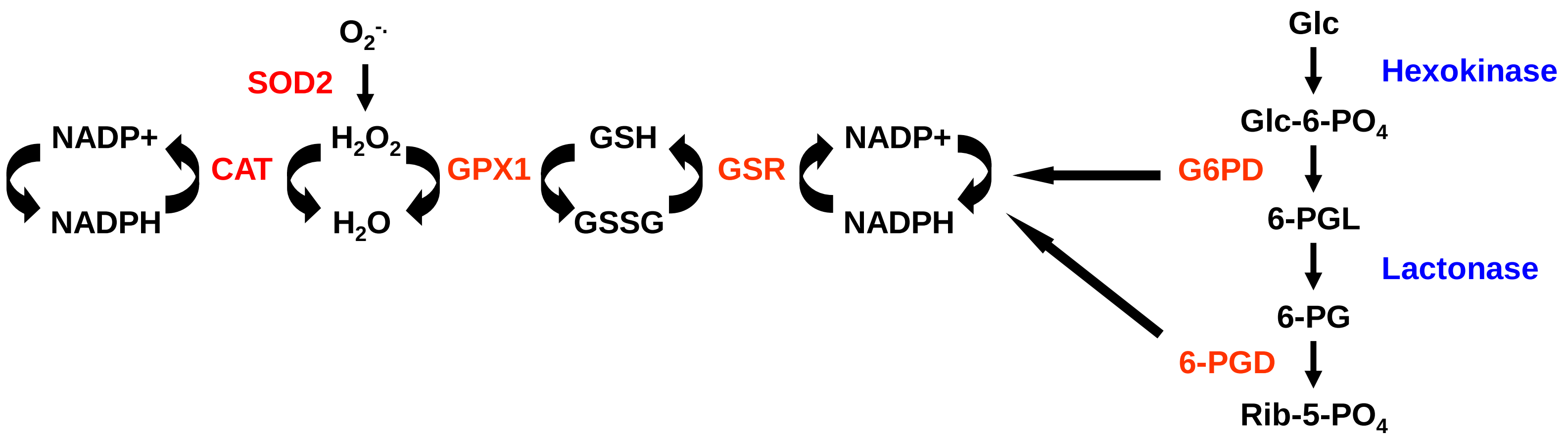
What are the consequences (if any) of the clearance of stored RBCs?

Insufficient protection against oxidative stress *in vitro*

↓

Decreased RBC recovery *in vivo*

The case for G6PD: Homeostasis



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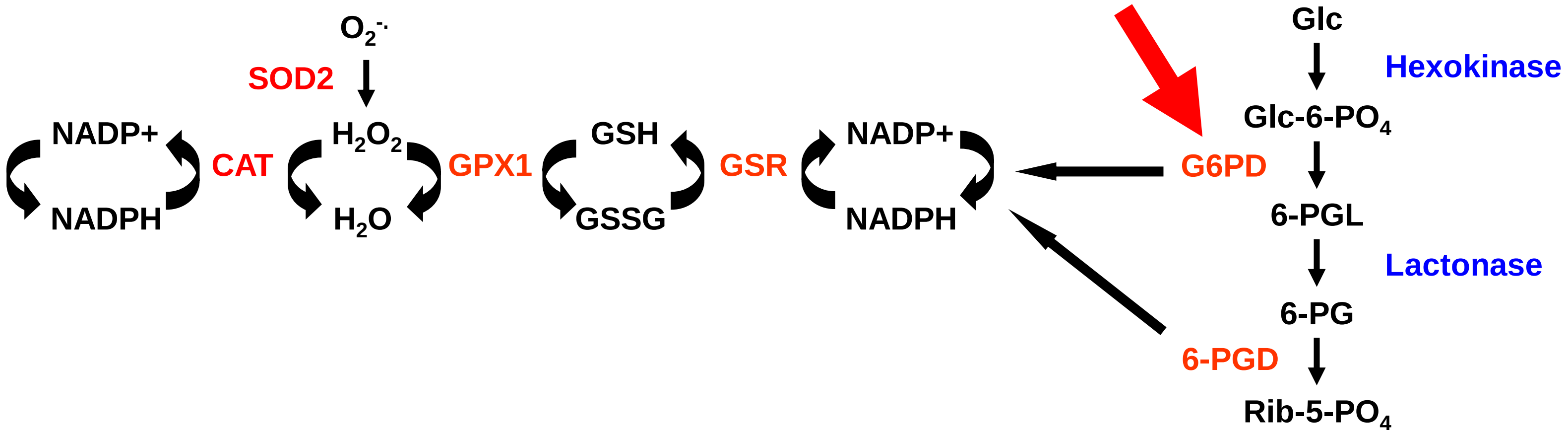

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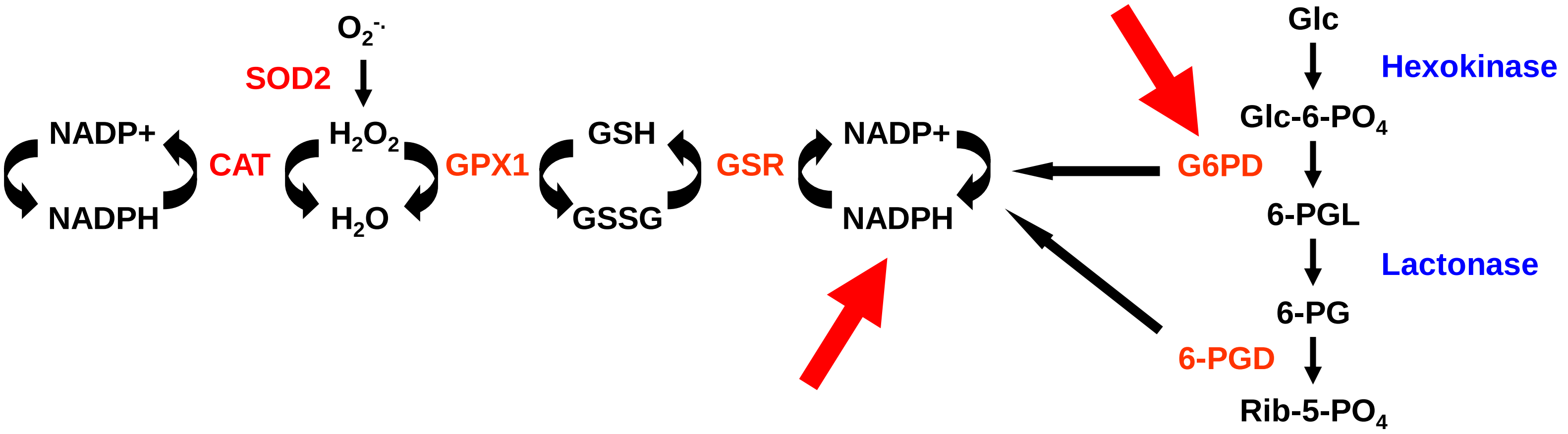

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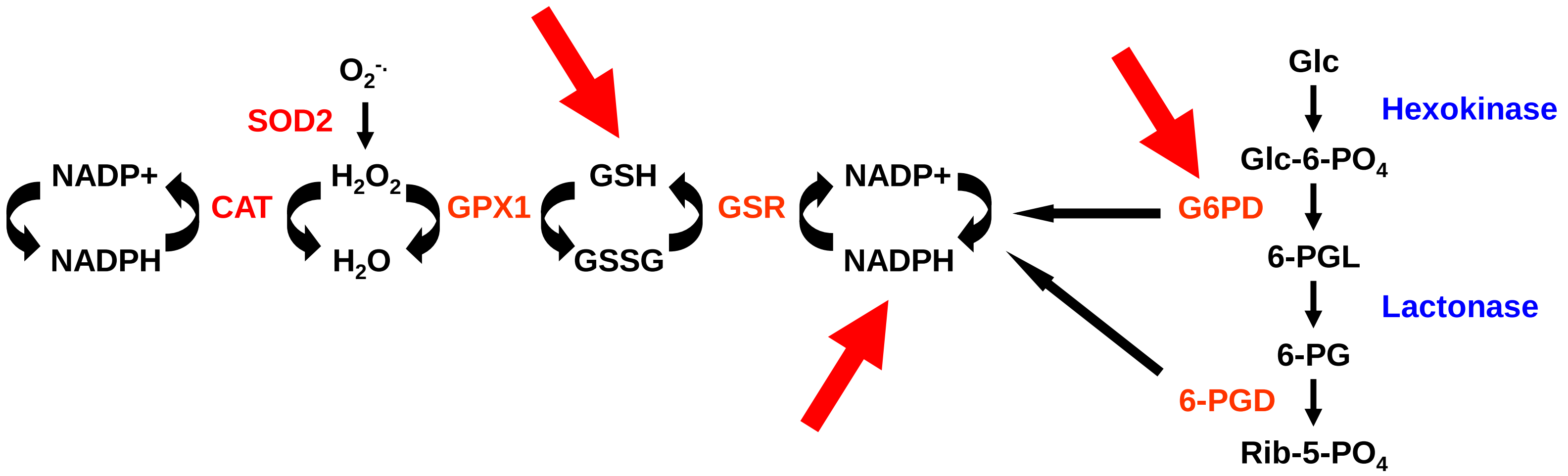

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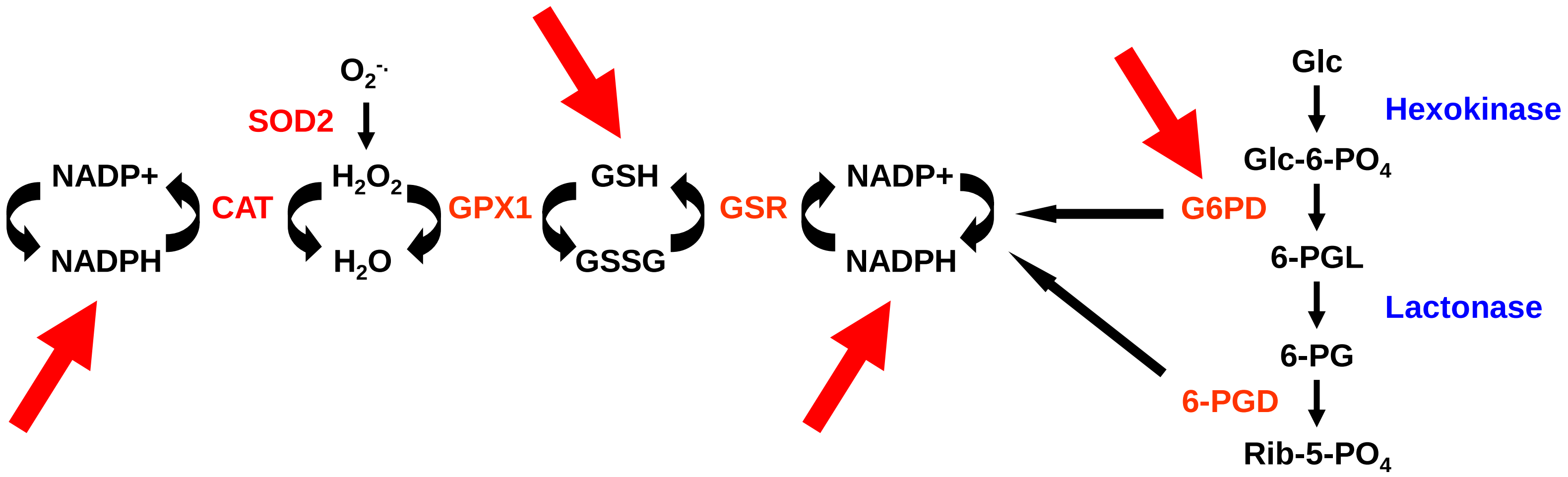

