Working differently with anaemia in Medicine and beyond

Claire Atterbury,
Clinical Nurse Specialist
Dept. Haematology and Blood Transfusion

claire.atterbury@qehkl.nhs.uk
Why do we need to work differently?

- Better for patients?
  - Accurate, newer tests, cheaper blood tests?
  - Less admissions?
  - Community based?
  - Consistent wellbeing rather than peaks and troughs
  - Reduced co-morbidities?
  - Safer? Longer lasting effects

- Costs? Blood, Admissions (numbers and LOS),

- Beds?
  - Surgical
  - Medical
  - Obstetrics

claire.atterbury@qehkl.nhs.uk
Where do we need to concentrate?

- Respiratory
- Cardiac
- IBD
- Palliative Care/Cancer
- Pre-op assessment
- Colorectal surgery
- Obstetrics

claire.atterbury@qehkl.nhs.uk
What problems does anaemia cause patients?

- Unpleasant symptoms
  - Lethargy
  - Dyspnoea
  - Fatigue & Insomnia
  - Light headedness & dizziness
  - Disorientation
- Increased susceptibility to infection
- Decrease in thermoregulation
- Increased bleeding
- Delayed wound healing
- Excessive fatigue and failure to cope
- Depression

Source: WHO
What problems does transfusion cause patients and hospitals?

- Increased infections
- Increased length of stay
- Transmitted infections (rarely)
- Transfusion associated cardiac overload
- Reactions (rarely)
- Discharge with “adequate” Hb but still anaemic. Rebound?
- Money
Figure 23
Number of viral and parasitic TTI incidents, by year of report and infection type
(Scotland included from October 1998)"
Anita Roddick: I’ve had hepatitis C for more than 30 years

Health warning

Anita Roddick, the founder of the Body Shop, warned last week about the dangers of hepatitis C, which can lead to serious illness and death. The warning was prompted by a recent outbreak of hepatitis C in the UK, which has been linked to the sale of contaminated blood products.

Roddick said: “I’ve had hepatitis C for more than 30 years and it’s not a disease that I’ve everdreamed of having.”

The outbreak is believed to have been caused by the use of contaminated blood products, which can lead to serious illness and death. The warning is aimed at people who may have been exposed to contaminated blood products.

“People should be aware of the risks,” Roddick said. “It’s a very serious condition and can be life-threatening.”

The outbreak has been linked to several cases in the UK, and the government has launched an investigation. The body has been working with a range of experts to understand how the outbreak occurred and what can be done to prevent it in the future.

The government has also announced a new programme of free hepatitis C testing for anyone who may have been exposed to contaminated blood products.

The warning has been published in the Queen Elizabeth Hospital, King’s Lynn, NHS Foundation Trust, which is one of the main providers of blood products in the UK.

NB We need blood for really sick people

claire.atterbury@qehkl.nhs.uk
Why are they anaemic?
Exclude everything you can.

- **Do the tests**
  - Full Blood Count,
  - Coagulation,
  - Reticulocytes,
  - Film
  - Liver function
  - Renal Function
  - Thyroid function
  - CRP,
  - Folate
  - B12
  - Iron Saturation or Ferritin?
  - Consider LDH
  - Direct Anti-globulin Test

- **Plus**
  - Endoscopy
  - Urine tests
  - Bleeding history
  - Recent surgery?
  - Examination
  - Medication

- **Decide on the appropriate treatment**
  - Blood?
  - Iron. Oral or IV?
  - \( B_{12}\)?
  - Folic acid?
  - Nothing?
  - Steroids?
  - Epo?

