Auto-immune Hemolytic Anemia and Transfusion 2: Still Out of Order

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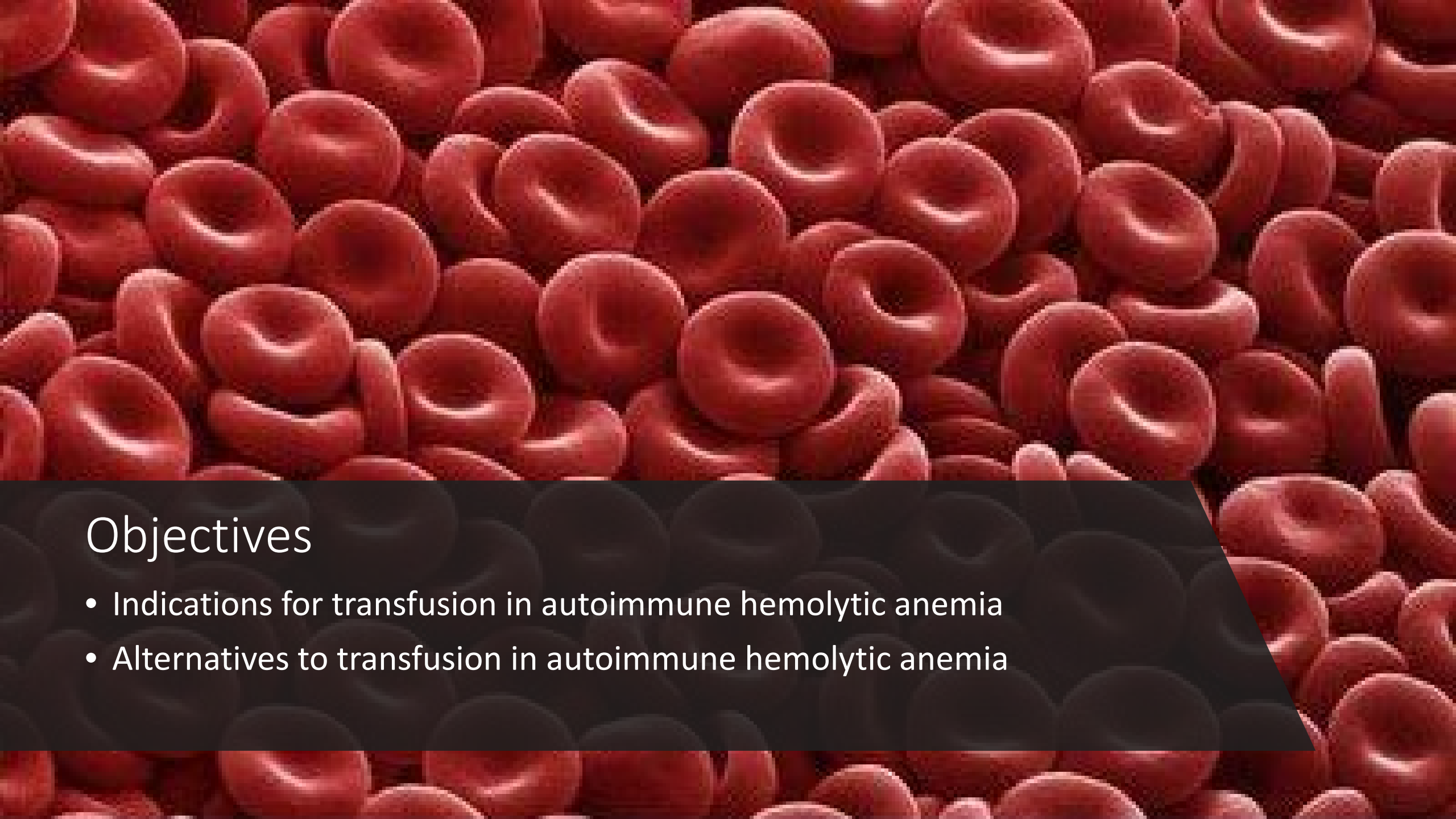
Disclosures

- I have no relevant conflicts of interest



Objectives

- Indications for transfusion in autoimmune hemolytic anemia
- Alternatives to transfusion in autoimmune hemolytic anemia

AIHA Case

- 51M, previously healthy
- Presented with weakness and dark orange urine, rigors and chills, exertional dyxpnea

- Hb 64-> 54 WBC 9.8 PLT 202
- Retics 4.1
- Haptoglobin <0.1
- LDH 964
- Bili 111/8
- DAT positive IgG, negative C3

Transfuse already!
Think of how *good* it will feel to have a higher Hb.

Transfuse!
Think of how good it will feel to have a higher Hb!