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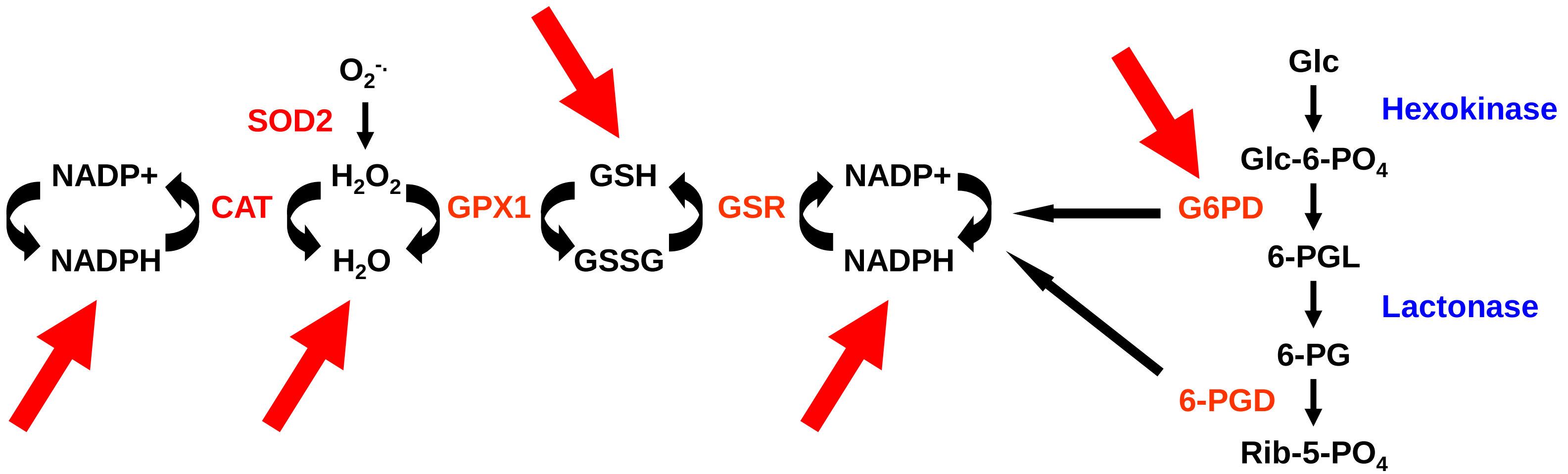
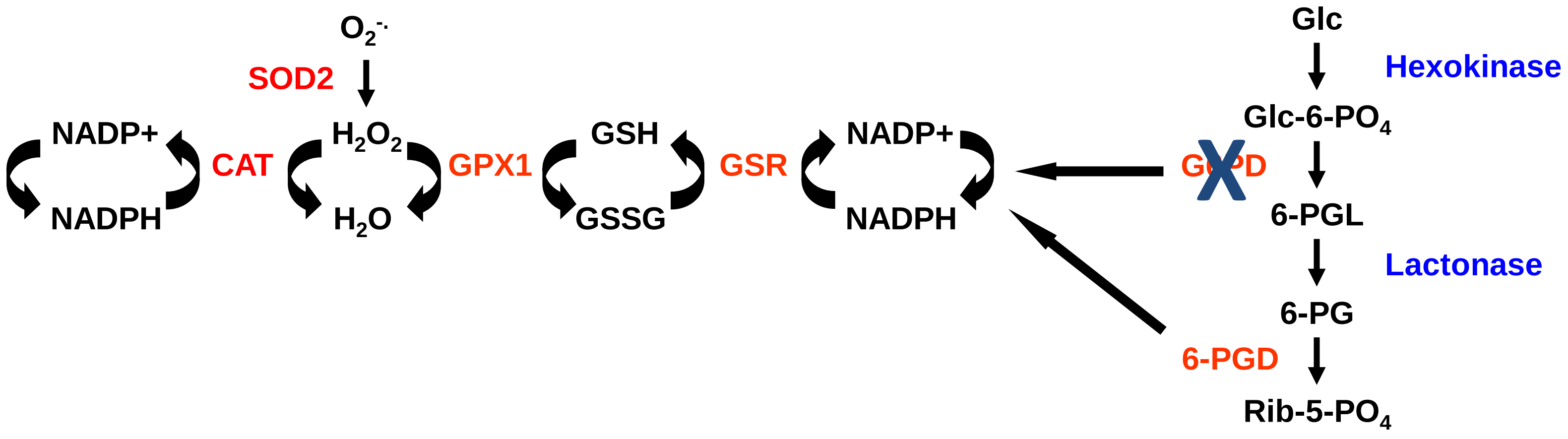


The case for G6PD: G6PD-deficiency



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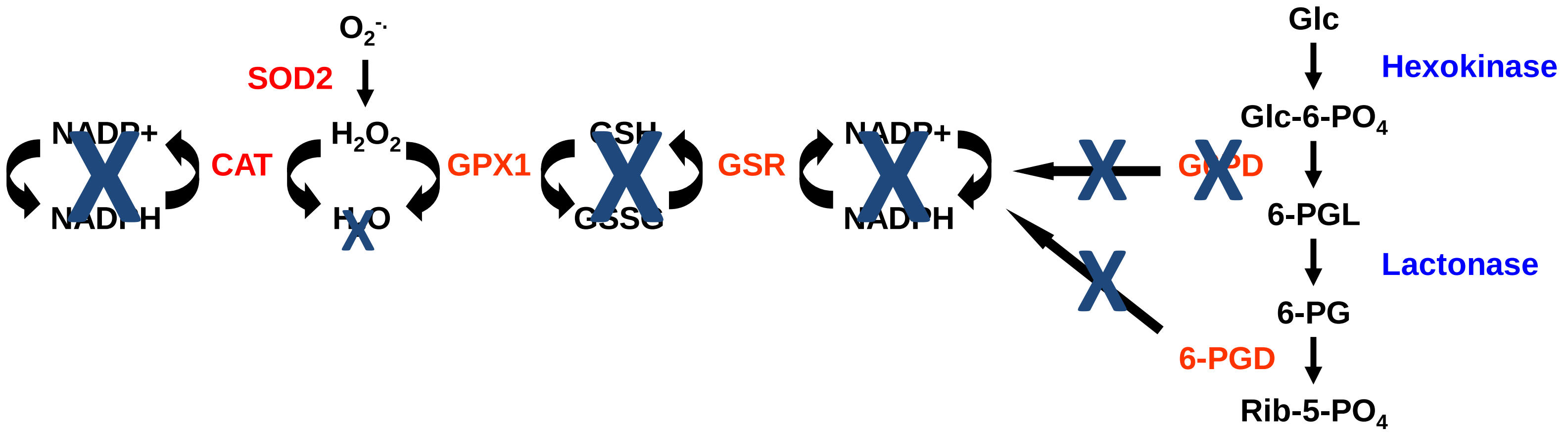

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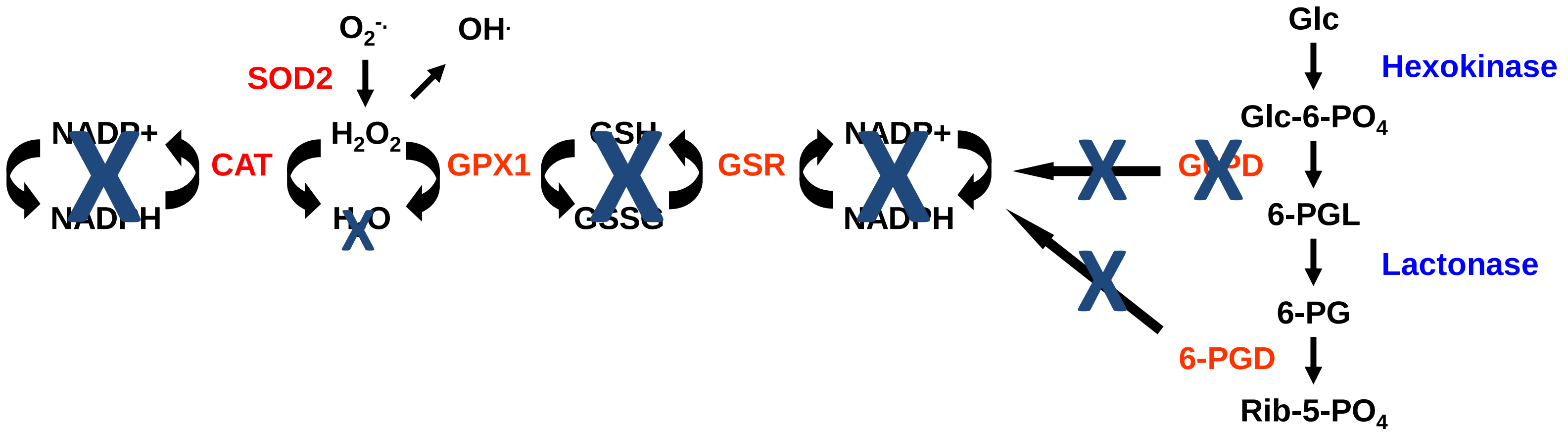

