

A microscopic view of red blood cells, showing their characteristic biconcave disc shape and pinkish-red color. The cells are densely packed and overlapping, creating a textured, cellular background.

# Tranexamic acid and Iron in Haematology

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A microscopic view of numerous red blood cells, which are biconcave discs, filling the frame. The cells are densely packed and appear in various shades of pink and red, with some showing their characteristic central indentation. The background is a soft, out-of-focus light pink.

Why consider an alternative?  
Can't we just give blood?

**NO!**

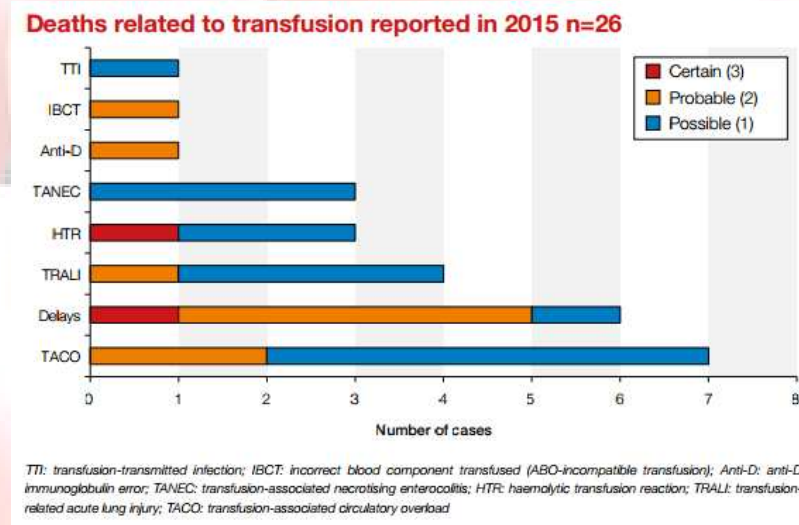
# Why consider an alternative?

## Can't we just give blood?

Blood transfusion not without its risks- SHOT report 2015 shows deaths as a result of transfusion

Entirely reliant on donors- donor pool ageing

Risk of TTI



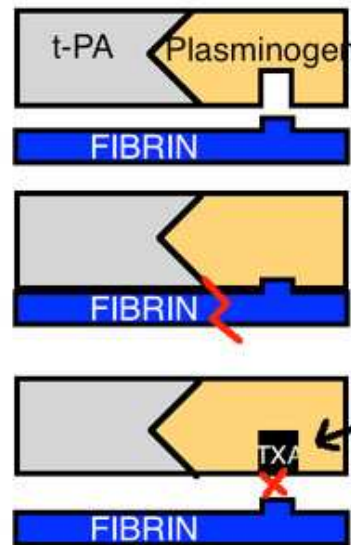
# What is Tranexamic acid

- Anti Fibrinolytic
- Developed in 1960's in Japan, used for menorrhagia
- More recently used for major Haemorrhage
- Cheap! (60-80p for a 500mg vial for IV)
- Effective (see NICE NG24)
- Available as oral tablets, IV and mouthwash and is available OTC for menorrhagia
- On the WHO list of essential medicines (minimum medicine needs for a basic health care system)

# How does it work?

- Anti Fibrinolytic- prevents clot breakdown by inhibiting the activation of plasminogen to plasmin, preventing plasmin degrading fibrin.

txa mechanism



normally...  
Activated Plasminogen  
binds to Fibrin

&

Breaks the Fibrin Clot

TXA interferes with the  
binding site

# Indications for Tranexamic acid

- Well used in major haemorrhage
- all expected bleeds >500mls in surgery (Nice NG24)
- Management of haemorrhage due to the administration of a fibrinolytic agent.
- Prevention and treatment of haemorrhages due to general or local fibrinolysis

# Contraindications and cautions

## Contraindications

- Acute venous or arterial thrombosis
- Fibrinolytic conditions following consumption coagulopathy except in those with predominant activation of the fibrinolytic system with acute severe bleeding
- Severe renal impairment (risk of accumulation)
- History of convulsions
- Intrathecal and intraventricular injection, intracerebral application (risk of cerebral oedema and convulsions)