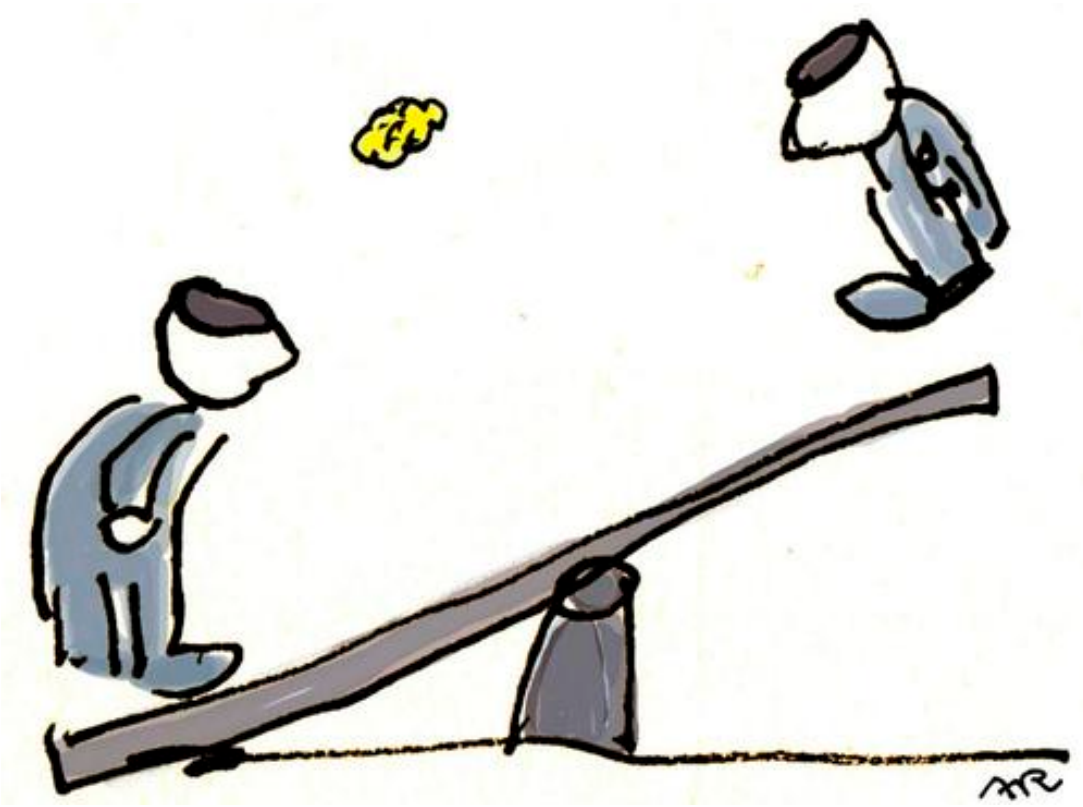
What if it makes things worse? A transfusion reaction is the last thing you need right now!

Reasons to be cautious…

- Transfused RBCs are as prone to hemolysis as the patient’s own RBCs
- More RBCs = more substrate for hemolysis and accumulation of products of hemolysis (free hemoglobin, RBC membranes)
- Auto-antibody interference with routine screening may mask presence of allo-antibody
- Availability of appropriate RBCs may be limited

However,

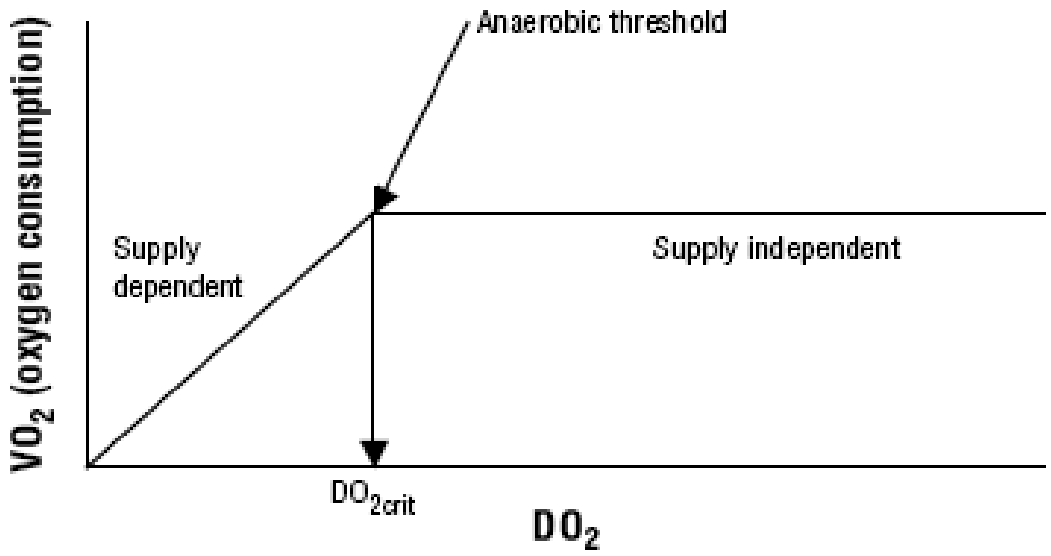
- Concern about hemolysis should not outweigh need to maintain adequate oxygen delivery
- Transfusion can be life-saving and may be necessary



Indications for transfusion

- Rationale for RBC transfusion is similar to other populations – support oxygen carrying capacity by maintaining sufficient hemoglobin concentration

- Very limited data to guide decision to transfuse: no equivalent to TRICC trial for AIHA



$DO_2 = (1.34 \times Hb \times SaO_2) \times (HR \times SVR)$

$VO_2 = CO \times 1.34 \times Hb \times (SaO_2 - SVO_2)$

Concern about transfusion safety can lead to harm:

"The patients' Hb decreased further; somnolence and hypoxemia were noted. The patient did not receive additional blood transfusions, as the attending haematologist was of the opinion that this would aggravate the underlying condition. On the following day, the patient was intubated and transferred to the intensive care unit at that hospital. On arrival, the patient had metabolic acidosis (pH 7.1), decompensated haemolysis (Hb <2 g/dL), circulatory failure (systolic blood pressure <50 mmHg), and the pupils were found to be enlarged. An emergency splenectomy was performed, but the patient died due to circulatory collapse."

