

Anaemia, Transfusion and TACO

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Caring Expert Quality

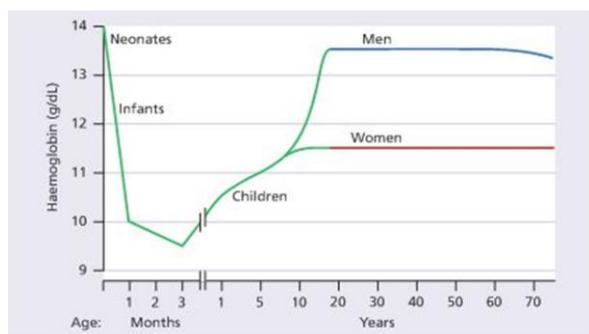
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Anaemia

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What is anaemia?



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Anaemia according to WHO


Blood and Transplant

Population	Non-Anaemia*	Anaemia*		
		Mild [†]	Moderate	Severe
Children 6 - 59 months of age	110 or higher	100-109	70-99	lower than 70
Children 5 - 11 years of age	115 or higher	110-114	80-109	lower than 80
Children 12 - 14 years of age	120 or higher	110-119	80-109	lower than 80
Non-pregnant women (15 years of age and above)	120 or higher	110-119	80-109	lower than 80
Pregnant women	110 or higher	100-109	70-99	lower than 70
Men (15 years of age and above)	130 or higher	110-129	80-109	lower than 80

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Anaemia in palliative care


Blood and Transplant

- Common (77% men 68% women)
- Symptoms often non-specific
- Some causes potentially reversible
- May be multifactorial

Dunn 2003. Anaemia at the end of life: prevalence, significance, and causes in patients receiving palliative care. *J Pain Symptom Manage.* 2003 Dec;26(6):1132-9.

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Clinical Features


Blood and Transplant

- Depend upon
 - Speed of onset
 - Severity of anaemia
 - Age/comorbidities
 - Predominant type of haemoglobin
- May be minimal symptoms or signs

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Symptoms



- Lethargy/fatigue/weakness
- Shortness of breath
- Headaches
- Palpitations
- Angina
- Symptoms of heart failure

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Causes



- Reduced production of red cells
 - Bone marrow infiltration
 - Epo deficiency
 - Haematinic deficiency
 - Dyserythropoiesis
- Increased loss of red cells
 - Bleeding
- Increased destruction
 - Haemolysis

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Classification of anaemia



- Often by size and colour of the red cell
- Microcytic, hypochromic
- Normocytic, normochromic
- Macrocytic

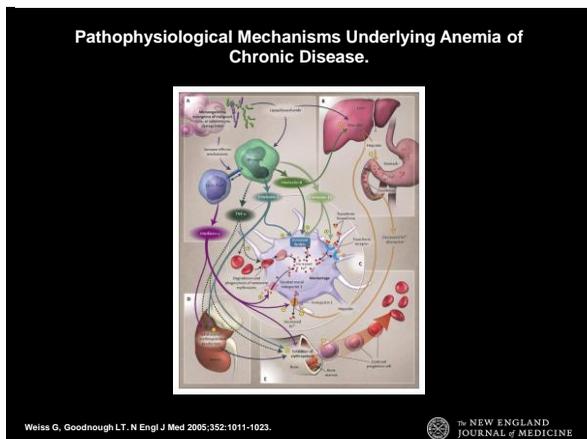
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Functional iron deficiency

NHS
Blood and Transplant

- Also known as anaemia of chronic disease or anaemia of inflammation
- Most common type of anaemia in palliative care
- Usually normochromic normocytic anaemia
- Can occur in conjunction with other types of anaemia

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Activation of T cells (CD3+) and monocytes.