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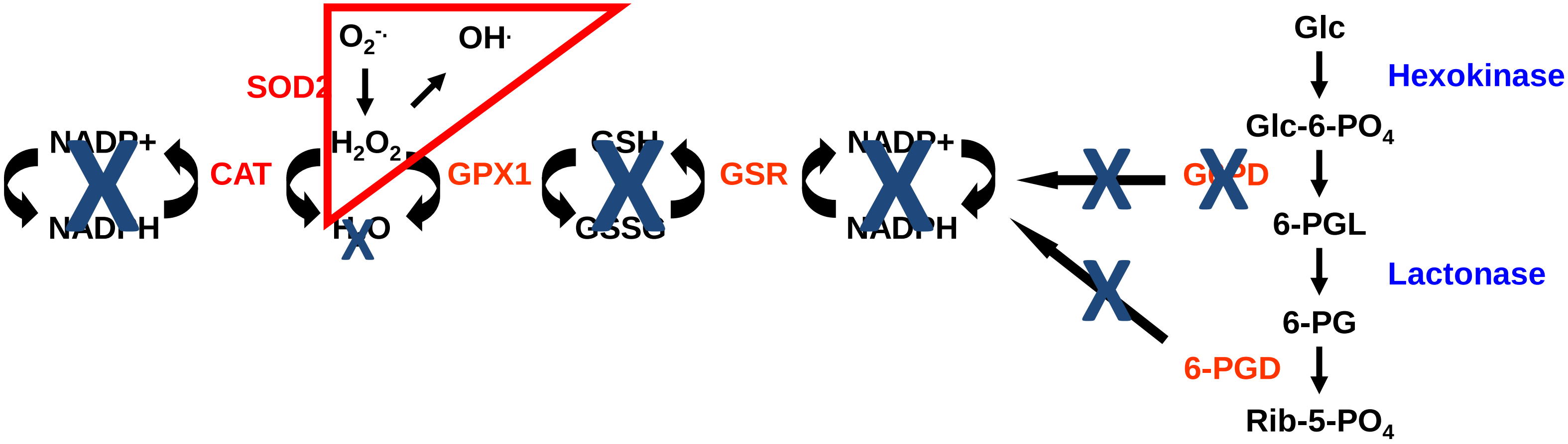

The case for G6PD: G6PD-deficiency

Unrelieved oxidative stress:

- **RBC structural damage →**
  - **Intravascular hemolysis (hemoglobinemia)**
  - **Extravascular hemolysis (NTBI)**

The case for G6PD: G6PD-deficiency

Most common human enzymopathy

The case for G6PD: G6PD-deficiency

Most common human enzymopathy

~400 million affected individuals

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Genetically-induced enzyme variation:

- Severely decreased activity
- Normal activity
- Increased activity

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- Normal activity
- Increased activity

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Most common human enzymopathy

~400 million affected individuals

Genetically-induced enzyme variation:

- Severely decreased activity: poor storers?
- Normal activity
- Increased activity: super storers?

The case for G6PD: G6PD-deficiency

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The case for G6PD: G6PD-deficiency

Prevalence of G6PD-deficiency in normal donors at CUMC-NYPH:

Random donors: 0.3%

Francis et al. Transfusion 53:606-611, 2013

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Prevalence of G6PD-deficiency in normal donors at CUMC-NYPH:

Random donors:	**0.3%**
R_0R_0/R_0r donors:	**12.3%**

Francis et al. Transfusion 53:606-611, 2013

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Exchange Transfusions for Sickle Cell Disease

Francis et al. Transfusion 53:606-611, 2013

Study Design

Study plan:

10 G6PD-deficient + 30 matched controls

Donate 1 unit; pre-storage leukoreduced; store for 40-42 days in AS-3; 24h 51-Cr PTR

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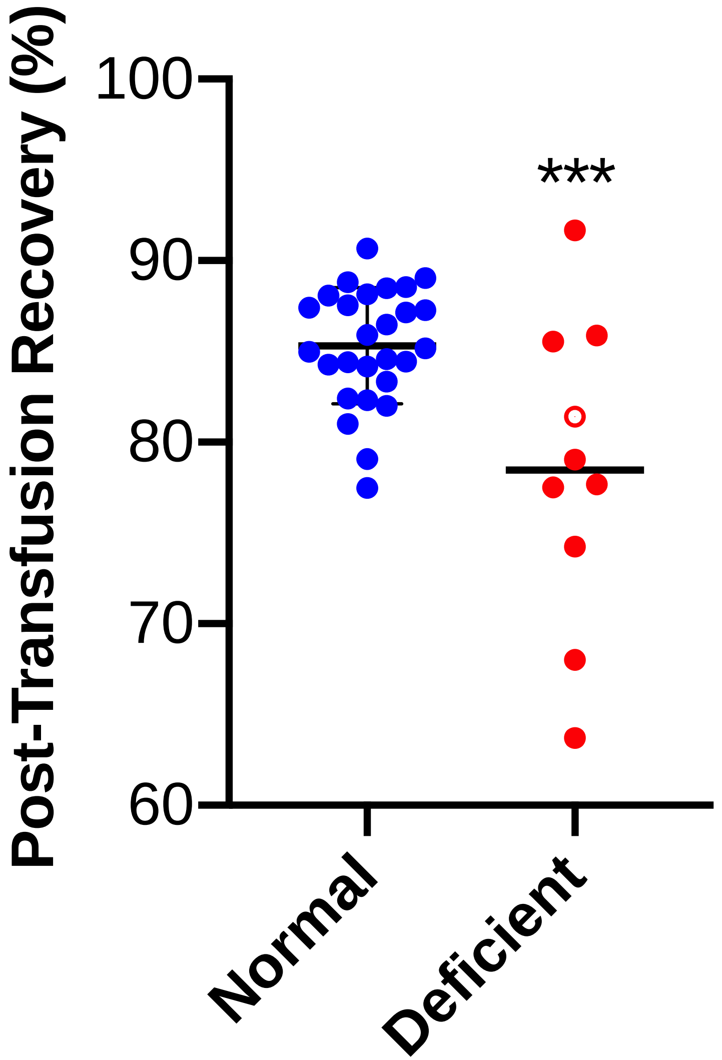
- 10 G6PD-deficient + 30 matched controls
- Donate 1 unit; pre-storage leukoreduced; store for 40-42 days in AS-3; 24h 51-Cr PTR

Completed study:

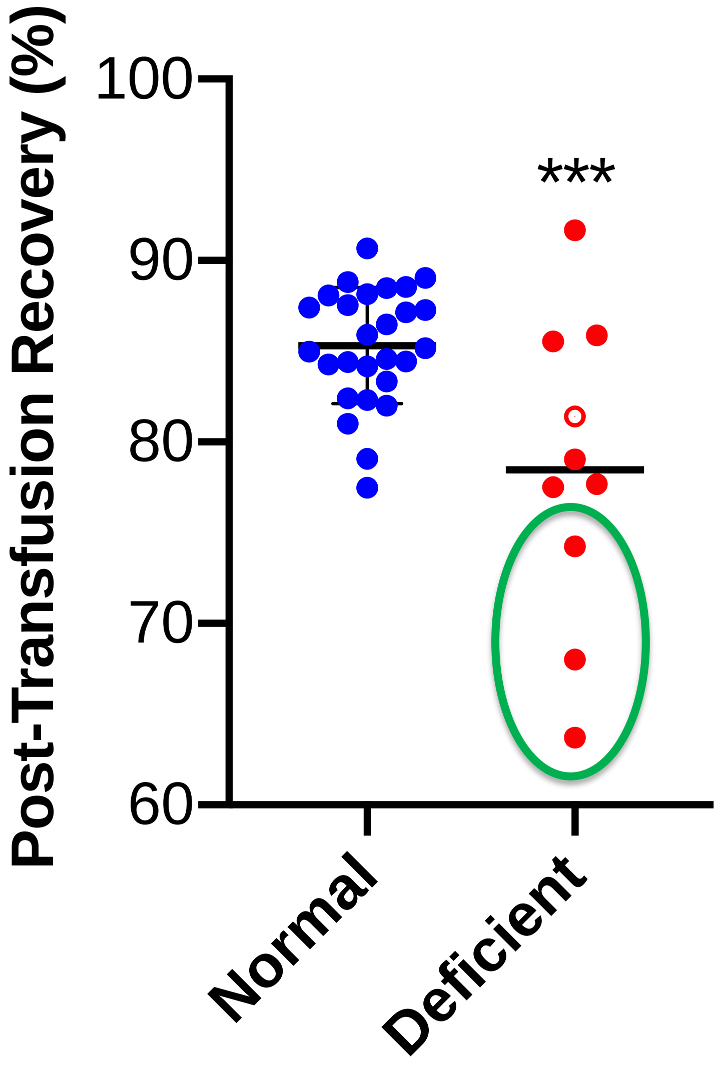
- 10 G6PD-deficient + 30 matched controls consented
- 10 G6PD-deficient + 27 controls completed study
- G6PD-deficient variants: 9 African, 1 Mediterranean
  - Exon sequencing
- None with hemoglobin variant or thalassemia
  - Hb screen (HPLC) + CBC

The case for G6PD: G6PD-deficiency



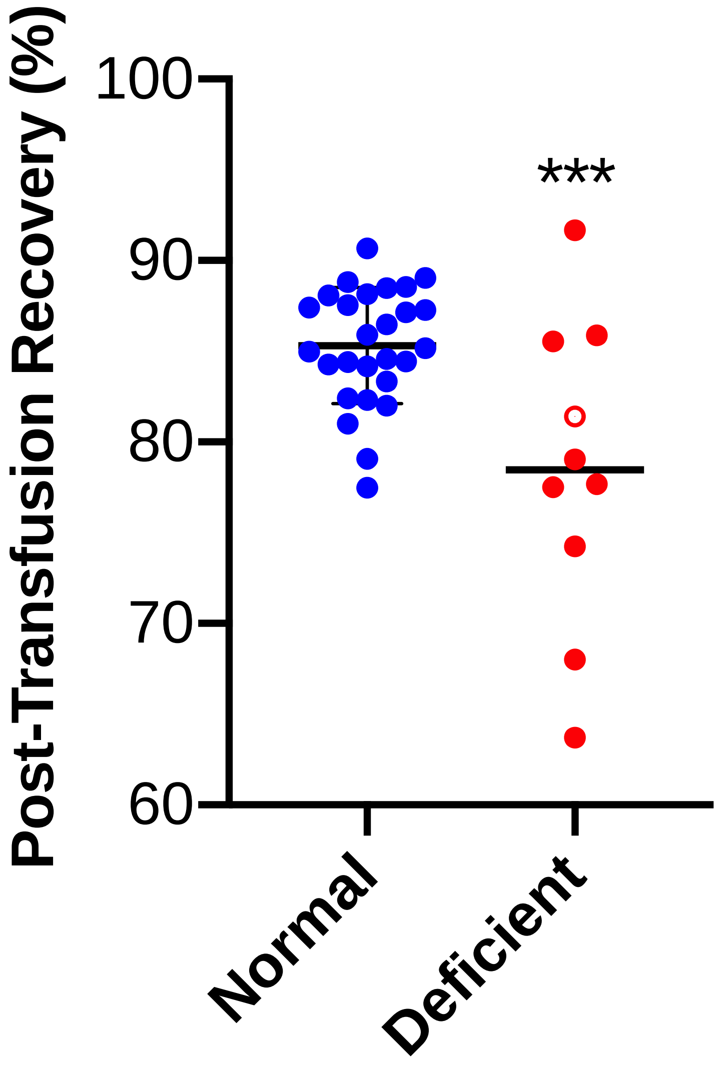
6.8% decreased recovery of G6PD-deficient RBCs