Patient	Age	Sex	Comorbidities	Hb g/dL	Blood transfusion
1	60	Female	DM, CAD	6.5-7.0	No
2	34	Female	Splenomegaly	<2	No
3	61	Male	-	2.4	Delayed
4	53	Male	Unrecognised bleeding	2.7	Inadequate

DM: diabetes mellitus; CAD: coronary artery disease; Hb: haemoglobin concentration.

Yurek et al. Blood Transfus. 2015; 13: 616.

Is it safe to transfuse in AIHA? Part I - reactions

- 450 patients with AIHA and Hb ≤110 g/L with hemolysis and DAT+
- Anemia:
  - Very severe (< 30 g/L) – 3%
  - Severe (30 - <60 g/L) – 34%
  - Moderate (60 - <90 g/L) – 46%
  - Mild (≥90 g/L) – 16.9%
- RBCs for transfusion selected using ‘least incompatible’ method

Chen et al. Medicine. 2020, 99(2):epub

Is it safe to transfuse in AIHA? Part I - reactions

- 60% transfused overall
  - Hb <60: 92% transfused
  - >60: 47% transfused
- 2509 units transfused to 269 patients in 1112 episodes; data on vitals available for 885 episodes
- Median of 5 RBC units (5-10)
- 58.5% had increase ≥5 g/L
- Transfusion reaction incidence: 1.6%
  - 13 febrile reactions
  - 1 allergic reaction
  - 1 'somatic'

Chen et al. Medicine. 2020, 99(2):epub

Is it safe to transfuse in AIHA? Part II - alloimmunization

Multicenter cohort study by BEST collaborative

- 8 centers from 5 countries
- 1 reference lab, 7 transfusion services
- 6/7 used prophylactic antigen matching (PAM)
- 1 122 245 patients

Review of 10-year period to identify patients with:

- IAT performed
- presence of warm autoantibody

Excluded:

- Drug-induced autoantibody
- Anti-CD38
- Sickle cell disease

Delaney et al. Vox Sang. 2020, 115: 515

Is it safe to transfuse in AIHA? Part II - alloimmunization

- WAA prevalence of 0.46%, 0.17%
- 1002 patients with complete data:
  - 67.9% WAA only; 32.1% WAA + alloAb
- 631 transfused (63.0%); 390 PAM, 241 no-PAM
  - WAA+alloAb more likely to be transfused (72.4% vs 58.5%, p<0.00001)
  - WAA+alloAb transfused more RBCs (17.5±28.1 vs 13.8 ±23, p=0.0676)

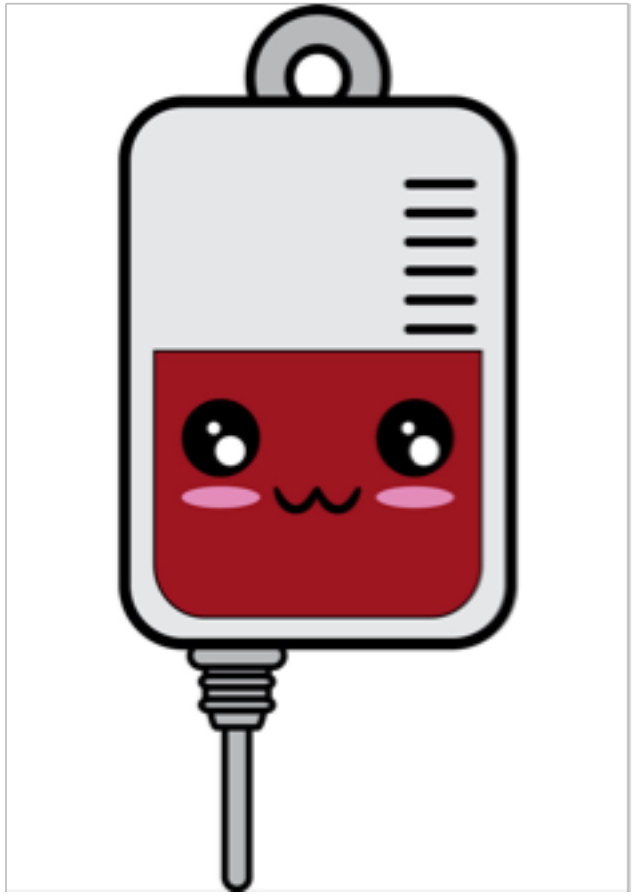
- 372 had IAT ≥30 days after transfusion
  - New alloAb in 56 (15.1%)
  - (14.6% vs 15.6%, p=0.8837)
  - No association between PAM and alloimmunization (14.6% vs 15.6%, p=0.8837)

	WAA with new alloimmunization (*n* = 56)	WAA without new alloimmunization (*n* = 316)	Absolute difference[a] (95% CIs)
Female	38 (67·9%)	148 (46·8%)	21·0 (7·6, 34·4)*
Autoimmune haemolytic anaemia (AIHA)[b]	7 (14·0%)	81 (29·1%)	−15·1 (−26·1, −4·1)*
Autoimmune and connective tissue diseases	8 (14·3%)	51(16·1%)	−1·9 (−11·9, 8·2)
Leukaemia/lymphoma	14 (25·0%)	91 (28·8%)	−3·8 (−16·2, 8·6)
Previous alloantibody (Yes)	29 (51·8%)	117 (37·0%)	14·8 (0·6, 28·9)*
PAM transfusion strategy (Yes)	31 (55·4%)	181 (57·3%)	−1·9 (−16·0, 12·2)
Average RBC units after WAA identification (range)	30·9 (1–192)	20·6 (1–221)	10·3 (−0·8, 21·4)

Delaney et al. Vox Sang. 2020, 115: 515

Efficacy of RBC transfusion?