claire.atterbury@qehkl.nhs.uk
Let’s just get one thing straight

- Inflammation increases the release of Hepcidin by the liver which binds with Ferroportin trapping Iron in the stores rather than releasing it into the circulation to be used.
- Inflammation = no iron absorption
- No Iron absorption = Iron deficiency either actual or functional
- Ferritin is misleading if patients have ANY inflammation (Chronic Disease, Cancer, Arthritis, Obesity) and oral Iron will not work in this situation
- Iron Saturation (TSat) more accurately describes the availability of Iron regardless of stores (ie the %of Transferrin bound by Iron). It should be >20%

claire.etterbury@qehkl.nhs.uk
Chronic Cardiac and Respiratory diseases

- Account for large percentage of urgent admissions – especially in the winter
- FAIR-HF study
  - Stefan Anker et al NEJM 2009:361
  - Improvement in Iron status with or without anaemia improves symptoms, functional capacity and quality of life.
- Could these patients be picked up and treated in the community?
- Could be reduce admissions in crisis or with infections?
Case study

- 82 year old woman
- Admitted with Hb 6g/dl
- “tired, SOB++, in failure”
- Longstanding Ischaemic Heart Disease
- Both hips replaced in the past year
- Hb in January 12g/dl
- No gut symptoms
- On oral Iron

claire.atterbury@qehkl.nhs.uk
<table>
<thead>
<tr>
<th>Specimen No. : HH204660Y</th>
<th>Haematology</th>
<th>&lt;PgUp/PgDn&gt; for more</th>
</tr>
</thead>
</table>

03/12/2012 16:07  Blood

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>White Blood Cell Count</td>
<td>12.50 x10^9/L</td>
<td>(4 to 10) Auth</td>
<td></td>
</tr>
<tr>
<td>Auto Neutrophil Count</td>
<td>11.69 x10^9/L</td>
<td>(1.8 to 7.7) Auth</td>
<td></td>
</tr>
<tr>
<td>Auto Lymphocyte Count</td>
<td>0.36 x10^9/L</td>
<td>(1.5 to 3.5) Auth</td>
<td></td>
</tr>
<tr>
<td>Auto Monocytes</td>
<td>0.37 x10^9/L</td>
<td>(0.2 to 1.0) Auth</td>
<td></td>
</tr>
<tr>
<td>Automated Eosinophils</td>
<td>0.01 x10^9/L</td>
<td>(0.02 to 0.5) Auth</td>
<td></td>
</tr>
<tr>
<td>Automated Basophils</td>
<td>0.01 x10^9/L</td>
<td>(0 to 0.1) Auth</td>
<td></td>
</tr>
<tr>
<td>Red Blood Cells</td>
<td>3.42 x10^12/L</td>
<td>(3.8 to 4.8) Auth</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>8.5 g/dL</td>
<td>(12.5 to 16.5) Auth</td>
<td></td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.274 L/L</td>
<td>(0.360 to 0.460) Auth</td>
<td></td>
</tr>
<tr>
<td>MCV</td>
<td>80.0 fL</td>
<td>(81 to 99) Auth</td>
<td></td>
</tr>
<tr>
<td>MCH</td>
<td>25.0 pG</td>
<td>(27 to 32) Auth</td>
<td></td>
</tr>
<tr>
<td>MCHC</td>
<td>31.2 g/dL</td>
<td>(31.5 to 34.5) Auth</td>
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<tr>
<td>Platelet Count</td>
<td>288 x10^9/L</td>
<td>(150 to 400) Auth</td>
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</table>
### MAU ANAEMIA