The case for G6PD: G6PD-deficiency



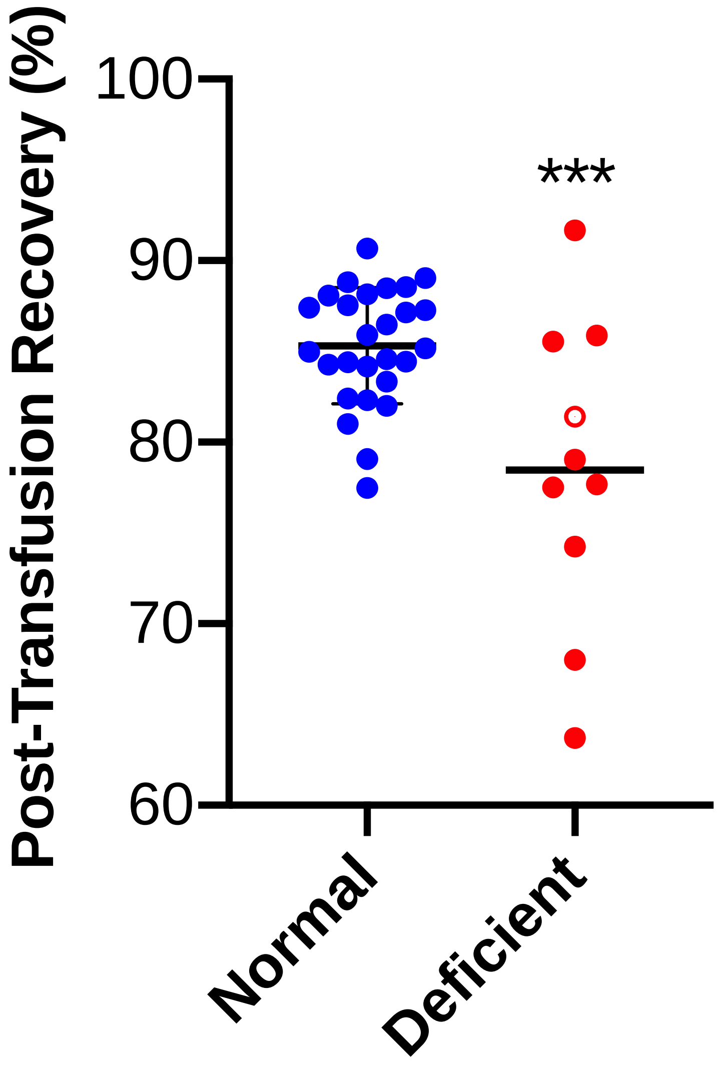
"FDA failures" in G6PD-deficient group

The case for G6PD: G6PD-deficiency



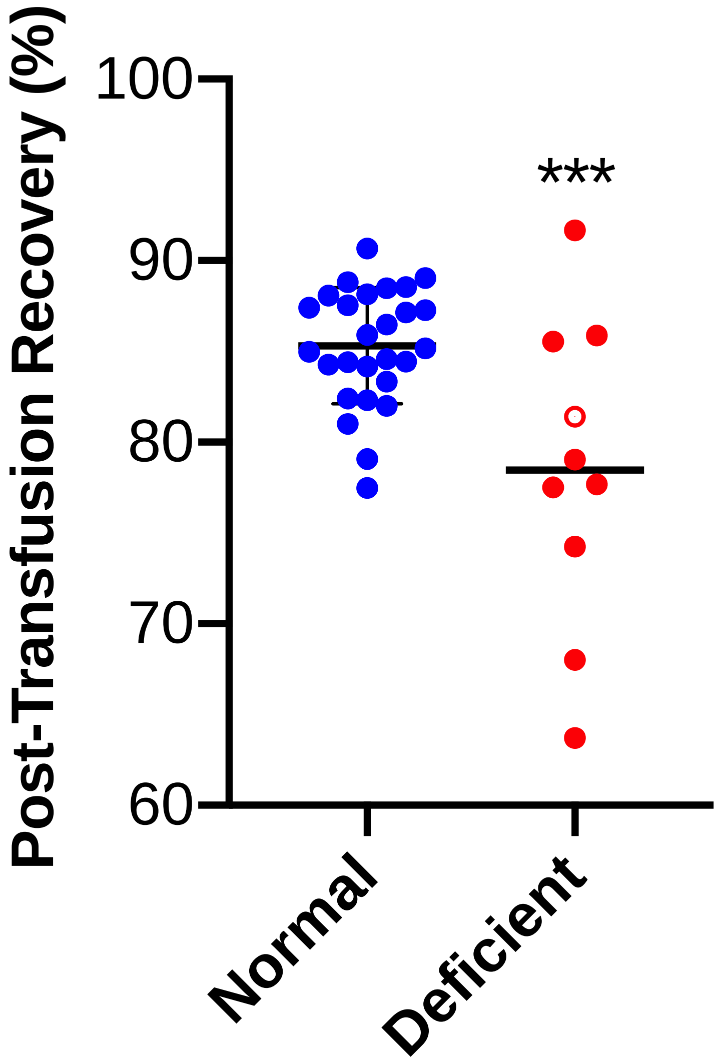
No correlation between PTR and G6PD enzyme activity within groups

The case for G6PD: G6PD-deficiency



No difference in hemolysis "in the bag" at outdate

The case for G6PD: G6PD-deficiency



Would 24-hour post-transfusion recoveries be worse in ill recipients?

The case for G6PD: Next steps

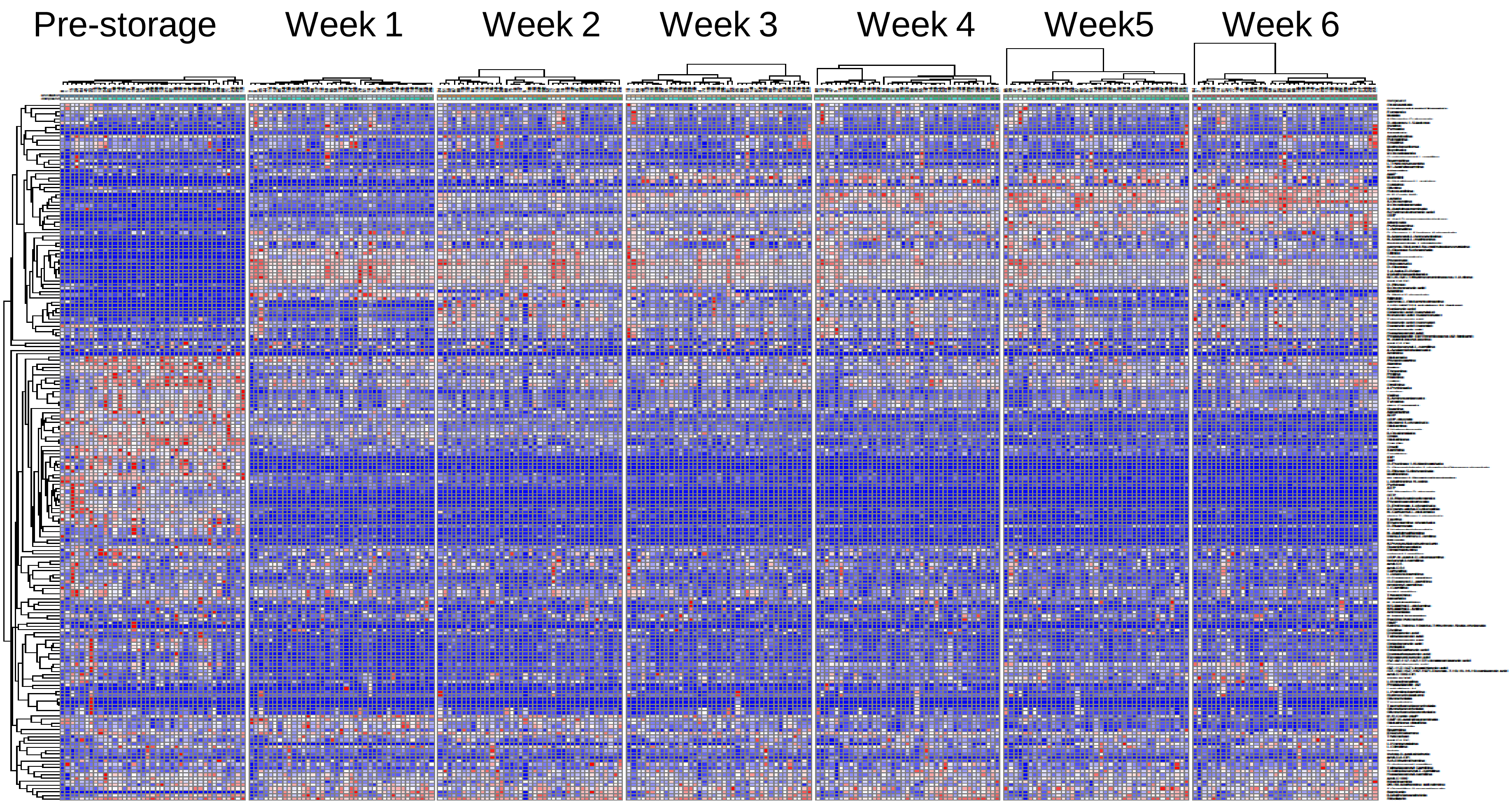
The case for G6PD:
Next steps

Metabolomics:

