University Hospitals Bristol NHS
NHS Foundation Trust

NHS
Blood and Transplant

Bucking the trend: Red cell demand in myelofibrosis

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The population is:

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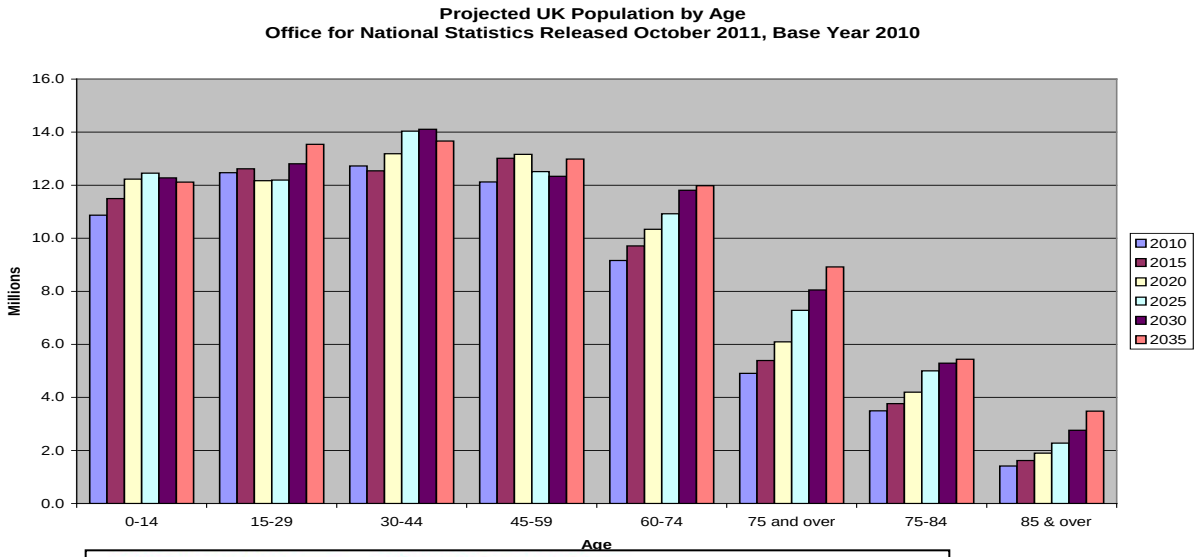
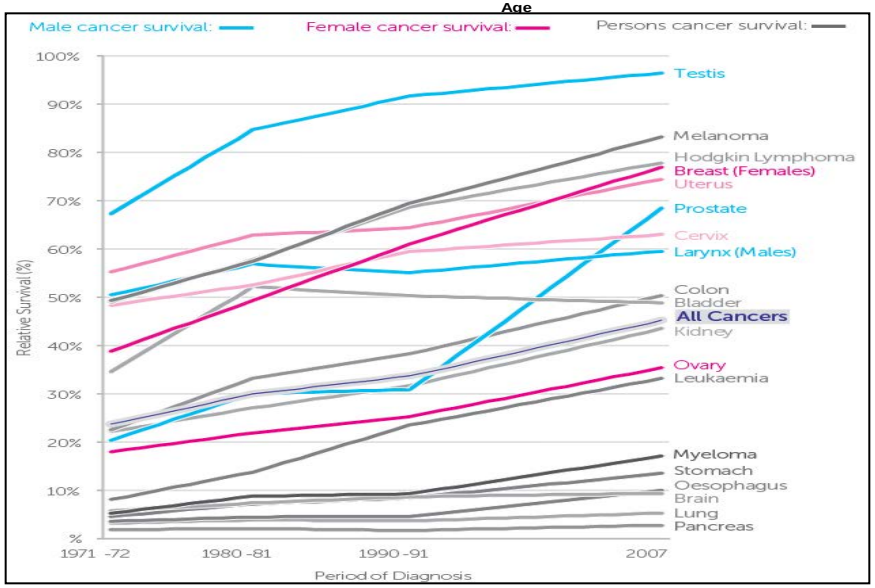


Growing
and aging
(Office for National Statistics)



Surviving cancers
(Cancer Research UK)

Older patients and cancer survivors:

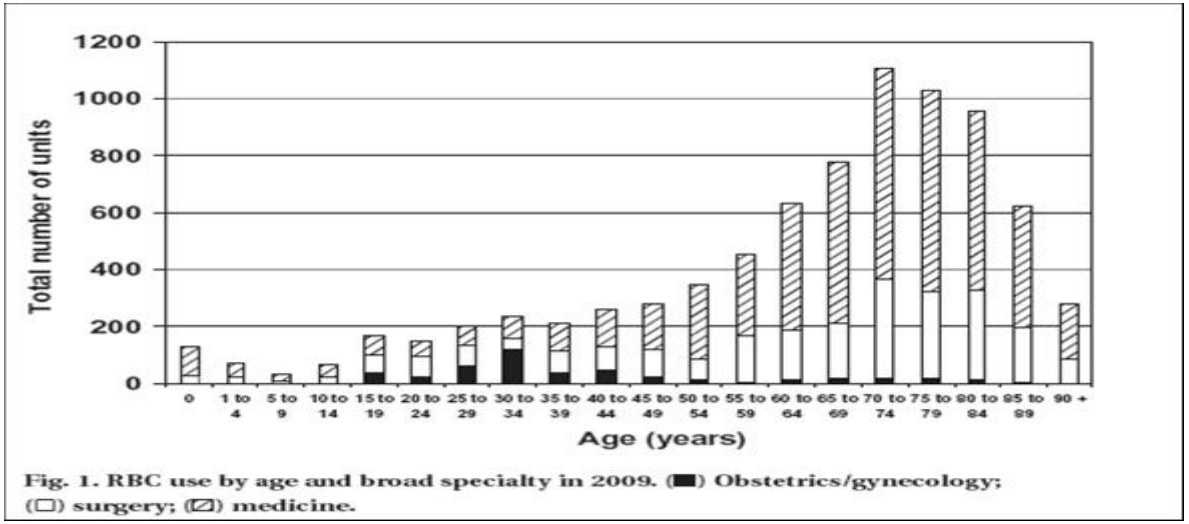
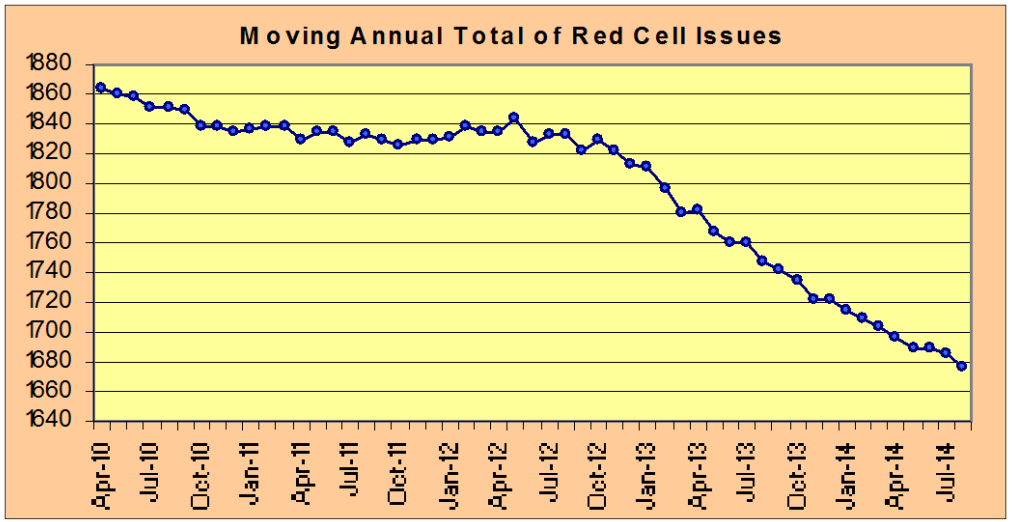


Fig. 1. RBC use by age and broad specialty in 2009. (■) Obstetrics/gynecology; (□) surgery; (▨) medicine.

Use more red cells (Tinegate 2013)

So demand must be up?



No!

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Introduction

- Haematology is one of the biggest users
- Advances in diagnosis, therapy and survival has occurred in nearly all disorders.

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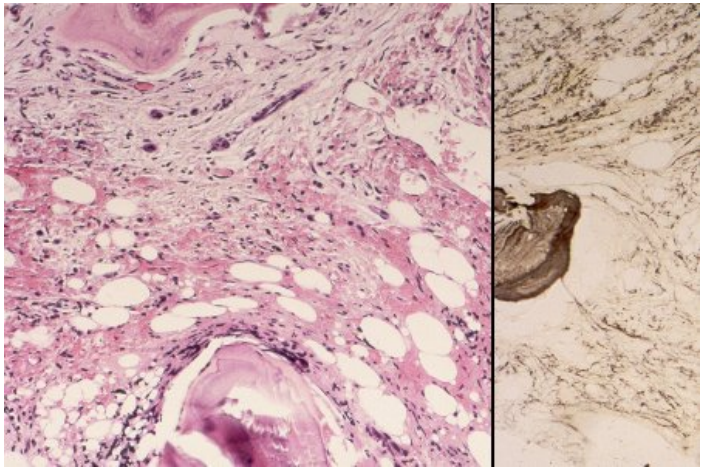
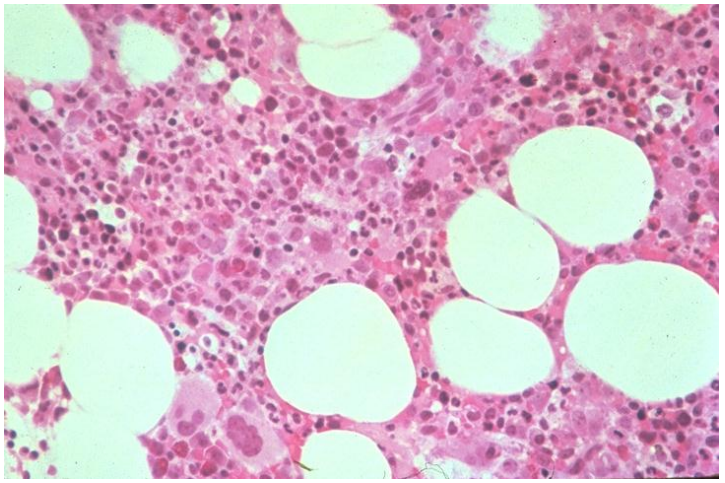
Myelofibrosis

