Anaemia

What is anaemia?

[Graph showing hemoglobin levels across different age groups: Neonates, Infants, Children, Women, Men]
Anaemia according to WHO

<table>
<thead>
<tr>
<th>Population</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 6–10 months of age</td>
<td>11/100</td>
<td>7–90</td>
<td>&lt; 70</td>
</tr>
<tr>
<td>Children 6–11 years of age</td>
<td>11/100</td>
<td>6–80</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Children 12–14 years of age</td>
<td>11/100</td>
<td>6–80</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Non-pregnant women (15 years of age and above)</td>
<td>11/100</td>
<td>6–80</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>11/100</td>
<td>6–80</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Men (55 years of age and above)</td>
<td>11/100</td>
<td>6–80</td>
<td>&lt; 80</td>
</tr>
</tbody>
</table>

Anaemia in palliative care

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


Clinical Features

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

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

Causes

• Reduced production of red cells
  • Bone marrow infiltration
  • Epo deficiency
  • Haematin deficiency
  • Dyserthropoiesis
• Increased loss of red cells
  • Bleeding
• Increased destruction
  • Haemolysis

Classification of anaemia

• Often by size and colour of the red cell
• Microcytic, hypochromic
• Normocytic, normochromic
• Macrocytic
**Functional iron deficiency**

- 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

**Pathophysiological Mechanisms Underlying Anemia of Chronic Disease.**

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
    - IL-10
IL-6 and lipopolysaccharide stimulate liver to produce hepcidin.

Hepcidin inhibits duodenal absorption of iron.

IFN-γ † DMT-1 & † Fe2+ uptake.
IL-10 † transferrin receptor expression and † uptake of transferrin-bound iron.
TNF-α † phagocytosis of old RBCs.
IFN-γ, hepcidin & lipopolysaccharide ↓ ferroportin 1 & ↓ iron export.
TNF-α, IL-1, IL-6 & IL-10 ↑ ferritin expression and ↑ storage and retention of iron within macrophages.

TNF-α and IFN-γ ↓ erythropoietin production in the kidney.
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 μg/L

• Recommend treat for absolute iron deficiency if ferritin < 100 μg/L and patient has renal impairment, chronic inflammation, cancer, or cardiac failure
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

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

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
Renal impairment & anaemia

- CKD can be a cause of anaemia when GFR <60 ml/min/1.73m²
- More likely when GFR < 30ml/min/1.73m² or <45/min/1.73m² if diabetic
- Treat any iron deficiency until iron replete
  - %hypochromic RBCs <6%
  - Ferritin >100 µg/L
  - Transferrin saturation >20%
- Only consider ESAs if still anaemic when iron replete and other causes of anaemia excluded.


Incidence of MDS

Transfusion

Caring Expert Quality

5 questions patients should ask

1. Do I really need this transfusion?
2. What are the benefits?
3. What are the risks or side-effects?
4. Are there simpler safer options?
5. What happens if I don’t have it?

What is the evidence?
Blood transfusions for anaemia in patients with advanced cancer (Review)

Preston NJ, Harlow A, Eiser J, Bennett M

THE COCHRANE COLLABORATION

• 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

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

Nicolas Chin-Yee,1 Joshua Taylor,2 Kaitlyn Bouette,2 Danielle Fatig,3 Alexandra Davis,1 Dean Ferguson,1 and Elanna Saldenberg1,2

13 studies (11 case series, 2 cohorts (1 prospective))
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
Restrictive red cell transfusion policy

Results

• Data from 121 (58%) UK adult hospices

• 38 sites confirmed they did not perform a transfusion

• 465 RBC transfusion episodes administered at 83 sites
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
Reason for anaemia

- Anemia of chronic disease: 38%
- Active bleeding: 24%
- Bone marrow failure: 21%
- Don’t know: 9%
- Other: 8%

Reason for Transfusion

- Low Hb: 51%
- SOB & low Hb: 39%
- Fatigue: 16%
- Other: 11%
- Maintenance Rx for haematology patient: 9%
- Patient request: 5%

Pre-transfusion haemoglobin

- No active bleeding: 32% transfused Hb > 80g/L
- 14% transfused Hb > 70g/L (low Hb)
## 30 day outcome

<table>
<thead>
<tr>
<th>Status</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient still admitted with no improvement</td>
<td>21  (5)</td>
</tr>
<tr>
<td>Patient still admitted with transient improvement</td>
<td>10  (2)</td>
</tr>
<tr>
<td>Patient at home with no improvement</td>
<td>29  (6)</td>
</tr>
<tr>
<td>Patient at home with transient improvement</td>
<td>73  (16)</td>
</tr>
<tr>
<td>Patient died</td>
<td>150 (32)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>40  (9)</td>
</tr>
</tbody>
</table>

83 (18%) had an improvement still noted at 30 days
142 (31%) transient improvement
50 (11%) no improvement
73 (16) patient at home with improvement in symptoms
150 (32%) were dead at 30 days, over double predicted
**TACO Definition (ISBT) 2016**

- 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


**SHOT Definition**

- Considers cases that occur up to 24 hours after transfusion


**TACO prevalence**

- 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
**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

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

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.
SHOT case 1

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.

SHOT case 2

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.

SHOT case 3

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.
Information provided to patients

Discuss risks of transfusion including TACO with all patients

Recommendations

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

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?
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 NICE.CustomerServices@nhsnet.uk

To transfuse or not to transfuse?

Is your patient anaemic;
Male - Hb < 130g/L
Female - Hb < 120g/L

Check Haematinics (Iron studies, B12 and folate.)

Symptomatic Fe deficiency anaemia
Haematinic deficiency
• Folate < 4.5 µg/l
• Oral folic acid
• B12 < 150 pmol/l (200ng/L)
• IM or oral Hydrexocobalamin
• Ferritin < 30 OR Ferritin < 100 – active infection/inflammation, renal impairment, cancer or cardiac failure
• Low iron, high TIBC AND transferrin Sats < 20%

Fe deficiency anaemia

Oral Iron

Is patient symptomatic or compromised from anaemia?
Is patient at risk of Transfusion - associated circulatory overload?

• TRANSFUSE
• Max 1 Unit per 24 hours
• Re-assess between units
• Re-check Hb
• Monitor for complications

Is cause of anaemia chronic blood loss?
Consider oral tranexamic acid to decrease blood loss

YES

Risk Factors for TACO
Low weight
Renal impairment
Hypotension/arrhythmia
Hypovolaemia
Tachycardia
SaO2 < 90%
Malignant or infection
Respiratory disease
Peripheral oedema
Significant positive fluid balance
Concurrent fluids

Do benefits of transfusion outweigh the risks?
Make decision with patient

YES

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