Mechanistic understanding

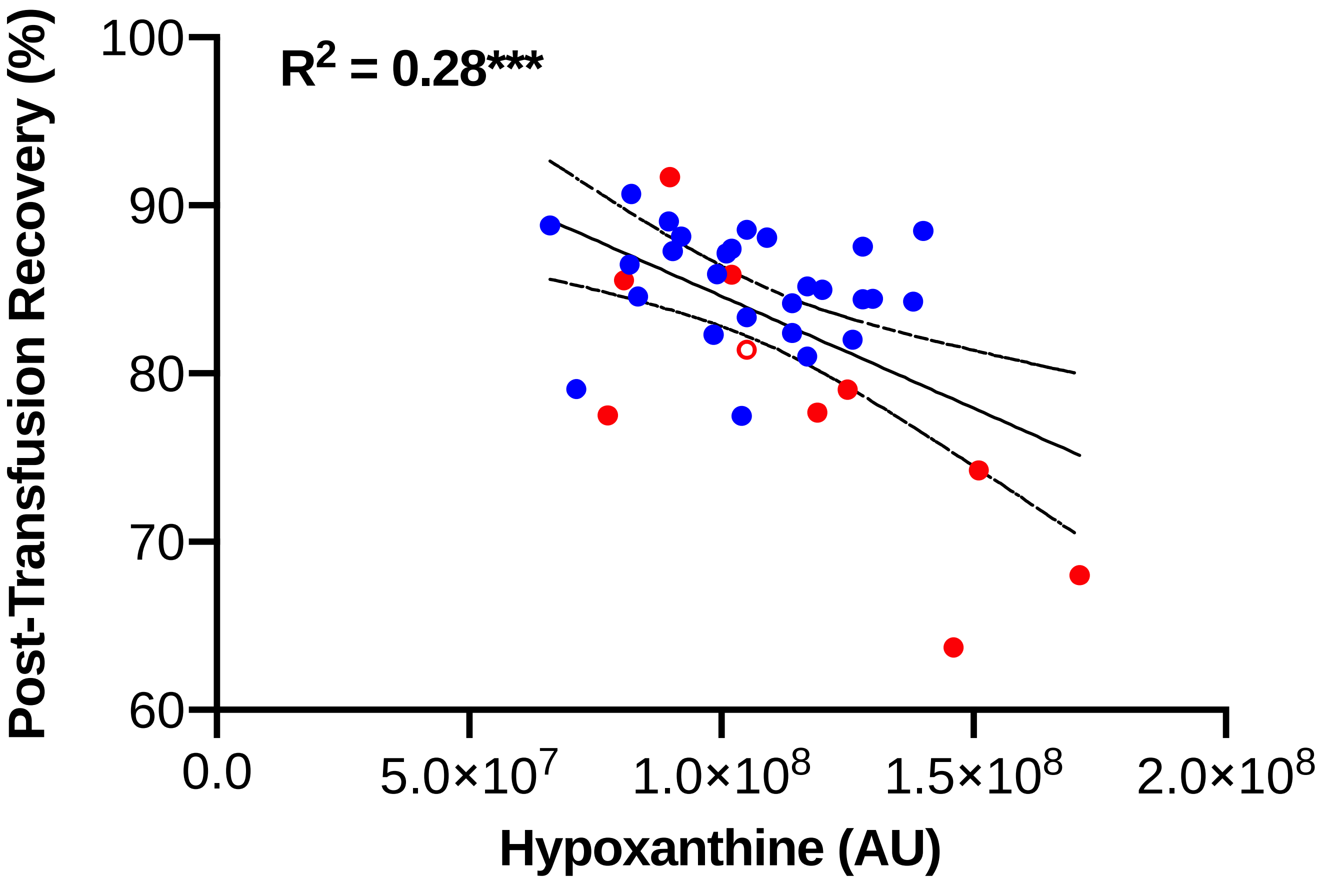
Develop predictive biosignature(s)

The case for G6PD: Next steps



Francis et al. Unpublished observations.

The case for G6PD: Next steps



Francis et al. Unpublished observations.

Metabolomics: Human RBCs

Jim Zimring

Angelo D'Alessandro

(Interim) Conclusions

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RBCs obtained from G6PD-deficient volunteers have inferior storage quality at 40-42 days

- **Statistically-significant difference of 6.8% ($p<0.001$)**

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Strongly suggests that the RBC's intrinsic ability to resist oxidative stress affects storage quality

(Interim) Conclusions

RBCs obtained from G6PD-deficient volunteers have inferior storage quality at 40-42 days

- Statistically-significant difference of 6.8% ($p<0.001$)

Strongly suggests that the RBC's intrinsic ability to resist oxidative stress affects storage quality

Is this difference clinically relevant?

- Acute transfusion setting
- Chronic transfusion setting
- Acute intercurrent illness

Diet

Diet

Vitamin C
Vitamin E
Vitamin D

Fe
Cu
Se

Ergothioneine
Olive oil & other lipids

Obesity

Diet

Vitamin C
Vitamin E
Vitamin D

Fe
Cu
Se

Ergothioneine
Olive oil & other lipids

Obesity

The “RBC storage lesion”
Final common pathway?

Metabolic dysfunction & oxidative stress ➔

↓ Deformability

↑ “Eat me” signals

↓ “Don’t eat me” signals

- ↑ Hemolysis *in vitro*
- ↑ RBC clearance *in vivo*
  - Intravascular and extravascular hemolysis

Iron deficiency (without anemia) is very common in blood donors

Iron deficiency (without anemia) is very common in blood donors

Iron-deficient erythropoiesis (IDE)

Iron deficiency anemia affects RBC lifespan & transfusion recovery

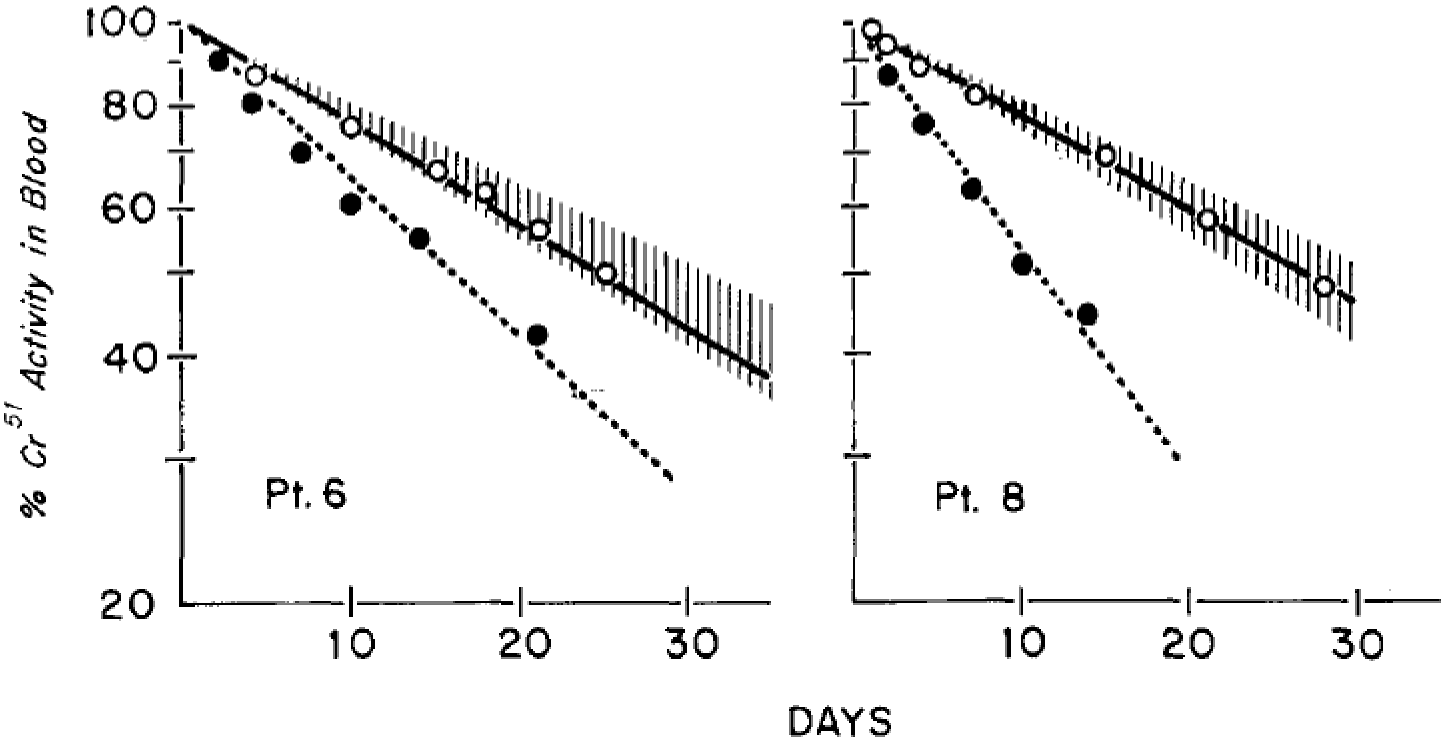
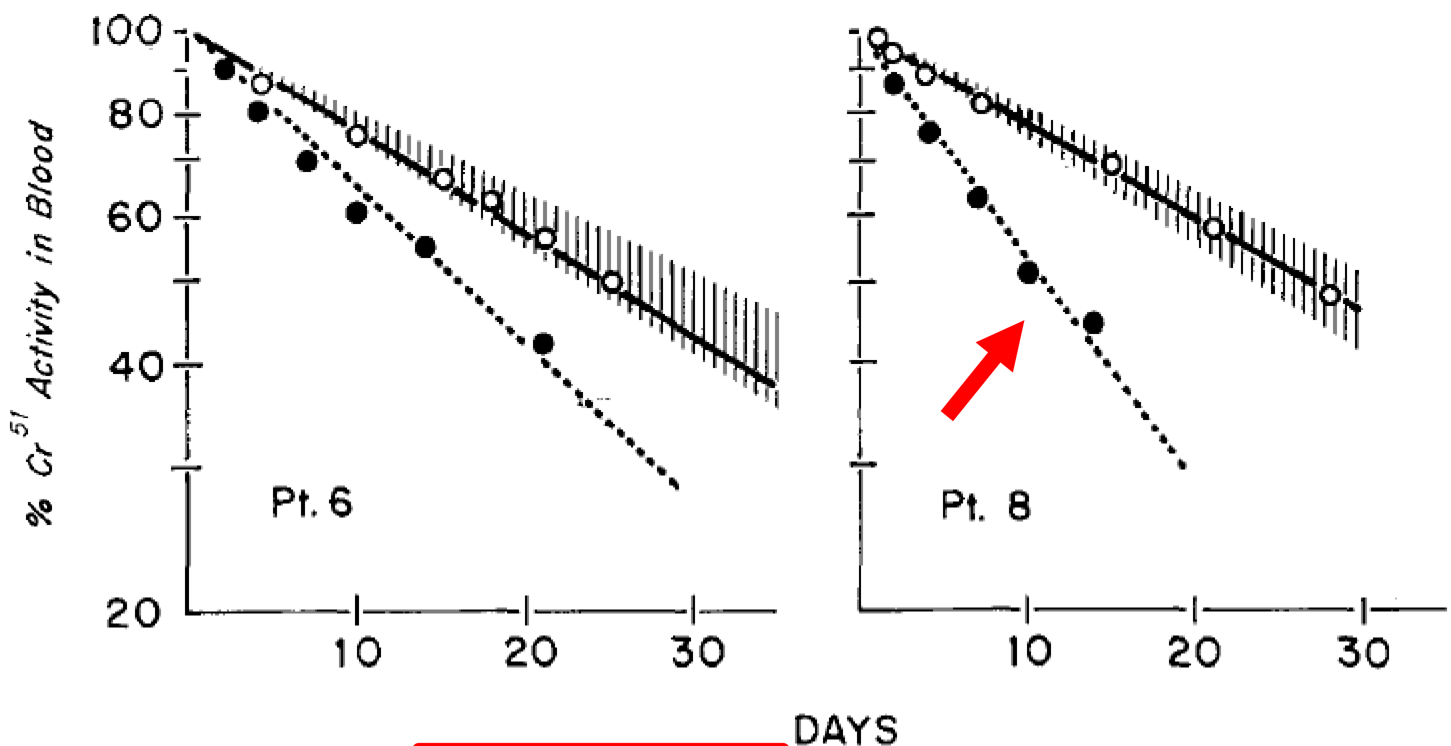


Fig. 4. Cr^{51} red cell half-life before (● — ●) and after (○ — ○) correction of iron deficiency anemia.