## Cautions

- Irregular menstrual bleeding (investigate cause first)
- Massive Haematuria (risk of obstruction)
- Patient on oral contraceptive (increased risk of Thrombosis)

# Case Study 1

- 76 year old man with Myelofibrosis
- Needs regular transfusions
- Hb could drop to 45-55 g/l, Plts ran 1-6
- Developed oozy GI Bleed
- Commenced on Tranexamic acid PO 1g TDS
- Difficult to judge effect as Myelofibrosis progressing



## Case study 2

- 73 year old lady
- Myeloma
- Plts 12 Hb 54
- Sores and localised bleeding to mouth
- Commenced on Tranexamic acid mouthwash to good effect (reported by Patient)

## Case Study 3

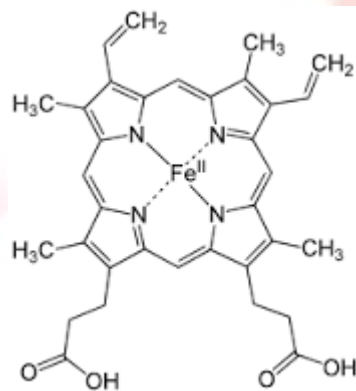
- 63 year old lady
- ITP
  - Difficult to control
  - Poor Response to steroids
  - And steroids not well tolerated by Patient
- Hb 143 Plts 29
  - As ITP would not respond to Plt Transfusion
- Tranexamic acid started whilst waiting to start rituximab

# Conclusion

- Cheap
- Quick
- Effective
- But be aware of contraindications (few absolute)
- Be aware of bleeding- may need additional treatments (Blood, Platelets, Iron etc)

# What is Iron?

- Element -atomic number 26
- Fundamental in structure of Haemoglobin
- Haemoglobin accounts for 65% of iron in body (between 2g and 4g total)



# Main Causes of iron deficiency

## **Inadequate Dietary Intake**

Poor nutrition  
Chronic alcoholism  
Decreased consumption of animal protein and ascorbic acid

## **Increased Iron Demands**

Pregnancy  
Infancy/adolescence

## **Iron Loss**

Menstruation  
Gastrointestinal bleeding  
Haemodialysis  
Puerperium  
Surgery  
Blood donation

## **Inadequate Gastrointestinal Iron Absorption**

Malabsorption syndromes  
Systemic inflammation  
Interference with certain foods/drugs