Tests added at 00:45 27/11

<table>
<thead>
<tr>
<th>Specimen No : CC506891R</th>
<th>Chemical Pathology</th>
<th>&lt;PgUp/PgDn&gt; for more</th>
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<tbody>
<tr>
<td>Calcium</td>
<td>2.00 mmol/L</td>
<td>( 2.20 to 2.60 ) Auth</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>14 umol/L</td>
<td>( 0 to 20 ) Auth</td>
</tr>
<tr>
<td>Alkaline Phosphatase(ALK)</td>
<td>55 U/L</td>
<td>( 20 to 140 ) Auth</td>
</tr>
<tr>
<td>Alanine Transaminase (ALT)</td>
<td>21 U/L</td>
<td>( 10 to 49 ) Auth</td>
</tr>
<tr>
<td>Iron</td>
<td>2.9 umol/L</td>
<td>( 9.0 to 30.4 ) Auth</td>
</tr>
<tr>
<td>Total iron binding capacity</td>
<td>35 umol/L</td>
<td>( 45 to 81 ) Auth</td>
</tr>
<tr>
<td>Iron Saturation</td>
<td>8 %</td>
<td>Auth</td>
</tr>
<tr>
<td>TSH</td>
<td>1.72 mIU/L</td>
<td>( 0.55 to 4.78 ) Auth</td>
</tr>
<tr>
<td>Free T4</td>
<td>11.3 pmol/L</td>
<td>( 11.5 to 22.7 ) Auth</td>
</tr>
<tr>
<td>IgG</td>
<td>9.28 g/L</td>
<td>( 5.3 to 16.5 ) Auth</td>
</tr>
<tr>
<td>IgA</td>
<td>2.38 g/L</td>
<td>( 0.8 to 4.0 ) Auth</td>
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<tr>
<td>IgM</td>
<td>0.58 g/L</td>
<td>( 0.5 to 2.0 ) Auth</td>
</tr>
<tr>
<td>Anti parietal cell Ab</td>
<td>In-progress</td>
<td>Auth</td>
</tr>
<tr>
<td>Ferritin</td>
<td>1601.7 ng/mL</td>
<td>( 10 to 291 ) Auth</td>
</tr>
<tr>
<td>Serum Folate</td>
<td>8.7 ng/mL</td>
<td>Auth</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>193 pg/mL</td>
<td>Auth</td>
</tr>
</tbody>
</table>

1 Date 2 Earlst 3 Latst 4 rep seQ 5 Spec 6 DFT 7 Matches 8 Options 9 eXit X

Cursor Up/Down for more
Symptoms of Anaemia, Investigation, Treatment and the Decision to Transfuse in the Macmillan Unit

Patient referred

Haematology
  - Full Blood Count, Complement, (serum) vitamin B12, folate, serum ferritin

Chemistry
  - Renal function, Liver function, BUN, Creatinine
  - Thromboplastin time, PT, INR
  - CRP, Fibro Test, FFA, and Ferritin
  - if CRP is high ask for Iron Studies

Transfusion
  - DAT (Direct Antiglobulin Test, used to be called Coombs) and group and antibody screen

Transfusion results
  - Positive DAT = Haemolytic
  - Positive (new) Antibody screen could also mean (false) Haemolytic — delayed transfusion reaction?
  - HLA antibodies?

Chemistry results
  - Alkaline Phosphatase — vitamin D deficiency
  - Renal function — Analysis of Creatinine, Protein on urinalysis for low level
  - Renal CRP Pseudocholinesterase — makes FSH rise, may need to hold for iron Studies
  - Thyroid function — patient may have Thyroid deficiency
  - Liver function and iron need replacing, Low haematocrit rules out anaemia, Iron deficiency, and liver failure

Haematology results
  - Low platelets may mean "thrombocytopenia"
  - Thrombocytopenia may indicate platelet dysfunction or bleeding disorder
  - high MCV could mean polycythaemia vera (too many red cells), but also liver disease
  - Patient may have hereditary sphaerocytosis, etc. RA and AS can cause anaemia
  - Iron deficiency or other liver problems

How much time do you have?
How bad are the symptoms?
Where should the blood transfusion take place?