- 161 patients with AIHA transfused 1-5 RBC units in single episode
- Adsorption performed to assess for allo-antibodies
- Daily Hb, Tbili, LDH assessed x 7 days
- Compared with other anemic patients:
  - 100 with negative DAT but *positive* screen
  - 100 with negative DAT and *negative* screen



Park et al. Ann Lab Med. 2015, 35(4): 436

Clinical variables	Patient groups			N of available samples in each patient group			*P* value*		
	(1) <5.0 g/dL (N=14)	(2) 5.0-8.0 g/dL (N=97)	(3) >8.0 g/dL (N=50)	(1)	(2)	(3)	(1) vs. (2)	(1) vs. (3)	(2) vs. (3)
Unit of transfused RBCs, median (range)	2.0 (1.0-5.0)	2.0 (1.0-3.0)	2.0 (1.0-5.0)				0.112	0.187	0.198
Volume of transfused RBCs (mL), median (range)	800 (400-1,920)	800 (320-1,200)	800 (320-2,000)				0.056	0.072	0.370
Transfused RBCs (mL)/kg of patient, median (range)	15.94 (11.03-31.74)	12.97 (3.99-24.00)	13.33 (5.20-42.64)				0.008	0.027	0.624
Hemoglobin (g/dL), median (range)									
Pretransfusion	4.4 (2.1-4.8)	7.2 (5.1-8.0)	8.9 (8.1-12.5)	14	97	50	<0.001	<0.001	<0.001
Day 1	6.7 (5.2-8.6)	9.0 (5.4-11.8)	10.7 (7.8-13.6)	14	97	50	<0.001	<0.001	<0.001
Day 7	8.1 (5.6-11.5)	9.2 (6.0-12.5)	10.0 (8.2-13.6)	8	68	28	0.165	0.009	0.001
Hemoglobin changes (g/dL) per transfused RBCs of 10 mL/kg, median (range)									
Day 1	1.30 (0.60-2.60)	1.50 (-0.20-4.50)	1.15 (-0.70-3.90)	14	97	50	0.828	0.155	0.012
Day 7	2.45 (1.50-5.50)	1.75 (-0.70-7.60)	0.80 (-0.80-2.50)	8	68	28	0.040	<0.001	0.001

Park et al. Ann Lab Med. 2015, 35(4): 436

No significant differences in LDH changes

Clinical variables	Patient subgroups			N of available samples in each patient group			*P* value*		
	(1) Autoantibodies ± alloantibodies (N=161)	(2) Alloantibodies only (N=100)	(3) No antibodies (N=100)	(1)	(2)	(3)	(1) vs. (2)	(1) vs. (3)	(2) vs. (3)
LDH (IU/L), median (range)									
Pretransfusion	210.5 (96.0-704.0)	187.0 (108.0-704.0)	240.0 (114.0-398.0)	161	100	100	0.083	0.227	0.001
Day 1	206.0 (120.0-798.0)	198.5 (117.0-739.0)	264.0 (128.0-588.0)	161	100	100	0.349	0.005	<0.001
Day 7	192.0 (100.0-698.0)	174.0 (132.0-868.0)	242.0 (90.0-542.0)	101	51	100	0.379	0.016	0.001
LDH changes (IU/L) per transfused RBCs of 10 mL/kg, median (range)									
Day 1	11.2 (-192.0-210.5)	13.7 (-135.1-272.6)	18.9 (-109.7-507.5)	161	100	100	0.640	0.219	0.366
Day 7	-18.2 (-498.8-240.5)	-9.8 (-148.9-131.8)	2.4 (-159.4-640.9)	101	51	100	0.305	0.101	0.168

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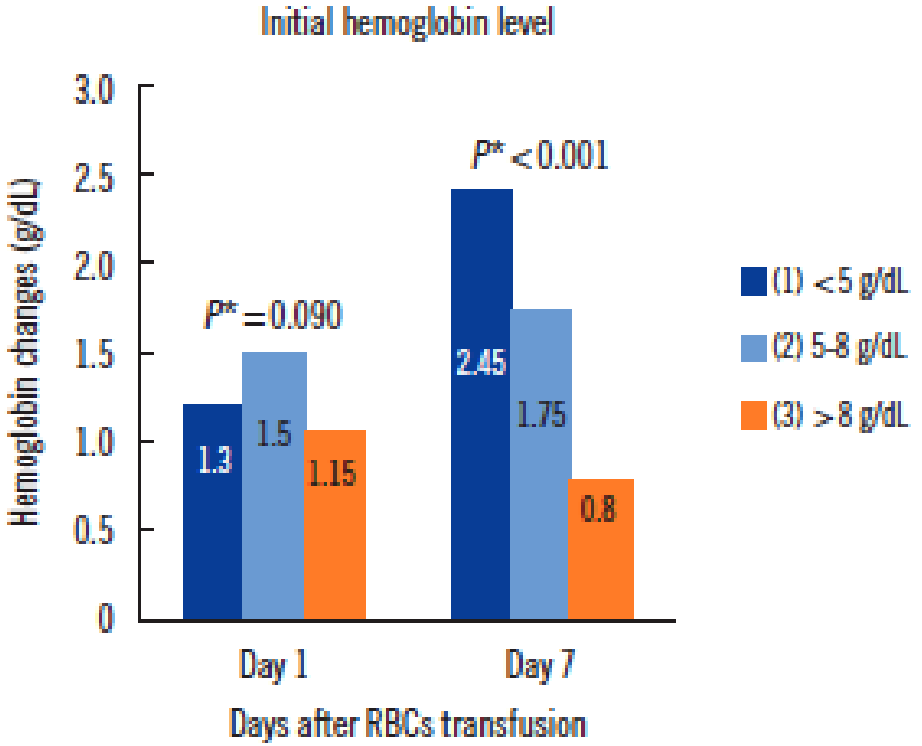