# Whats the fuss?- small numbers?

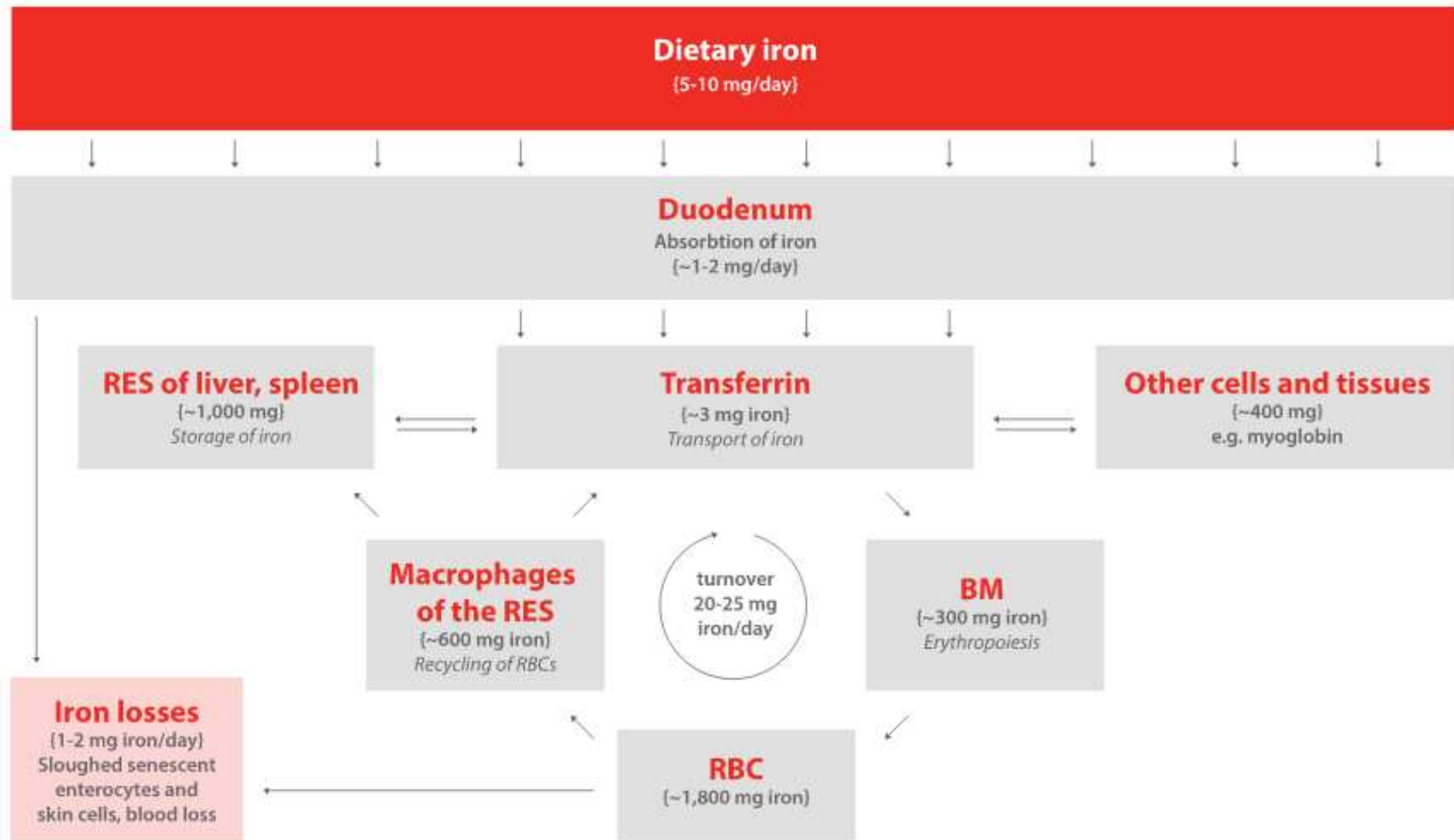
- The most common and widespread nutritional disorder in the world
- Most Common cause of Anaemia
- 2 billion people – over 30% of the world’s population – are anaemic, many due to iron deficiency
- Iron deficiency affects more people than any other condition
- Modern “epidemic”
- Iron deficiency exacts its heaviest overall toll in terms of ill-health, premature death and lost earnings.

- WHO 2016

# What does that mean in Haematology?

- Often multifactorial –patients with multiple conditions
- Linked with cause- Bleeding means increased risk of iron deficiency