Treatment decisions
  - Blood Transfusion
    - Although usual practice to keep Hb > 10, some patients require Hb levels to fall
    - 12 to 14 cm of flat platelet
  - Iron Transfusion

Intravenous iron
  - Fed/Not for home care or day case

Transfusion choices
  - Red Cells, or PRP
  - PRPs for 2 units

Hydroxyurea
  - Patients who refuse blood
  - Patients with renal failure

Other options
  - On Haematology/Best physician advice only
  - Patients with Myeloma

Review letter
  - If the patient is still in difficulty due to Anaemia please ring Haematology/Transfusion CNS or Consultant Haematologist for advice.
Palliative Care

• Appropriate Treatment
• Flow chart for diagnosis
• Support from all Palliative Care Staff
• Discuss at MDT
• Junior Doctor led
• Measure QOL using FACT-AN
• Choice of treatments?
Case Study

- 78 year old man
- Hb 7-8 g/dl
- Ca Prostate – mild Haematuria
- Cardiac failure - unstable
- No obvious other bleeding
- 2-3 units Transfusion weekly
- Utterly exhausted and becoming more frail

claire.atterbury@qehkl.nhs.uk
Plan

- Check bloods
- FBC, Reticulocytes, Film, Clotting
- Renal & Liver function
- B₁₂ Folate and Iron studies
- Direct Antiglobulin test
- Ferinject 800 mg
- Maintenance 200mg Venofer 6 weekly to death
Case Study

- 23 year old woman
- Ca Cervix – end stage
- Multiple treatments
- Small daughter
- Refusing transfusion
- Needlephobic

claire.atterbury@qehkl.nhs.uk
Plan

- Single dose Ferinject 900 mg
- Lived 14 weeks
- Acceptable QOL
IBD

• Oral Iron is contraindicated in IBD
• Maintenance IV Iron therapy reduces crises
• IBD therapy clinics
• Remember; reduce anaemia reduce infections and bleeding
• Increase QOL
Surgical Pre-assessment

- Reduced LOS for surgical patients
- Reduced complications
- Therefore happier patients
- Speedier patient throughput
- Partnership working between GP commissioners and Hospital teams
- Savings to be made for everyone?
Colorectal Surgery

- PREVENTT RCT
- Pilot study on 3 sites
- Does reducing transfusion
  - Reduce LOS?
  - Reduce post op infections?
  - Reduce other complications?
  - Increase survival?
  - Save the NHS money?
Obstetrics @ QEH

claire.atterbury@qehkl.nhs.uk
Number of PPH
Units used by year

The Queen Elizabeth Hospital
King's Lynn
NHS Foundation Trust

claire.atterbury@qehkl.nhs.uk
How did we achieve this?

- **Regular** interdepartmental meetings
- Midwife education and understanding
- Find a champion or two
- Make it easy (algorithms)
- Back the staff up – easy access for advice
- Make sure systems are in place
- Dietary information in “Bounty packs” explained to Mums
What were (are) the challenges?

• Doing something new
• Taking the calls
• Some medical colleagues
• Goldfish memories
• Changing the culture
• Other hospitals
• The cost of IV Iron (Iron deficiency is epidemic when you go looking for it)
• The B$_{12}$ battering
Iron Therapy Timeline in O&G

The Pregnancy Time Line - Potential for Fe Therapy in Pregnancy

Potential (%)

Oral Fe
Venofer

1st trimester
2nd Trimester
3rd Trimester

Conception
Birth

Weeks

claire.atterbury@qehkl.nhs.uk
Hb less than 11 g/dl at booking (or less than 10.5 if above 12 weeks gestation) = **ANAEMIA**

- **MCV below 81 fl**
  - See Flow Chart 1b

- **MCV 81-99**
  - See Flow Chart 1c

- **MCV above 99**
  - See Flow Chart 1d

**Flow Chart 1a – Anaemia at Booking**
Flow Chart 1b – Anaemia at Booking and MCV less than 81

Hb less than 11 g/dl at booking (or less than 10.5 if above 12 weeks gestation)

= ANAEMIA

AND

MCV less than 81fl

Check Haemoglobinopathy Screen

Thalassemia Trait

Check Ferritin

Normal

No action

Normal

Check Ferritin

Low

Dietary advice and Oral Iron

Re-check Hb in 2 weeks

Unable to tolerate oral iron or failure to show rise in Hb after 2 weeks oral iron

Check Ferritin (if not previously done)

Ferritin below 30

Consider intravenous iron in second trimester

Ferritin above 30

Re-check Hb in 4 weeks after IV Iron

No response

Seek Haematology Advice

claire.atterbury@qehkl.nhs.uk
And for the wee ones........