Produce cytokines

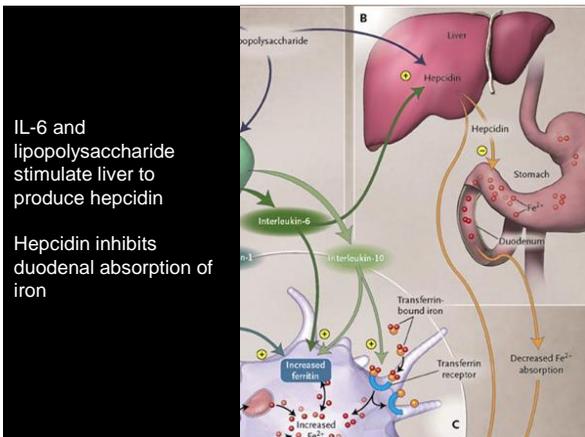
T-cells

- Interferon- γ

Monocytes and macrophages

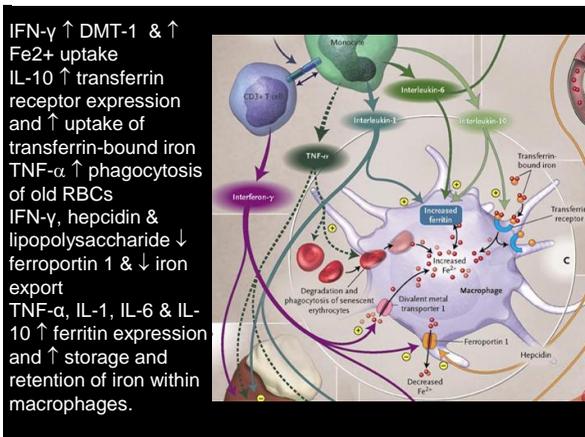
- tumor necrosis factor(TNF) α
- Interleukin (IL)-1
- IL-6
- IL10

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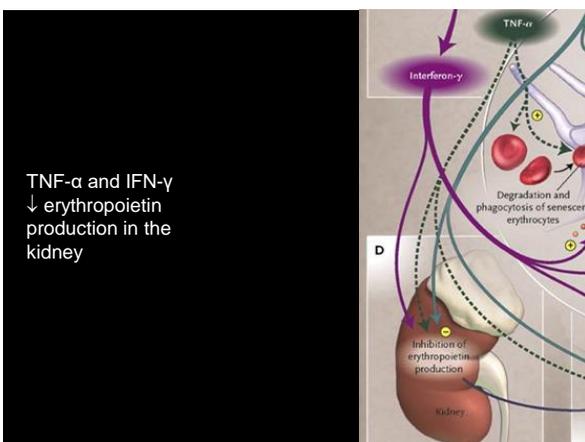
IL-6 and lipopolysaccharide stimulate liver to produce hepcidin
 Hepcidin inhibits duodenal absorption of iron

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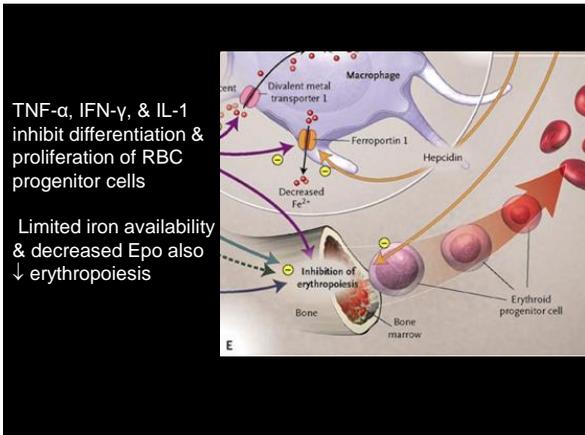
IFN- γ \uparrow DMT-1 & \uparrow Fe^{2+} uptake
 IL-10 \uparrow transferrin receptor expression and \uparrow uptake of transferrin-bound iron
 TNF- α \uparrow phagocytosis of old RBCs
 IFN- γ , hepcidin & lipopolysaccharide \downarrow ferroportin 1 & \downarrow iron export
 TNF- α , IL-1, IL-6 & IL-10 \uparrow ferritin expression and \uparrow storage and retention of iron within macrophages.