# Iron Turnover in the body

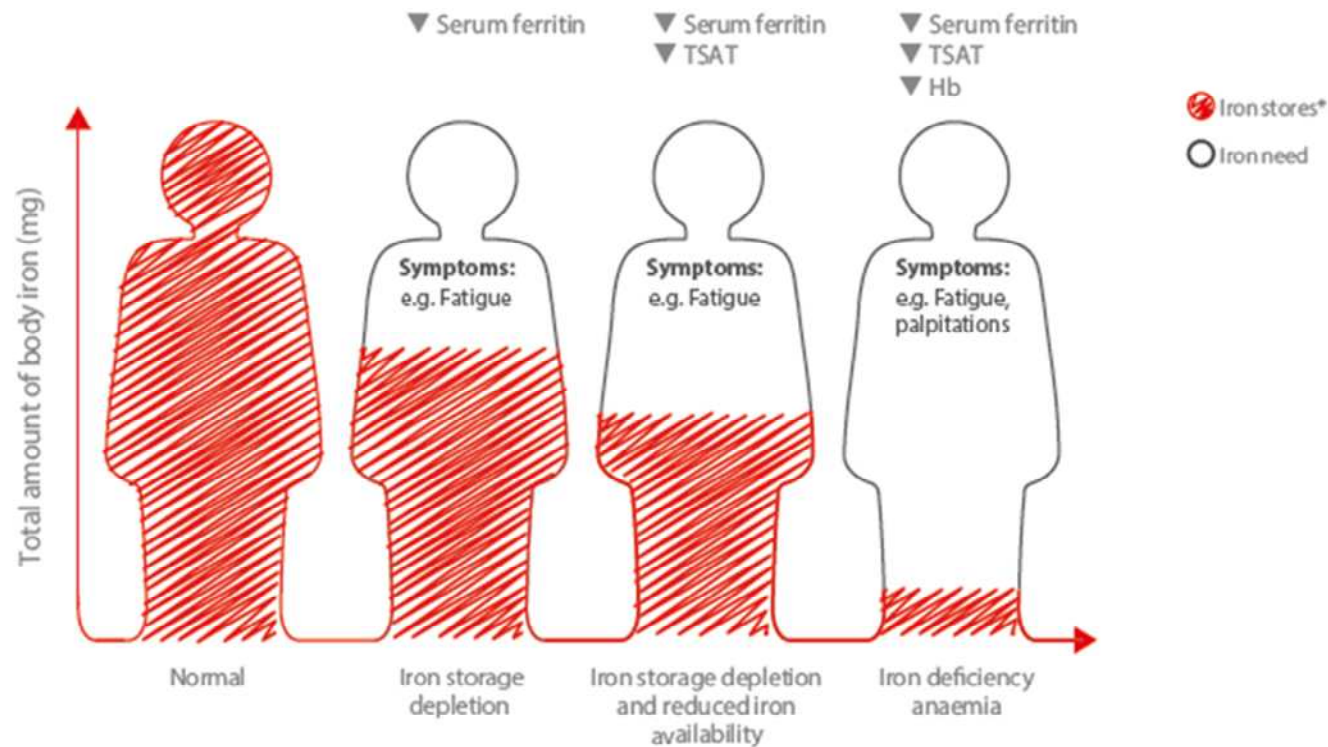


RES – reticuloendothelial system; BM – bone marrow; RBC – red blood cell



# Progression of Iron deficiency

- Iron deficiency anaemia is the result of a process that starts with iron store depletion<sup>1</sup>



\*Storage iron, transport iron and functional iron  
TSAT = Transferrin saturation, Hb = Haemoglobin  
Adapted from Tussing-Humphreys, 2012 and Ponikowski, 2015

**In patients with CHF, repletion of iron stores with oral iron could take more than 6 months<sup>3</sup>**

# Treatment 1- increase Nutritional intake

- Simple
- Also need to increase vitamin C intake
- Not to drink Tea or coffee with meals (inhibits absorption)

But

- can take months to resolve anaemia
- Limited by patients diet
- Usually too late for the haematology Patient



# Treatment 2 Oral Supplementation

- Tablets or Liquid
- But still absorbed via GI Tract
- Cheap
- Relatively safe

BUT

- Side effects common
- Patients often stop taking if side effects are intolerable
- Takes weeks to months to take effect
- Side effects can include abdo pain, constipation, diarrhoea with a relatively high frequency
- OTC preparations are low doses
- Cannot be used in children
- Usually too progressed if they make it to Haematology referral- often tried by GP



# Treatment 3 IV Iron

Ferinject used at Hinchingsbrooke

- Dose is dependent on weight and Hb
- Given direct into blood- bypasses Gut
- Peak response 3-4 weeks post dose
- Short infusion time (30 mins)
- Relatively fast acting

But

- High reaction risk
- Relatively expensive
- Used when fast response needed or intolerant of Oral iron
- Not licensed for children