- Poor uterine growth
- Decreased liquor
- Asymmetrical growth patterns
- Small for dates
- Premature delivery
- Low birth weight
- Failure to thrive (poor lactation)
- And if it continues - poor concentration and reduced scholarly achievements (Source SMA!)

- And for the Midwife..................?

claire.atterbury@qehkl.nhs.uk
Case study

- 36 year old Journalist on the Mirror
- Not keen on blood transfusion
- On Pregaday
- Best friend a Transfusion Nurse Specialist!
- Hb 9.0 at 28 weeks
- MCV slightly lower than pre-pregnancy (91→87)
Plan

- Increase oral Iron to FeSO₄ 200mg TDS from week 28
- Continue folic acid to delivery

- Delivered at 42/40
- 1250 ml bleed
- Hb at 2 days PP 10g/dl
Oral Iron vs Venofer in the Postpartum
(Dr Nav Bhandal, John Radcliffe, Oxford, personal communication but in BJOG April 2007)

- Oral Iron 200mg bd for 6 wks
- Venofer 200mg on Day 2 and 4
Low $\text{B}_{12}$ - Risks to Mother and child.....

- Symptoms of anaemia
- Neuropathy – can be severe in extreme cases
- Increased susceptibility to infection
- Neural tube defects
- Bone Marrow Failure

- But VERY difficult to say where a true deficiency is in pregnancy due to increased plasma volume
Hb less than 11 g/dl at booking (or less than 10.5 if above 12 weeks gestation) and MCV above 99 = **ANAEMIA**

AND

**MCV above 99fl**

Check B₁₂/Folate

**Low Folate**

Dietary advice and oral folic acid (5mg daily)

Re-check Hb in 4 weeks

No response

Seek Haematology Advice

**Low B₁₂**

**B₁₂ <211 = DEFICIENT**

High risk if: Vegan Diet, Ileal Disease, Malabsorption, Bariatric Surgery or Family History PA;

Hydroxycobalamin 1mg x 6 doses im

Take sample for intrinsic factor antibodies. Take sample **before** giving B₁₂ (but do not wait for result)

If antibodies positive = Pernicious Anaemia

Refer to GP

If antibodies negative

**B₁₂ 211-246 INDETERMINATE**

Hydroxycobalamin 1mg one dose im if still 211-246

**B₁₂ 211-246 INDETERMINATE**

Repeat in 4-8 weeks

**B₁₂ normal**

Reschedule FBC in 2 weeks

**Normal**

**Hb less than 11, seek Haematology advice**
Case Study

- 22 year old – 2 other children
- 37/40
- Admitted to Antenatal ward with Norovirus
- Christmas.
- Septic
- Distressed baby → Section
- Hb 3.1g/dl, Platelets 41 x10⁹/l, Neutrophils 0.3 x10⁹/l
- B₁₂ 99, Folate 1.6, CRP 280
Then...

- 14 days as inpatient
- Septic shock (managed on Labour Ward)
- 8 units of Red cells
- 1 unit of Platelets
- IV antibiotics +++
- Lots of stress and anxiety for everyone.........
Back up a bit...........

- 30.9.08 - 28 week血液 showed MCV 109 and film comment “macrocytic anaemia. Probable B₁₂ deficiency”

- 6.11.08 MCV 116. Hb 9.0 Film comment “Macrocytic picture ? Liver ?B₁₂ /Folate deficiency.”

- 13.11.09 B₁₂ 117, Folate 0.9 (3-20) Red Cell Folate  48 (93-641)

- Patient given oral iron. Usual Midwife on AL. Patient moved house.

- 10.12.09 UTI – E-Coli


claire.atterbury@qehkl.nhs.uk