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TNF- α and IFN- γ \downarrow erythropoietin production in the kidney

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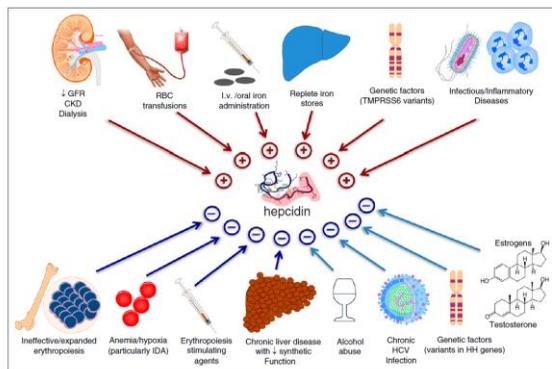


Figure 1. Clinical conditions known to influence circulating hepcidin levels. Clinically relevant conditions include CKD,^{11, 18} RBC transfusions,²⁷ iron administration,^{28, 29} repetitive iron stores,^{10, 12} TMPRSS6 variants,^{10, 12} infectious/inflammatory disorders,^{10, 12} ineffective erythropoiesis,^{10, 12} hypoxia,^{10, 12} administration of erythropoietic stimulating agents,¹⁰ chronic liver disease,¹⁰ alcohol abuse,¹⁰ HCV,¹⁰ hemochromatosis-related mutations,^{10, 11, 15} and administration of the sex hormones testosterone¹⁰ and estrogens.^{10, 11} CKD, chronic kidney disease; GFR, glomerular filtration rate; HCV, hepatitis C virus; HH, hereditary hemochromatosis; IDA, iron deficiency anemia; RBC, red blood cell; TMPRSS6 (transmembrane protease serine 6), the gene encoding for matriptase-2.

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Iron deficiency



- Is common, estimates vary depending on the population tested
- In national audit of people transfused in hospices 38% (46/125) of those tested had ferritin < 100 $\mu\text{g/L}$
- Recommend treat for absolute iron deficiency if ferritin < 100 $\mu\text{g/L}$ and patient has renal impairment, chronic inflammation, cancer, or cardiac failure

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Folate deficiency



- In Ireland estimate 1 in 7 people aged over 50 years has low folate
- In national audit of people transfused in hospices 41% of those tested had low (< 3 µg/l) or borderline (3 to 4.5 µg/l) serum folate (43/105)
- Recommend treat for folate deficiency if folate < 4.5 µg/l

Voluntary fortification is ineffective to maintain the vitamin B12 and folate status of older Irish adults: Evidence from the Irish Longitudinal Study on Ageing (TILDA). British Journal of Nutrition, 120(1), 111-120. doi:10.1017/S0007114518001356

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B₁₂ deficiency



- In UK prevalence is 6% in people < 60 years and 20% in people > 60 years
- In national audit of people transfused in hospices 12% of those tested had B12 deficiency (12/102)

Vitamin B₁₂ deficiency *BMJ* 2014; 349 doi: <https://doi.org/10.1136/bmj.g5226>

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B₁₂ deficiency



- No gold standard to define deficiency
- MCV normal in 25% of cases of B12 deficiency causing neurological symptoms
- Treat for B12 deficiency if cobalamin levels < 200ng/l (150pmol/l) and anaemic (BSH guidance)
- Always check folate at same time as B12

Vitamin B₁₂ deficiency *BMJ* 2014; 349 doi: <https://doi.org/10.1136/bmj.g5226>
Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Haematol, 166: 496-513. doi:10.1111/bjh.12959

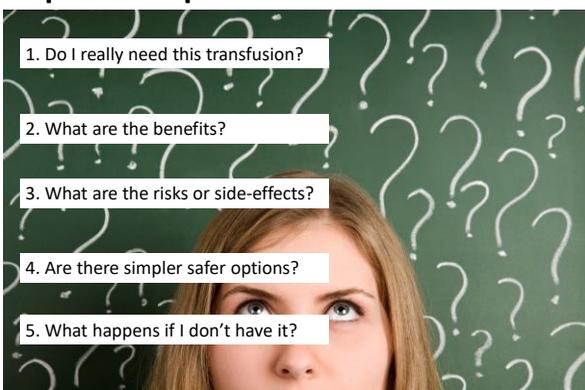
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Transfusion