- Bone marrow fibrosis
- Extramedullary haematopoiesis.
- Splenomegaly- often massive
- Weight loss, fatigue, bleeding
- JAK2 mutation 60% (NEJM 2005)
- MPL mutations in 8%
- CALR mutations in 72% of JAK2 wildtype cases (NEJM 2013)





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Case 1

- 63 year old male. Myelofibrosis and “gastrointestinal failure” as a result of adhesions and repeated operations on total parenteral nutrition
- Admitted via A&E to ITU with indwelling line sepsis.
- Treated with broad spectrum antibiotics, fluids and continued total parentral nutrition intravenously.

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Case 1

- Recovering but falling Hb and platelets
- Hb: 72 g/L (Normally 90-110) Wbc: 2.92 x 10^9/L Plt: 299 x 10^9/L (normally >500 for him)
- Creatinine 234 umol/L (59-104)
- Questions
  - What could lead to a fall in counts?
  - Does he need a transfusion?

Case 1

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- Folate level 2ug/L (4.6-18.7)
- TPN focuses on protein and energy, containing no folate supplementation
- Even if supplementary preparations are used the folate content is only 400ug/day
- Typically patients with increased folate demand (haemolysis / myelofibrosis) need 5mg folate / day
- We added folinic acid 15mg/day iv daily to his feeds.
- He recovered and remained transfusion free.

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Case 2

- 59 year old man from the Caribbean with 11 full siblings (and 2 half sibs)
- Life threatening thrombotic history, myocardial infarction, intra cardiac thrombus with emboli. Malignant hypertension and diabetes.
- Drugs: Warfarin and anti-hypertensives
- Noted to have a thrombocytosis. Hb **87** g/L (130-170) WBC 9.66 x 10^9/L Plt **1074** x 10^9/L Creatinine **146** umol/L (59-104)
- Fibrotic marrow, Jak-2 mutation present
- Erythropoietin 98.2 mIU/mL (3.0-18.0)

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Case 2

- Does he need to start a transfusion program now?
- Is he likely to become chronically transfusion dependent?
- What treatment options might work for him?

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Treatment

- BMT? – 11 full sibs!
- Commenced on escalating erythropoietin and hydroxycarbamide
- Marked improvement in quality of life
- Haemoglobin 123g/L, white count 5.6 x 10^9/L, platelets 540 x 10^9/L.

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Case 3

- 78 year old man. Myelofibrosis, chronic obstructive pulmonary disease rheumatoid arthritis, Sweet syndrome and pulmonary fibrosis requiring home oxygen and steroids.
- Very lethargic difficult to ambulate with O2
- Marked splenomegally
- Hb 82g/L WCC 18 $x10^9$/L, neutrophils14$x10^9$/L , platelets 860 x 10^9/L
- Does he need transfusion?

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Case 3

- Monthly transfusions initially.
- Increased steroid dose,
- Thalidomide, and hydroxycarbamide
- Walked into clinic. No transfusions for 7 weeks, No oxygen. **Hb 104g/L, WCC 4.1x10^9/L, platelets 280x10^9/L**
- “It’s a miracle”
- Sadly he died 7 months later

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Summary

- Haematological disorders are an important area for patient blood management
- Simple things still count (eg folate)
- Specific therapy in myelofibrosis
  - Splenectomy (many decades)
  - Myelosuppressive therapy (Hydroxycarbamide 2 decades)
  - Erythropoietin (1-2 decade in MF)
  - Specific anti-proliferative therapy (thalidomide last decade)
  - Transplant (many not fit enough)
  - JAK2 inhibitors provide new therapeutic options

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Thanks / discussion

- Fiona Regan
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