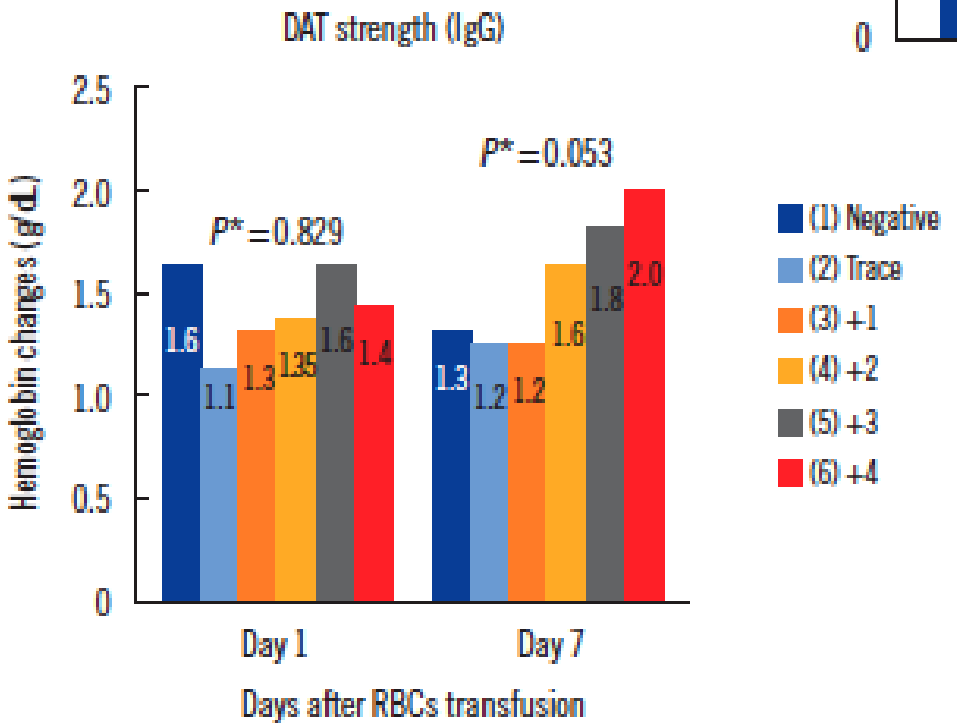

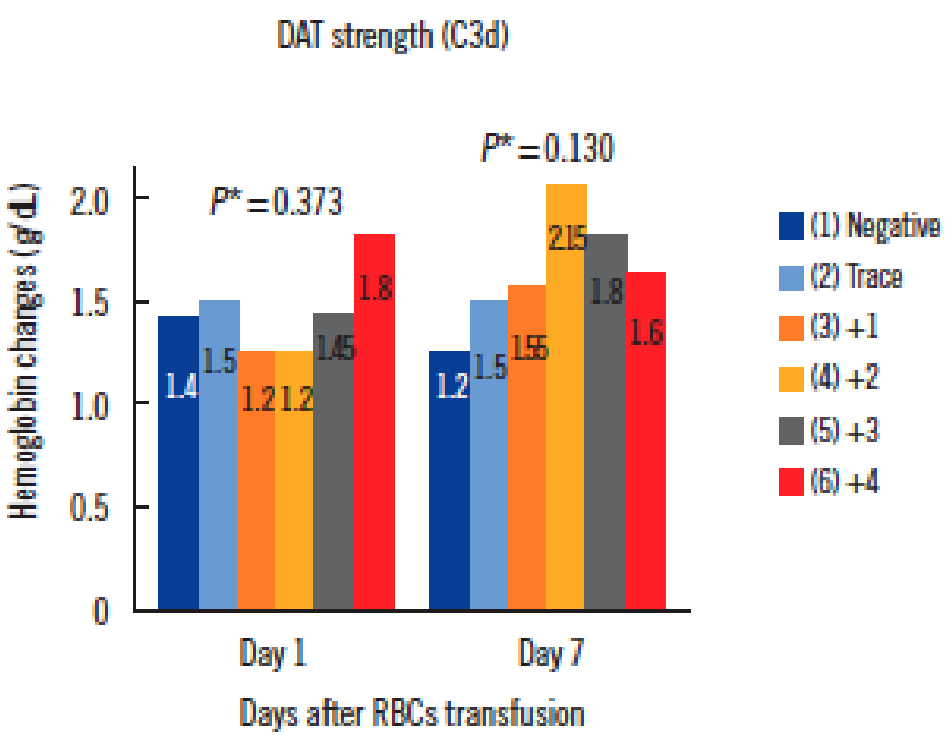

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When to transfuse?