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5 questions patients should ask



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Blood transfusions for anaemia in patients with advanced cancer (Review)



Preston NJ, Hurlow A, Brine J, Bennett MI



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- No RCTs
- Only 12 before and after studies
- Improved fatigue and breathlessness occurred in 31% to 70% of transfused patients, but this is often transient, lasting no more than 10 to 14 days
- Median survival post first transfusion 42 days
- 25% to 35% patients died within two weeks of transfusion

Preston NJ et al, Cochrane pain, palliative and supportive care group 2012

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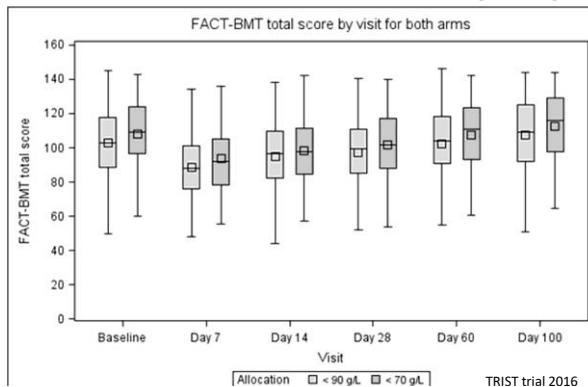
Red blood cell transfusion in adult palliative care: a systematic review

Nicolas Chin-Yee,¹ Joshua Taylor,² Kaitlyn Bourke,² Danika Faig,² Alexandra Davis,¹ Dean Fergusson,² and Elianna Saldenberg^{1,2}

13 studies (11 case series, 2 cohorts (1prospective))
Only 2 studies had a comparator group who were not transfused
9 studies assessed symptom relief, only 1 had a control group.
8 uncontrolled studies suggested short term symptom relief. 1 controlled study did not demonstrate any relationship between transfusion and cancer-related fatigue

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Restrictive red cell transfusion policy



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2016 National Comparative Audit of Red Blood Cell Transfusion in Hospices



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Results

- Data from 121 (58%) UK adult hospices
- 38 sites confirmed they did not perform a transfusion
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- 465 RBC transfusion episodes administered at 83 sites

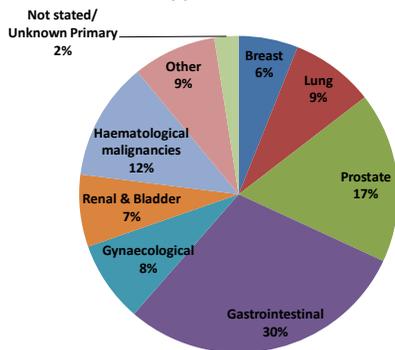
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Patient characteristics

- Mean age: 71 years (92% were over 50; 30% were over 80 years)
- 53% men
- Pre-transfusion performance status score was recorded in 194 (42%) episodes (AKPS most common scale used)
 - Median AKPS score was 60
- Nearly all patients (448; 96%) had cancer