# Treatment 4- Transfusion

## THE LAST RESORT!

- Only for patients with symptoms that need immediate resolution

- Acts straight away

BUT

- Reaction Risk

- Infection risk

- Immunosuppresses

- Risk of ARF

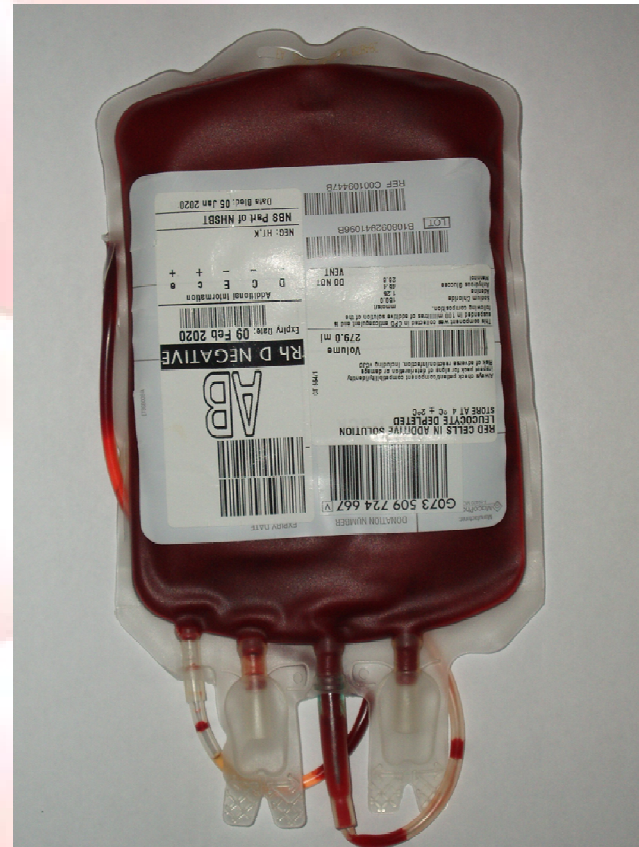
- Stops people donating in the future

- Relatively expensive

- Contains a small amount of Iron (about 250mg per bag)- does not replenish Iron Stores effectively

- Relatively long infusion time

- Potentially SHOT reportable (if not used as last resort)



# Case Study 1

- 90 year old man
- Myelodysplasia
- Managed with regular transfusions (for years), but ferritin always  $<100$  (unusual!!)
- Added periodic Iron infusions, in conjunction with blood Transfusions (shorter infusion time)
- Appears to have slightly reduced blood requirements.

## Case Study 2

- 94 year old male
- Lives alone, independently
- Longstanding iron deficiency- investigated repeatedly- NAD
- Subsequent referral to Haematology
- Has had 22 units of red cells since 2008 for IDA- multiple admissions (had developed atypical antibodies)
- Patient initially reluctant, but after iron said “that was much quicker” and happy to swap to iron infusions.
- No Transfusions Feb. 2015- May 2017 (Subsequent Cancer found- bone marrow failure)

## Case Study 3

- 58 year old lady
- Longstanding Carcinoid Tumour being regularly resected- referred to Haematology for anaemia.
- Hb 134
- Ferritin 20, CRP 4, TF Sats 8%, TF 3.62
- Iron deficient- unclear Mechanism – being re-investigated
- Given IV iron infusion (intolerant of oral tablets)



# IV Iron Service

- Often run by Transfusion Practitioner as an adjunct
- Different models- Telephone clinics, outpatient clinics
- Referred into service (GP, or within hospital (count as part of treatment))
- Have initial consult (phone/ in person)
- Booked into infusion suite (Haematology OPD/ Ambulatory Care/ Infusion suite)
- Generally bloods checked 3-6 weeks post IV iron
- Follow up (ie if needs referral and for monitoring of bloods)

# Sounds Great! What are the problems?

- Perception issue- Iron deficiency perceived as diagnosis, but it's a symptom- must have follow-up!
- Iron deficiency often falls between camps- “not haematology”, “not Gastro” or “not Gynae”
  - Makes where to administer difficult- Haematology OPD? Gastro Outpatient OPD?
  - Also makes setting up service difficult, where do the patients go? Who takes responsibility?
- What happens to Patients when investigations have been exhausted? Follow up can be patchy
- Demand v Supply – balancing resources

# What next?

Continue to increase Iron use across the hospital  
(blood use also dropping)

Optimise the pathways for Iron deficiency

- ? One stop Clinics
- Better tie in with PBM

Specific follow up clinic

Uses of Iron still being researched- research into  
exercise tolerance and iron deficiency, and Heart  
failure ongoing

# Conclusion

- Iron supplementation +/- Tranexamic acid can be very effective
- Iron Appropriate *alternative* to transfusion
- Consideration to route needs to be given
- Increased role for Iron in NICE, and BCSH guidance, in optimisation of patients prior to surgery

BUT we are treating *symptoms*, a cause for iron deficiency should be identified.

# Sources/ Further reading

- Vifor Pharma
- WHO
- Electronic Medicines Compendium
- Nice NG24
- BNF