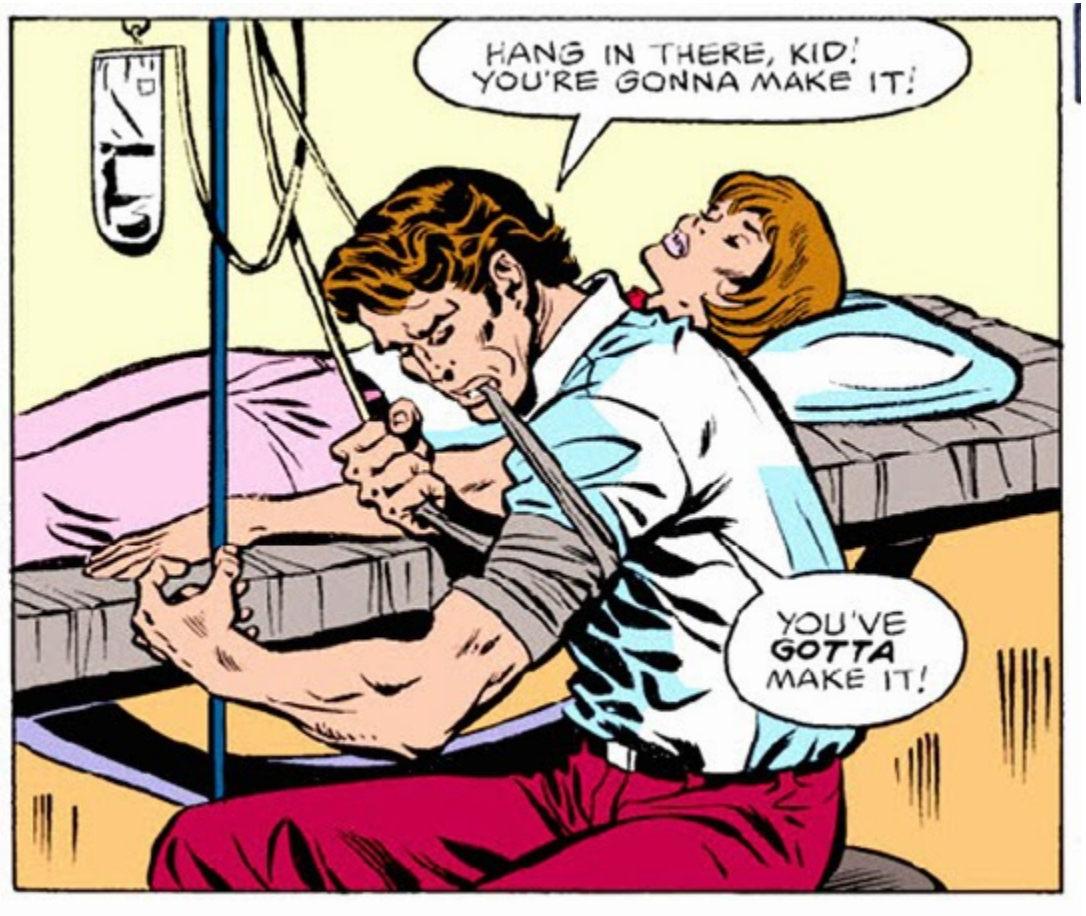
- Decision to transfuse should be individualized according to:
  - Symptoms of anemia or signs of inadequate oxygen delivery
    - Biomarkers: troponin, lactate
  - Co-morbidities
  - Availability of RBCs
  - Severity of hemolysis

Consider:

- 50-year-old man with Hb 85 g/L with symptoms of angina
- 75-year-old man with Hb 55 g/L and asymptomatic