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Type of cancer

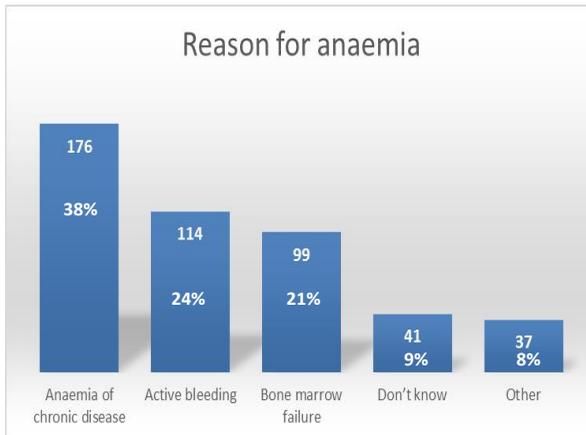


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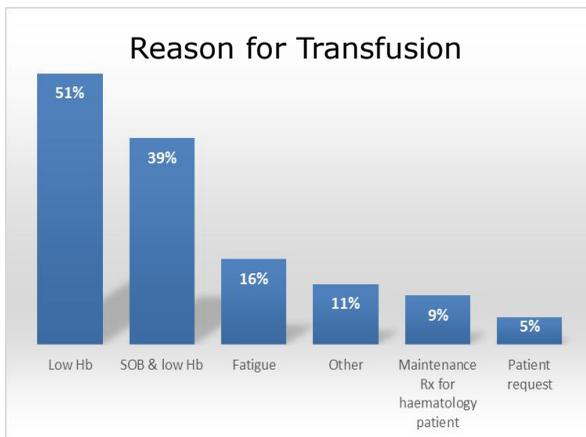
Life expectancy



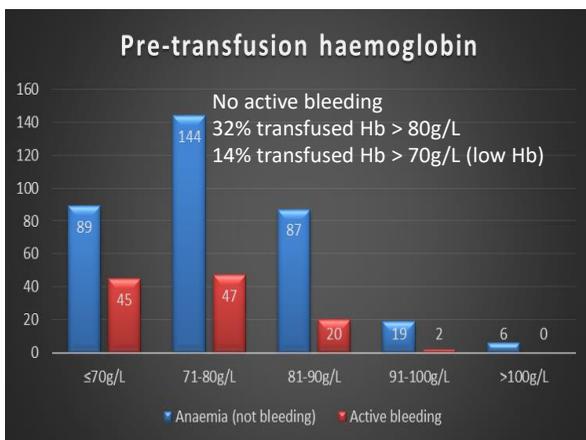
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TACO Definition (ISBT) 2016

 Blood and Transplant

- Acute onset or worsening respiratory distress during or up to 12 hours after transfusion, plus two or more of the following:
- Acute or worsening pulmonary oedema
- Unanticipated cardiovascular system changes (↑ HR, ↑ BP, ↑ JVP, peripheral oedema)
- Fluid overload (positive fluid balance, response to diuretic therapy with clinical improvement, change in the patient's weight)
- ↑ natriuretic peptide (NP) levels to greater than 1.5 times the pre-transfusion value

http://www.isbtweb.org/fileadmin/user_upload/Working_parties/WP_on_Haemovigilance/TACO_reporting_criteria_draft_Nov_2016.pdf

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SHOT Definition

 Blood and Transplant

- Considers cases that occur up to 24 hours after transfusion

<https://www.shotuk.org/wp-content/uploads/myimages/SHOT-Report-2017-WEB-Final-v4-25-9-18.pdf>

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TACO prevalence

 Blood and Transplant

- Under-reported
- Active surveillance estimates that it affects between 1 and 10% of transfusions
- Large audit of transfusions in people age 60 years or above in UK hospitals
 - 4% of inpatients required non-invasive ventilation or transfer to intensive care or high dependency within 24 hours of the transfusion
 - 1.7% of outpatients required admission to hospital

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TACO risk factors



- Age > 50 years
- Weight < 50kg
- Hypoalbuminaemia
- Congestive cardiac failure, left ventricular failure or aortic stenosis
- Chronic kidney disease
- Liver dysfunction
- Peripheral oedema
- Pulmonary oedema
- Prescription of concomitant IV fluids
- Undiagnosed respiratory symptoms
- Use of regular diuretics