Macdougall et al. J Pediatrics 76:660-675, 1970.

Iron deficiency anemia affects RBC lifespan & transfusion recovery



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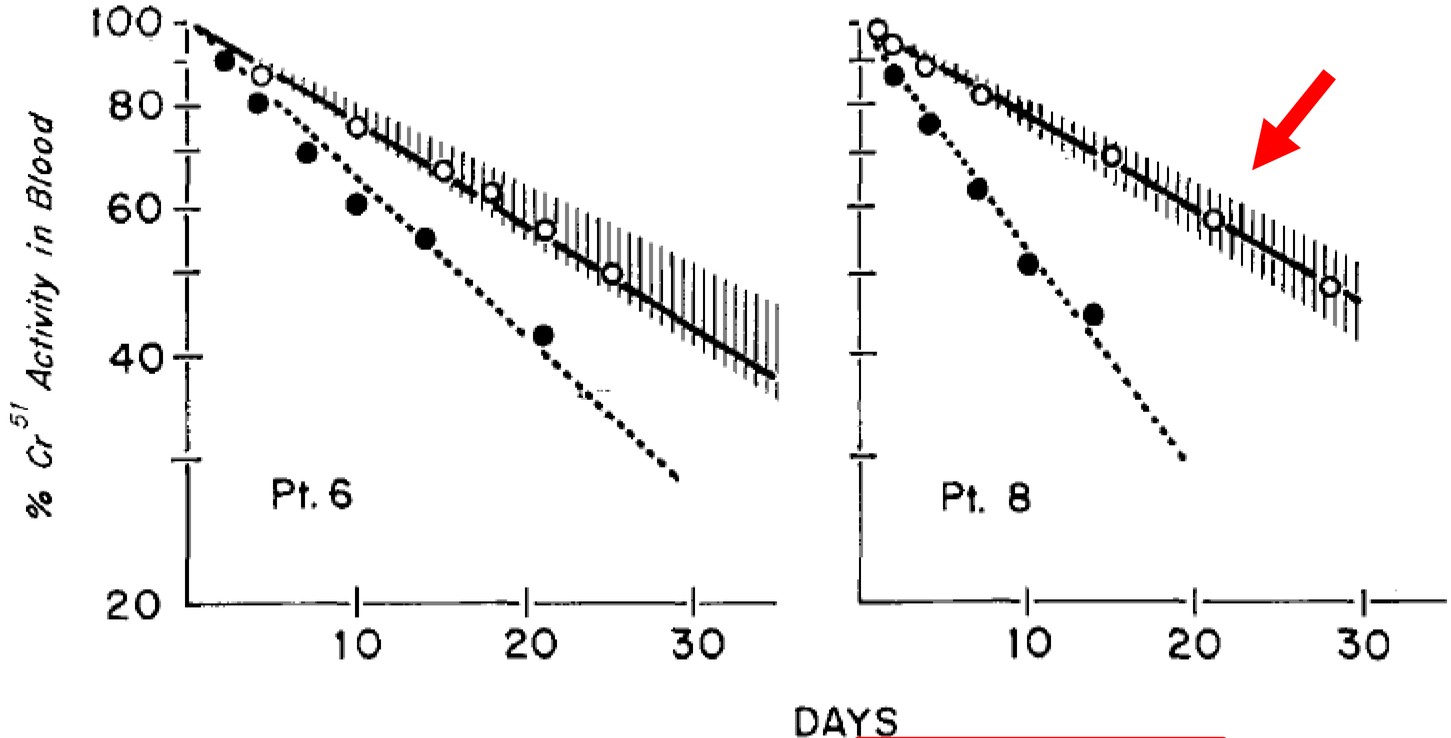

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Iron deficiency anemia affects RBC lifespan & transfusion recovery

- ↓ Resistance to oxidative stress
- ↑ Oxidative damage
- ↓ Resistance to low pH
- ↑ Phosphatidylserine exposure
- ↓ Deformability
- ↑ Splenic clearance

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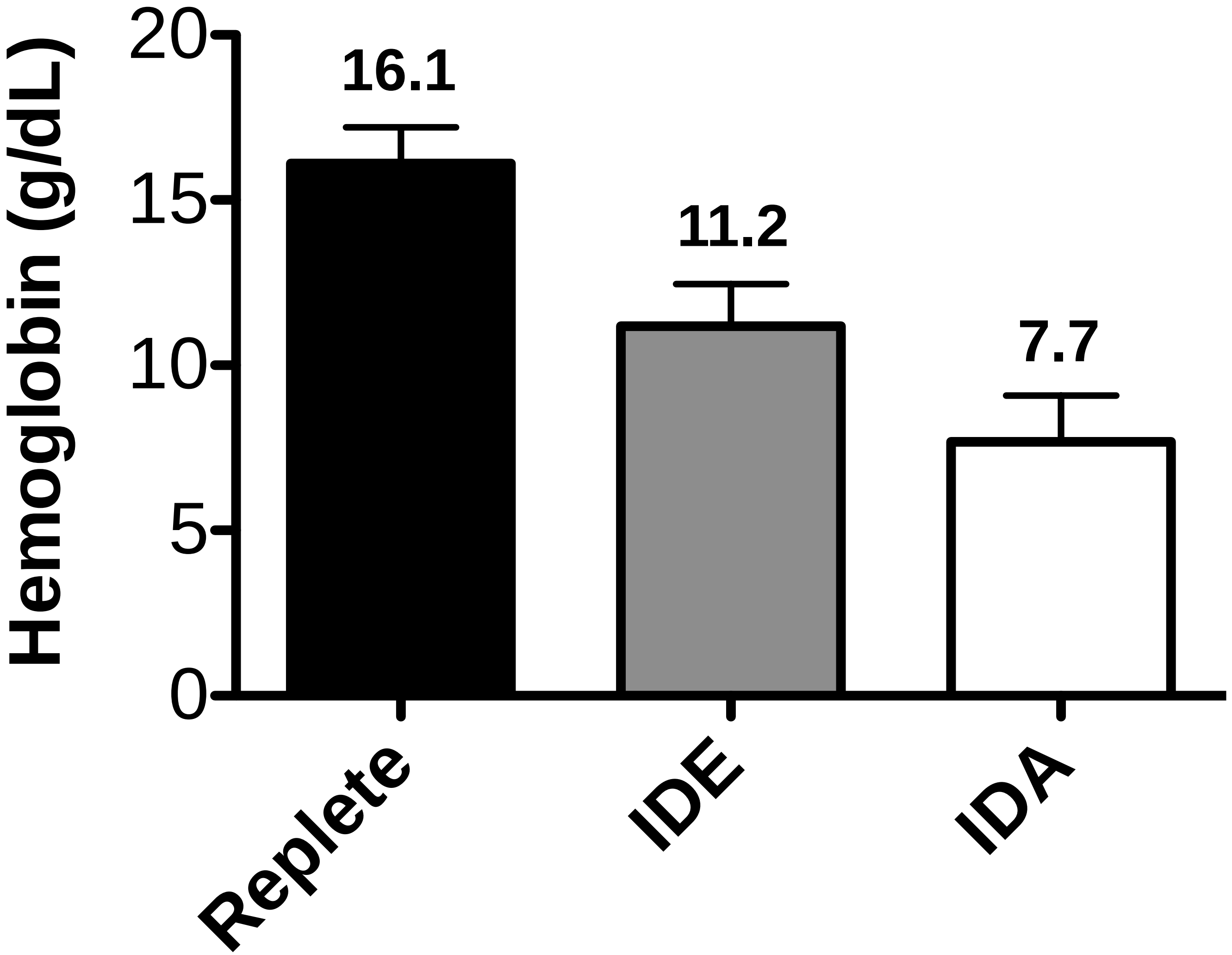
Do these apply to RBCs in IDE?

Mouse model

Weanling, male C57BL/6 mice:

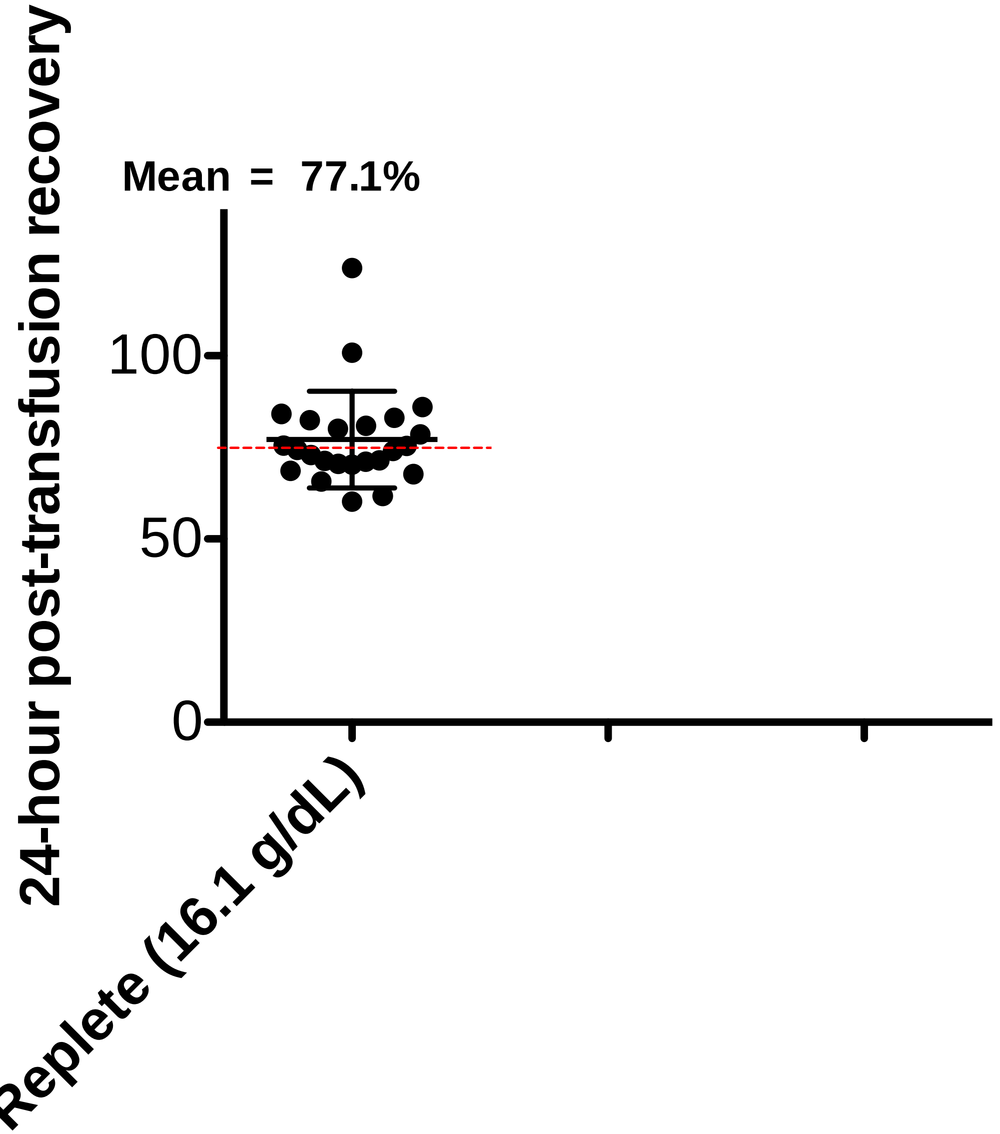
1. **Control diet: 45 ppm of iron** **(normal)**
2. **Iron-deficient diet: 0-4 ppm of iron** **(IDE)**
3. **Iron-deficient diet + weekly phlebotomy** **(IDA)**