- Response to transfusion should be monitored to guide therapy

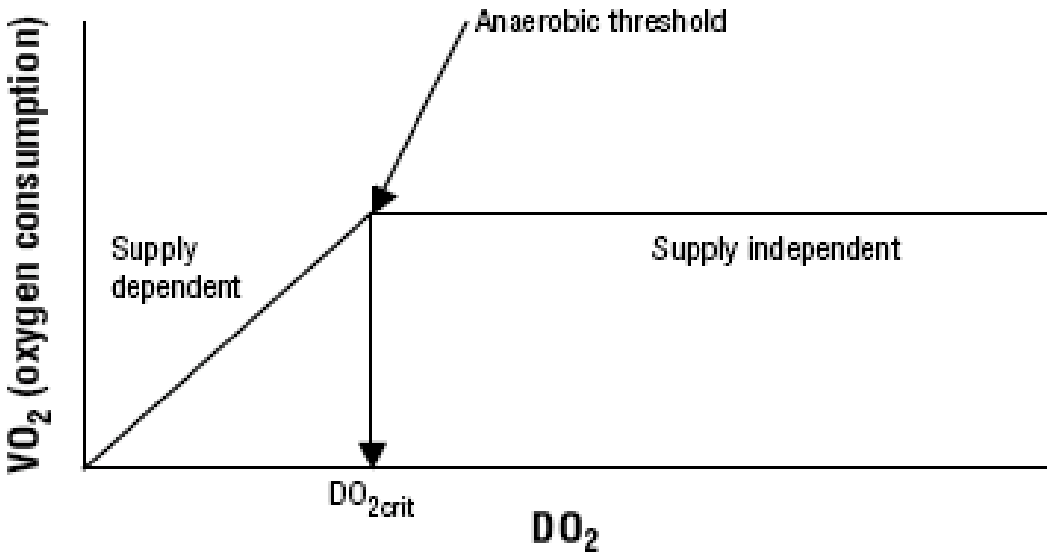
Alternatives to transfusion



Transfusion should not be discouraged because of incompatible cross-match

Alternatives to transfusion

- Basic physiology – increase oxygen delivery and decrease oxygen consumption



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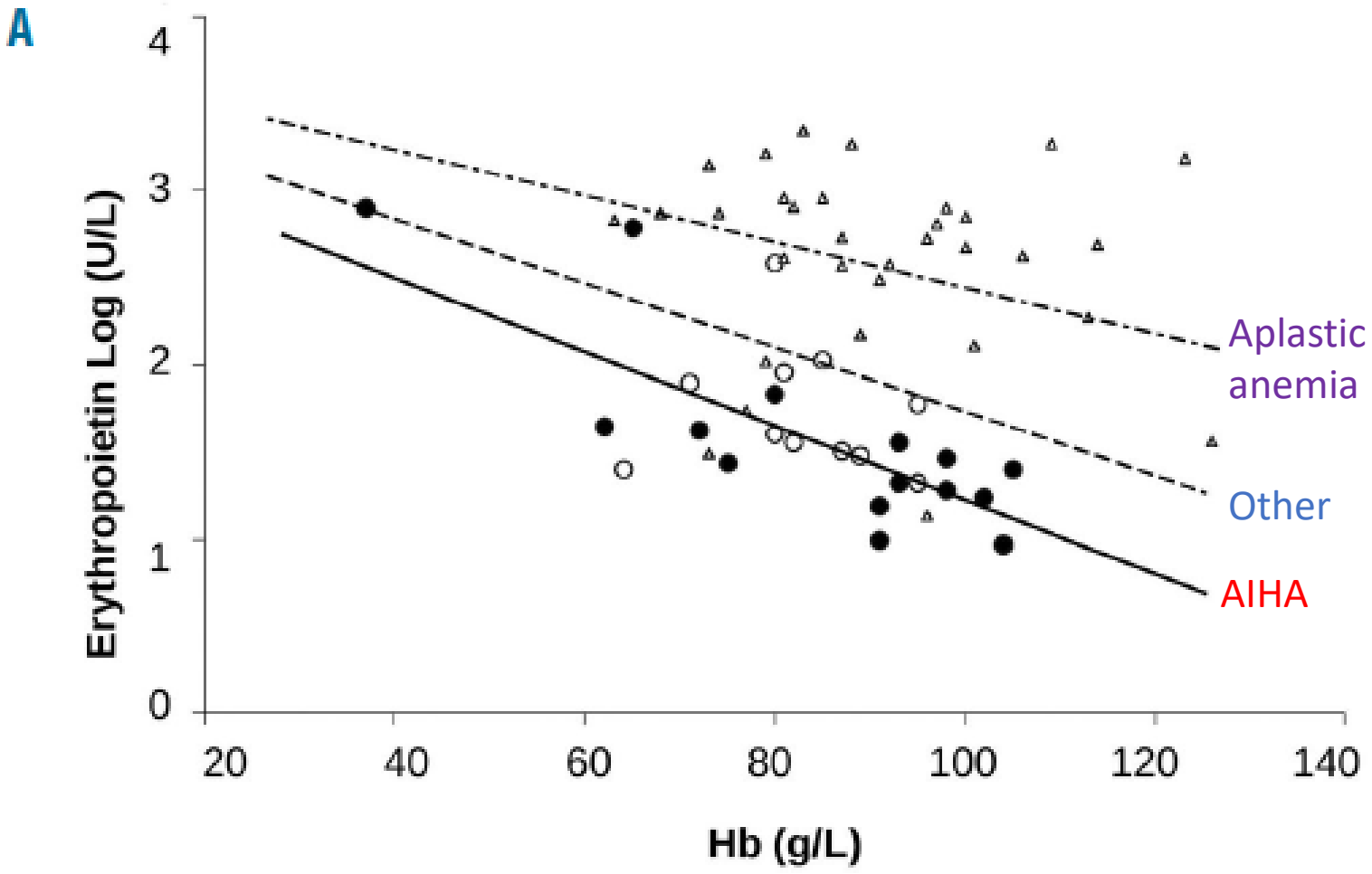
$VO_2 = CO \times 1.34 \times Hb \times (SaO_2 - SVO_2)$

Erythropoeitin

- Fattizzo et al evaluated safety and efficacy of exogenous EPO
- 51 patients with AIHA treated with EPO
- 9 centers across Europe
- 90% pretreated with ≥1 other therapy
- 67% not responding to concomitant therapy
- EPO started median of 24 months after AIHA diagnosis