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TACO risk factors



- 15% of cases reported to SHOT occur during the first unit transfused

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TACO Checklist	Red cell transfusion for non-bleeding patients	If 'yes' to any of these questions
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic?	<div style="font-size: 2em; font-weight: bold; color: white; background-color: #c00000; padding: 10px; margin: 0 auto;">1</div> <ul style="list-style-type: none"> Review the need for transfusion (do the benefits outweigh the risks)? Can the transfusion be safely deferred or resolved?
	Use a checklist prior to transfusion Does the patient have respiratory symptoms of undiagnosed cause?	<div style="font-size: 2em; font-weight: bold; color: white; background-color: #c00000; padding: 10px; margin: 0 auto;">3</div> <ul style="list-style-type: none"> Consider body weight dosing for red cells (especially if low body weight) Transfuse one unit (red cells) and review symptoms of anaemia Measure the fluid balance Consider giving a prophylactic diuretic Monitor the vital signs closely, including oxygen saturation
	Is the fluid balance clinically significantly positive? Is the patient on concomitant fluids (or has been in the past 24 hours)? Is there any peripheral oedema? Does the patient have hypoalbuminaemia? Does the patient have significant renal impairment?	

Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.

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SHOT case 1


Blood and Transplant

90 year old man (75kg), newly diagnosed haematological condition was admitted with sepsis and a Hb level of 79g/L.

Patient known to have heart failure, renal impairment and peripheral oedema (risk factors for TACO).

Two units of red cells were prescribed with prophylactic diuretics. During transfusion of the second unit the patient became breathless, began coughing up frothy sputum, developed bilateral crackles, tachycardia and hypertension. The chest X-ray was consistent with pulmonary oedema.

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SHOT case 2


Blood and Transplant

Elderly man with disseminated malignancy including pulmonary metastases was admitted to his community hospital for transfusion of 2 units of red cells.

He had congestive cardiac failure and renal impairment, and was short of breath. Later the same day (between 6 and 12 hours later) the man was admitted to hospital with fluid overload, and with treatment produced a diuresis of more than 4L but later died. The transfusion was considered contributory to his death.

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SHOT case 3


Blood and Transplant

A 67 year old female was transfused 3 units of red cells for chronic anaemia related to myelodysplastic syndrome (MDS), between 10:00 and 17:00, in the haematology day unit.

She was sent home after the transfusion, but felt ill on the way home and returned immediately to the ED, where she suffered a respiratory arrest and was admitted to ITU. The chest X-ray appearances were reported to be in keeping with LVF. She made a full recovery

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Information provided to patients



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Recommendations


Blood and Transplant

In patients at risk of TACO:

- Monitor fluid balance
- Prescribe one unit at a time and consider prescribing according to body weight (4ml/kg)
- Transfuse at a slower rate
- Consider use of a prophylactic diuretic
- Monitor the observations closely, including oxygen saturations
- Transfuse maximum of one unit per 24 hours

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SINGLE Unit Blood Transfusions
reduce the risk of an adverse reaction

Don't give unit two without review

Before you transfuse your patient:

- What is your patient's current haemoglobin level?
- What is your patient's target haemoglobin level and would this be achieved by transfusing one unit?



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Each unit transfused is an independent clinical decision

Clinically re-assess your patient after each unit is transfused.

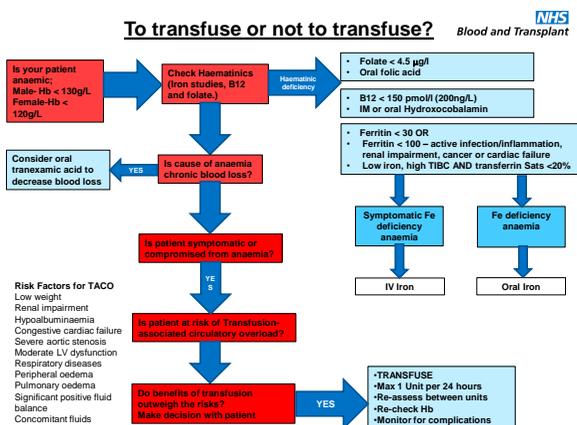
- ✓ Is your patient still symptomatic?
- ✓ Is further transfusion appropriate?

Only order one unit at a time for non-bleeding patients.

Document the reason for the transfusion.¹

Further copies are available from NHSBT.CustomerService@nhsbt.nhs.uk

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Key points

- Avoid transfusion if anaemia can be treated with an alternative
- Benefits of transfusion are often short-lived
- TACO is common
- Only transfuse if benefits outweigh the risks

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