Results



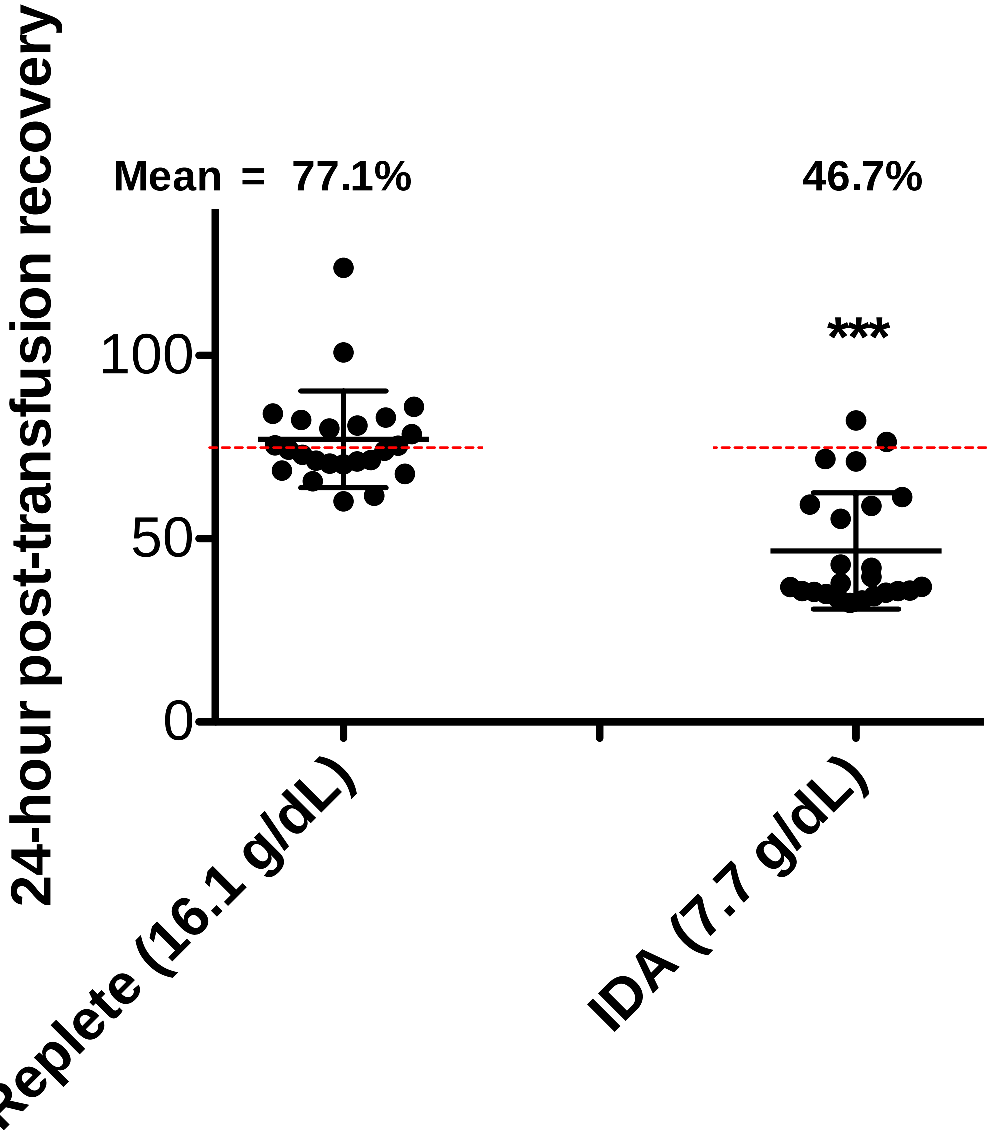
All comparisons: $p<0.001$

Results



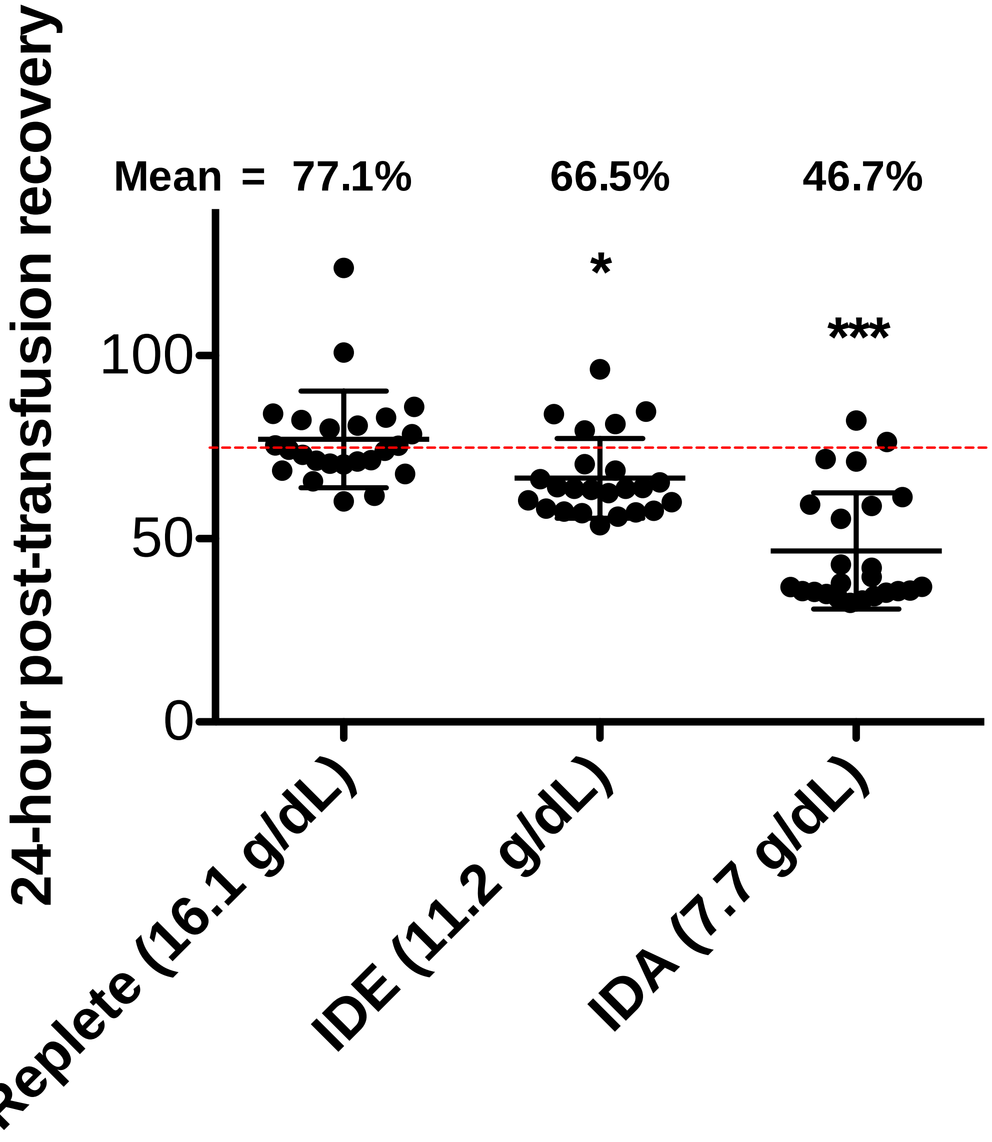
Mean = 77.1%
24-hour post-transfusion recovery
100
50
0
Replete (16.1 g/dL)

Results



***: $p<0.001$

Results



*: p<0.05

Interim Conclusions

Interim Conclusions

RBCs from mice with iron deficiency anemia exhibit poor storage quality

Interim Conclusions

RBCs from mice with iron deficiency anemia exhibit poor storage quality

RBCs from mice with “iron-deficient erythropoiesis” exhibit suboptimal storage quality

Would this be true for human recipients of RBC transfusions from donors with IDE?

Would this be true for human recipients of RBC transfusions from donors with IDE?

ClinicalTrials.gov

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Trial record **3 of 5** for: eldad hod

Previous Study | Return to List | Next Study

Donor Iron Deficiency Study - Red Blood Cells From Iron-deficient Donors: Recovery and Storage Quality (DIDS)

This study is enrolling participants by invitation only.

Sponsor:
Columbia University

Collaborators:
New York Blood Center
National Heart, Lung, and Blood Institute (NHLBI)

Information provided by (Responsible Party):
Eldad Arie **Hod**, Columbia University

ClinicalTrials.gov Identifier:
NCT02889133

First received: August 25, 2016
Last updated: March 20, 2017
Last verified: March 2017
History of Changes

Full Text View | **Tabular View** | **No Study Results Posted** | Disclaimer | How to Read a Study Record

Would this be true for human recipients of RBC transfusions from donors with IDE?