Fattizo et al. Haematologica. 2021, 106(2): 622

For same Hb, erythropoietin levels lowerin AIHA than other types of anemia



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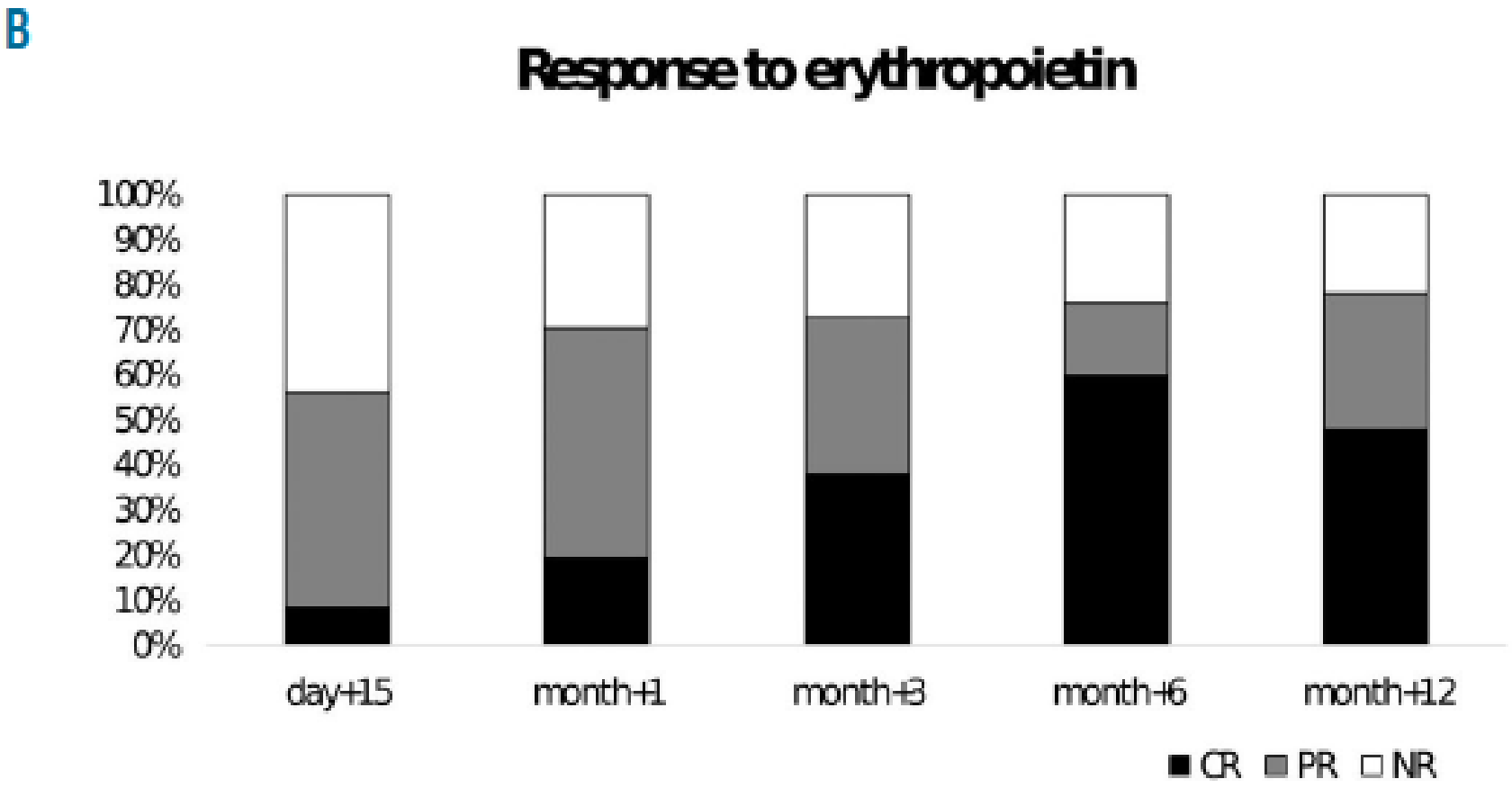
≥20 g/L increase observed in ~50% patients by 15 days



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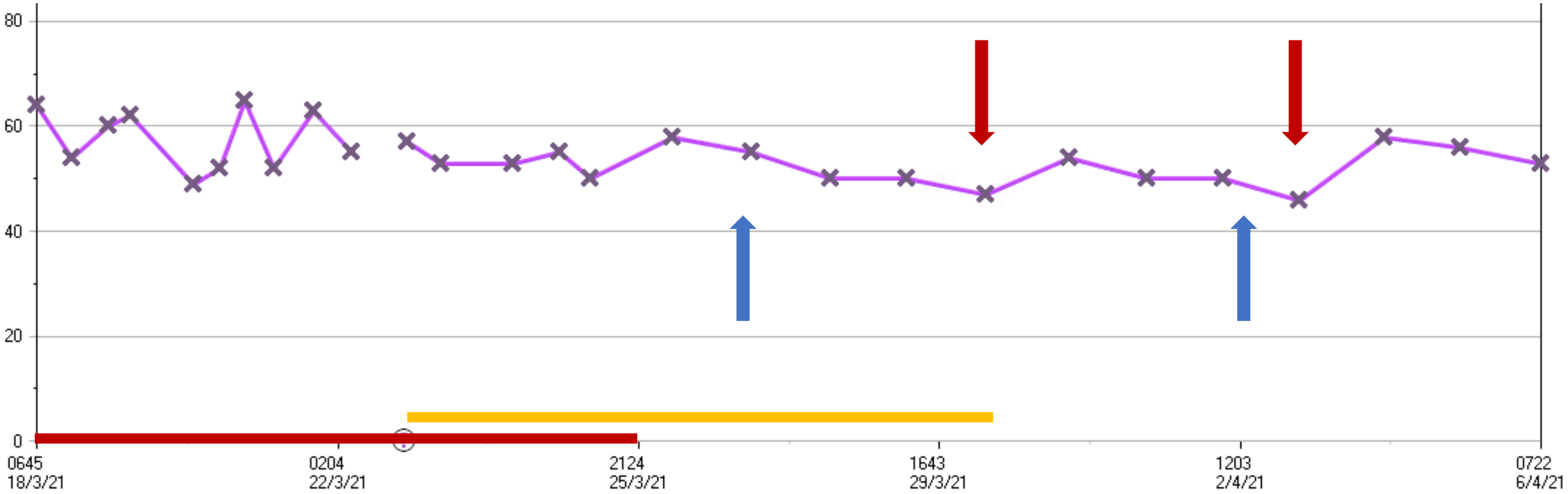
Alternatives to transfusion

- Acuity of need a limit to EPO as practical alternative
- Other alternatives:

Return to case…



Summary

- Indications for transfusion in AIHA similar to other patient populations, decision to transfuse should be individualized
- Response to transfusion should be monitored and over-transfusion avoided for patients tolerating anemia
- Concerns around transfusing ‘incompatible’ blood should be tempered with strategies to mitigate hemolysis from allo-antibodies
- Limited alternatives to transfusion support at present