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E. Hod

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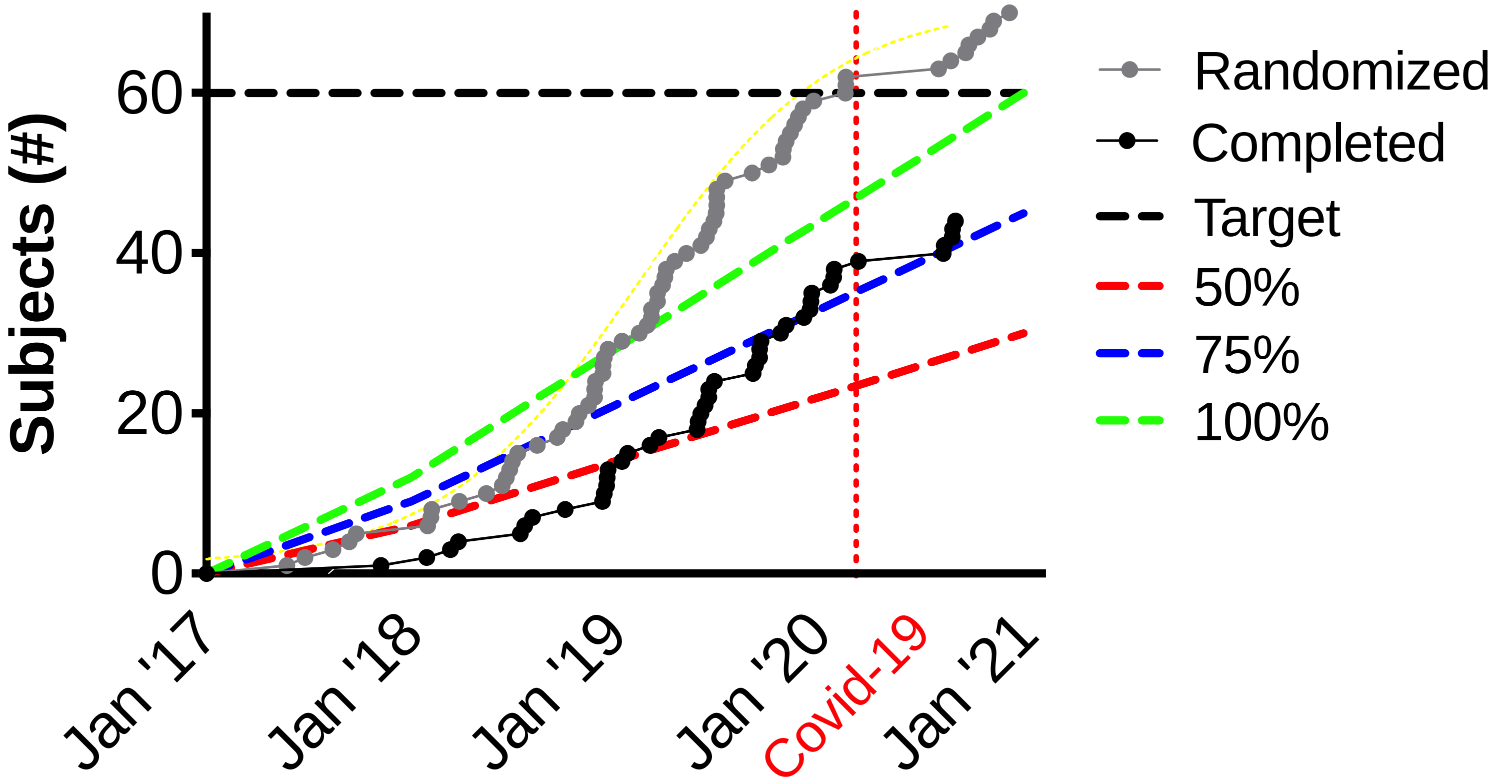

All volunteers have been randomized; various stages of completion.

“Environment”

“Environment”

Aging

Smoking

Microbiome

Lead

Others?

“Environment”

Aging

Smoking

Microbiome

Lead

Others?

Lead

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Neurotoxicant (synapses, myelin, etc.)

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No threshold effect

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Young children particularly vulnerable

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↑ blood lead level: >5 μg/dL (0.2415 μmol/L)

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No threshold effect

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↑ blood lead level: >5 µg/dL (0.2415 µmol/L)

In whole blood, 75% of lead is in RBCs

Lead

Do donor pRBC units contain high lead levels?

Lead

Do donor pRBC units contain high lead levels?

If so, who cares?

Lead

BLOOD DONORS AND BLOOD COLLECTION

A population-based study on blood lead levels in blood donors

Gilles Delage,[1] Suzanne Gingras,[2] and Marc Rhainds[2,3]

TRANSFUSION 2015;55;2633–2640

TABLE 2. Characteristics of study participants and estimated GM, 95% CI, and proportion of BLLs of more than 0.15 µmol/L among blood donors population, Québec, Canada 2006 to 2007

Variable	Number (%)	GM (µmol/L)	95% CI	p value	% > 0.15 µmol/L	p value
	BLLs					
Sex						
Men	2098 (60.1)	0.095	0.038-0.241	<0.001	15.93	<0.001
Women	1392 (39.9)	0.070	0.020-0.242		8.32	
Age (years)						
18-24	655 (9.8)	0,053	0.018-0.154	<0.001	1.28	<0.001
25-34	778 (11.6)	0.060	0.017-0.212		4.64	
35-44	1252 (18.6)	0.075	0.026-0.219		6.07	
45-54	2038 (30.4)	0.095	0.041-0.222		13.62	
55-64	1618 (24.1)	0.122	0.056-0.266		27.44	
≥65	374 (5.6)	0.135	0.063-0.290		36.59	
Level of education						
Primary school	454 (10.2)	0.089	0.039-0.278	0.008	22.97	<0.001
High school	1466 (32.8)	0.086	0.029-0.253		14.42	
College or university	1566 (57.0)	0.083	0.025-0.231		8.18	
Number of previous blood donations						
0	310 (8.9)	0.092	0.018-0.246	0.025	8.43	<0.001
1-3	598 (17.1)	0.089	0.021-0.225		6.76	
4-10	789 (22.6)	0.092	0.026-0.245		10.88	
11-25	879 (25.2)	0.086	0.033-0.231		11.86	
>25	914 (26.2)	0.088	0.044-0.256		21.55	
Age of dwelling (years)						
<10	354 (10.2)	0.079	0.022-0.236	<0.001	8.32	<0.001
10-29	1139 (32.8)	0.083	0.027-0.228		10.10	
30-49	1161 (33.4)	0.084	0.028-0.248		12.90	
≥50	818 (23.6)	0.091	0.030-0.274		15.93	
Smoking status						
Never smoker	2540 (73.5)	0.085	0.026-0.240	<0.001	11.30	0.106
Ex-smoker (≥1 year)	337 (9.7)	0.091	0.038-0.232		14.78	
Ex-smoker (<1 year)	86 (2.5)	0.107	0.034-0.280		16.44	
Occasional smoker	142 (4.1)	0.091	0.022-0.254		11.22	
Regular smoker (pack-years)	352 (10.2)	0.109	0.033-0.278		14.71	
<5	42	0.093	0.023-0.172	0.219	1.24	<0.001
5-9	36	0.104	0.025-0.248		9.43	
10-19	84	0.099	0.032-0.258		11.92	
20-29	64	0.103	0.044-0.261		12.97	
≥30	111	0.115	0.058-0.309		30.08	
Alcohol consumption						
Never	355 (10.3)	0.080	0.024-0.257	<0.001	13.19	<0.001
<1/month	536 (15.5)	0.076	0.021-0.229		9.66	
1-3/month	786 (22.7)	0.079	0.024-0.217		8.02	
1-2/week	1100 (31.8)	0.088	0.031-0.237		12.26	
3-6/week	508 (14.7)	0.094	0.038-0.246		13.84	
Daily	171 (5.0)	0.109	0.054-0.309		30.39	
Employed in the past 12 months						
Not	763 (21.9)	0.085	0.034-0.293	<0.001	22.77	<0.001
Not at risk of lead exposure	2584 (75.2)	0.084	0.026-0.223		8.70	
High risk of lead exposure	100 (2.9)	0.129	0.038-0.472		37.11	

Lead

Highest prevalence:

Lead

Highest prevalence:

Frequent blood donors, who are:

Lead

Highest prevalence:

Frequent blood donors, who are:

unemployed, uneducated, and older males,

Lead

Highest prevalence:

Frequent blood donors, who are:

unemployed, uneducated, and older males,

who:

smoke, drink, and have lived in the same home for a long time.

Lead

Lead exposure in preterm infants receiving red blood cell transfusions

Hijab Zubairi[1], Paul Visintainer[2,3], Jennie Fleming[1], Matthew Richardson[1,3] and Rachana Singh[1,3]

Pediatric RESEARCH Volume 77 | Number 6 | June 2015

Lead

One transfused aliquot had a lead level of 56 mcg/dl and only one infant received a single transfusion from this aliquot with a total lead load of 7.84 mcg from the single transfusion. This infant's pretransfusion lead level was <1 mcg/dl with the post-transfusion lead level increasing to 9 mcg/dl. The infant's discharge lead level was 1 mcg/dl. This aliquot was not used for any further transfusions and no other infants were exposed to this elevated lead level.

Interim Conclusion

The effects of donor environmental factors on RBC storage quality have not been well studied

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The effects of donor environmental factors on RBC storage quality have not been well studied

Blood donor exposome and impact of common drugs on red blood cell metabolism

Travis Nemkov,[1,2] Davide Stefanoni,[1] Aarash Bordbar,[3] Aaron Issaian,[1] Bernhard O. Palsson,[4] Larry J. Dumont,[5] Ariel Hay,[6] Anren Song,[7] Yang Xia,[7] Jasmina S. Redzic,[1] Elan Z. Eisenmesser,[1] James C. Zimring,[6] Steve Kleinman,[8] Kirk C. Hansen,[1,2] Michael P. Busch,[9] Angelo D'Alessandro,[1,2] and the Recipient Epidemiology and Donor Evaluation Study III Red Blood Cell–Omics (REDS-III RBC-Omics) Study[10]

JCI Insight 2021;6(3):e146175 https://doi.org/10.1172/jci.insight.146175

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The effects of donor environmental factors on RBC storage quality have not been well studied

Blood donor exposome and impact of common drugs on red blood cell metabolism

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Future Directions

Making better products: Ideal RBC unit

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Optimal post-transfusion recovery & lifespan

“Equivalent to fresh”

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"Equivalent to fresh"

Randomized controlled trial of 7, 28, vs 42 day stored red blood cell transfusion on oxygen delivery (VO_2 max) and exercise duration

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No WBCs

Avoid febrile NHTRs, HLA alloimmunization, TA-GVHD

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Avoid allergic NHTRs, anaphylactic NHTRs, and TRALI

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- "Equivalent to fresh"

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Lacking clinically-significant RBC blood group antigens
- Avoid RBC alloimmunization and HTRs

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Lacking hemoglobin S (and others?)
  Can use in exchange transfusions for SCD patients

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    Novel storage solutions, select & prepare better donors?
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No plasma
- Washing? Change in donor selection?

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- Phenotypic and/or genotypic matching? Pharm-ing?

Lacking hemoglobin S (and others?)
- Sickledex. Change in donor selection?

No transfusion-transmitted infections
- New screening tests; pathogen reduction/inactivation

Thank you